



**ABSTRACTS**

**International Workshop  
on Lung Health**

Prague, Czech Republic  
16–18 January 2020



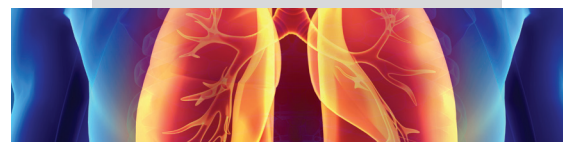
**European  
Respiratory  
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**SUPPLEMENT**

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# European Respiratory & Pulmonary Diseases

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<sup>th</sup>  
**7** **INTERNATIONAL WORKSHOP**  
**ON LUNG HEALTH**  
Rethinking Lung Diseases: towards tailored management

**Abstract Book**

**PRAGUE**  
16–18 January 2020



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Francesco Blasi  
G. Walter Canonica

**Chairmen:**

Stefano Centanni  
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Tobias Welte

# International Workshop on Lung Health



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## ABSTRACTS

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#### **Important note:**

The abstracts in this book are in alphabetical order (first author, last name). The abstract are presented during the Strolling Poster Session of the Workshop (with the presenter underlined)

## [P01] Obstructive Sleep Apnea and Metabolic Syndrome: Is there a Correlation?

Adelina Anton<sup>1</sup>; Doina Tofolean<sup>1</sup>; Gheorghe Ionel Comsa<sup>1</sup>

<sup>1</sup>Ovidius University, Constanta, Romania

**Background:** Obstructive sleep apnea syndrome (OSA), a disease with increasing prevalence, but underdiagnosed, is disclosed to cause metabolic changes increasing cardiovascular risk. The purpose of this study was to evaluate the association between OSA and metabolic syndrome (MS) or its components and to assess the role of hypoxemia on metabolic abnormalities.

**Method:** To this end, we conducted a prospective study of patients investigated in Constanta Sleep Disorders Center, between 2015–2019. The study group included 146 patients and all patient underwent nocturnal polygraphy, blood sampling and measurement of anthropometric variables. MS was identified in 59% of patients. The prevalence of metabolic changes increased proportionally with the severity of OSA and with the increase of the desaturation index. Obesity, especially visceral one, although an intricate determinant, was a predictor of both pathologies. In conclusion, OSA and MS are interdependent pathologies that act synergistically and have multisystemic involvement. This association should certify the need for OSA screening in patients with metabolic abnormalities.

## [P02] Telemedicine Experience for Severe Asthma Care: A Developing Country Perspective

Carolina Barbosa Souza Santos<sup>1</sup>; Mayara Sousa Silva<sup>1</sup>; Bianca Matos Magalhães<sup>1</sup>; Ana Carla Carvalho Coelho<sup>1</sup>; Carolina Souza-Machado<sup>1</sup>

<sup>1</sup>Universidade Federal da Bahia, Salvador, Brazil



**Background:** Telemedicine can be defined as the provision of health care and services through information and communication technologies, when distance is a critical factor. In developed countries, telemedicine is already well established as an integrated part of professional-patient care and is effective in preventing and controlling chronic diseases, such as asthma. However, in developing countries such as Brazil, where approximately 20 million people have the disease, telemedicine has not been widely adopted as a potential tool for asthma control.

**Aim:** To describe the experience of telemedicine use for patients with severe asthma in a specialized center in the city of Salvador, Bahia, Brazil.

**Method:** Experience report on a clinical study that used a telemedicine tool to monitor patients with severe asthma seen at a specialized center in Brazil. The telemedicine tool consisted of a telemonitoring platform and a protocol for telemedicine procedures focused on the care of patients with severe asthma. The clinical study was approved by the research ethics committee in Brazil.

**Result:** A total of 129 severe asthmatic patients were followed for a period of 6 months to 1 year by the telemedicine tool. A team of nurses was responsible for performing the procedures. The experience was divided into steps, described below. 1) *Usability of the telemedicine tool:* the telemedicine platform consisted of the installation of computers, communication and call recording software, and the creation of a guiding protocol that standardized the informations given by professionals. The use of easily accessible and relatively inexpensive material resources, combined with the use of a guiding protocol, based on up-to-date scientific evidence appropriate to the study site, has enabled a good practical use of the telemedicine. 2) *Health outcomes:* after telemedicine intervention it was noticed that the participants had an improvement in the correct use of inhaler devices and knowledge about asthma, as well as a reduction in reports of hospitalizations and emergency visits.

3) *Ethical aspects:* the main ethical issues related to telemedicine processes were respected, ensuring the participant's data security and privacy. The space where the telemedicine platform was installed is reserved, where only research nurses had access to ensure the confidentiality of interventions. 4) *Challenges and perspectives:* The use of telemedicine can be an ally in the way health care is produced. However, in developing countries such as Brazil, where the population attended by the public health system, in general, has low socioeconomic and educational level, there is difficulty in accessing expensive technologies and the implementation of this tool can be a challenge. Therefore, simple and easily accessible alternatives should be chosen for effective use of telemedicine in developing countries, focusing on the patient and their individualities, based on current scientific evidence, especially in chronic conditions such as asthma.

**Conclusions:** The use of telemedicine-based interventions is a complementary and clinically viable alternative for effective health care for asthmatic patients. For developing countries, experiences such as ours may be able to encourage self-management of asthma, reducing direct and indirect disease costs, as well as being an applicable and reproducible model for other chronic diseases.

## [P03] Acute Exacerbations of Chronic Obstructive Pulmonary Disease (AECOPD) as a Cardiovascular Risk Factor

Daniela Buklioska Ilievska<sup>1</sup>; Jordan Minov<sup>2</sup>

<sup>1</sup>General Hospital "8th September", Skopje, Macedonia; <sup>2</sup>Institute for Occupational Health of R. Macedonia - WHO Collaborating Center, Skopje, Macedonia

**Background:** AECOPD are accompanied by increased cardiovascular risk because of systemic inflammation, hypoxia, age, cigarette smoking. Recent data suggest an increased risk of myocardial infarction in the following days of a severe exacerbation of COPD, and around 30% die from cardiovascular diseases. Cardiac dysfunction in AECOPD is often underestimated and underdiagnosed at the time of admission, because decompensated cardiac failure and AECOPD share symptom similarities.

**Objective:** To investigate the presence of increased cardiovascular risk in hospitalized patients with emphysema and AECOPD.

**Materials and Methods:** Observational study, 120 hospitalized AECOPD patients and 60 stable COPD controls, matched by age, gender and body mass index. Inclusion criteria: age 40–75, cigarette smoking history  $\geq 10$  pack/years, signed consent for participation. All patients underwent laboratory tests, pulmonary function tests, chest-X ray, electrocardiogram (ECG), 2D-Doppler echocardiography.

**Results:** Systolic or diastolic left ventricular dysfunction was noted in 66.7% of investigated group. Right ventricular (RV) abnormalities were significantly higher in investigated group than controls ( $p < 0.001$ ), with RV systolic dysfunction in 62.5%, pulmonary hypertension 54.2%, tricuspid regurgitation 53.3%. According to ECG findings 67% had abnormal ECG, and 33% had a new abnormality from baseline. Atrial premature beats were detected in 66.7%, ventricular premature beats 41.7%, un-sustained ventricular tachycardia 5%, atrio-ventricular block of first degree 5%, right bundle branch block 33.3%, atrial fibrillation 15%, T-wave changes 33.3%, ECG signs of previous infarction in 25%. An abnormal ECG, particularly with ischemic changes, on presentation to the emergency department with AECOPD, is correlated with a prolonged hospital stay (Image 1). AECOPD is associated with greater prolongation of P wave dispersion than in stable COPD. Patients with fatal arrhythmias had QTc interval greater than 440ms. Elevated troponins have been associated with the elderly, comorbid heart failure, chronic renal failure, atrial fibrillation. Correlation between pH value and fatal arrhythmias risk in investigated

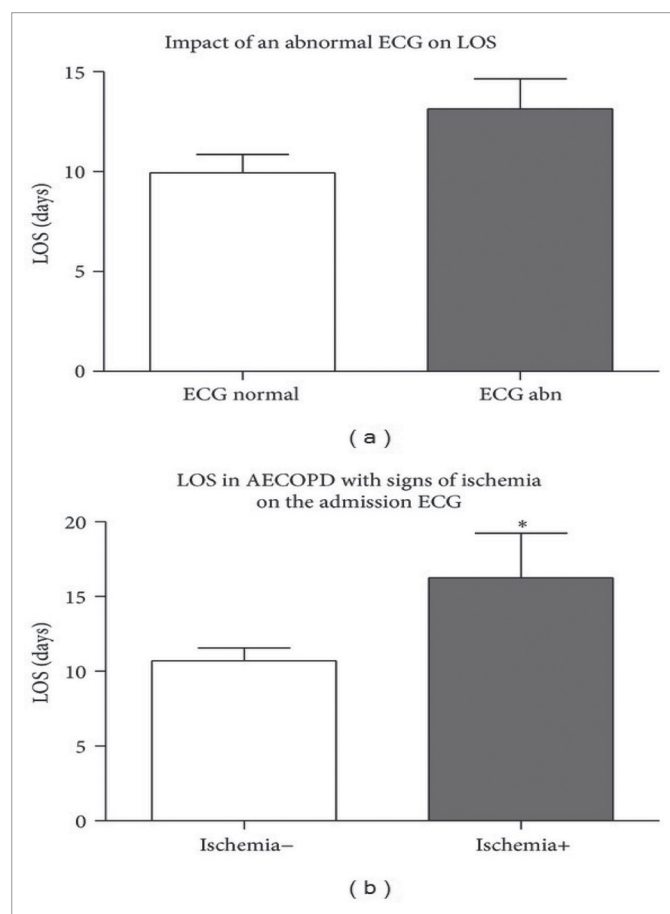
group, showed that respiratory acidosis was associated with higher risk of fatal outcome ( $p < 0.001$ ).

**Conclusions:** Acute exacerbations of COPD may trigger cardiac events. Cardiac treatments could improve AECOPD outcomes induced by respiratory infections in COPD patients, so early detection of unrecognized coexisting cardiac disorders is significant. Further research into the pathogenesis and treatment of acute cardiac dysfunction in COPD exacerbations are needed.

**Keywords:** Chronic Obstructive Pulmonary Disease, acute exacerbations, systemic inflammation, cardiovascular risk.

*I declare all commercial interests.*

**Figure 1: Presence of an electrocardiogram (ECG) abnormality and length of stay (LOS) of subjects admitted with an AECOPD**



**[P04] Respiratory Function Prediction After Lung Resection in Different Postoperative Periods in Pulmonary Tuberculosis Patients**

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**Introduction:** Currently, with the increase in the share of drug-resistant pulmonary tuberculosis (PT), the relevance of the surgical method in the complex treatment of this disease is growing. However, surgery is challenging for PT patients because the risk of postoperative complications and mortality is high, and careful assessment of patient operability is critical. The predicted postoperative (ppo) function

calculation is important for assessing operational risks. We aimed to investigate the possibility of applying the ppo calculating formulas according to ERS/ESTS guideline (2009) for lung cancer patients in different postoperative periods in PT patients.

**Methods:** 20 patients undergoing segmentectomy (SE) (11M/9F, mean age 39.9±14.9 yrs), 45 lobectomy (LE) (31M/14F, mean age 40.8±12.7 yrs) and 70 patients after pneumonectomy (PE) (47M/23F, mean age 41.1± 9.9 yrs) in complex PT treatment were evaluated with complete preoperative and repeated postoperative measurements of FEV1, TLC, VC and DLCO in 1, 6 months and 1 year. The ppo respiratory values were compared with the observed postoperative (po) values. We used for calculating the SE and LE ppo values the following equation: ppo values = pre-operative value\*(R/T), in which T - total number of functioning segments before the operation; R - residual number of functioning segments after the operation. For PE we used the formula: ppo values = pre-operative value\*[1-a], in which a - the proportion of blood flow from the total volume in the removed lung. Mann-Whitney test was used to compare differences between groups.

**Results:** After SE, no differences were noted between ppo and po values of all respiratory parameters at each evaluation time. After LE, there were no differences between ppo and FEV1, TLC, VC and DLCO for one month ( $p > 0.05$ ), but RV and DLCO/AO were higher compared to the ppo value ( $p = 0.006$  and  $p = 0.004$ ). 6 months and 1 year after the LE, the ppo was significantly lower than the real values. 1 month after PE, the po values were lower than the ppo values ( $p < 0.05$ ), but after 6 months and 1 year, no significant differences between the predicted and observed values were revealed ( $p > 0.05$ ).

**Conclusions:** There were no significant differences between the po and ppo values of respiratory parameters according to the simplified calculation formula without taking into account atelectasis of ERS/ESTS segments at the whole stage of observation after SE. There were no significant differences in po and ppo values in 1 month after LE, but in 6 months and 1 year - the po values were higher than the ppo ones. When comparing the predicted and real values in 1 month after PE, the po values were lower than the ppo, but after 6 months and 1 year, no significant differences between the predicted and real values were revealed.

**[P05] Mental Status in Patients with Non-Cystic Fibrosis Bronchiectasis (BE) in Stable Phase**

Valeriia Dmytrychenko<sup>1</sup>; Kateryna Gashynova<sup>1</sup>; Kseniia Suska<sup>1</sup>

<sup>1</sup>State Institution "Dnipropetrovsk Medical Academy of the Ministry of Health of Ukraine", Department of Occupational Diseases and Clinical Immunology, Dnipro, Ukraine

**Background:** Patients (pts) with chronic pulmonary diseases frequently have depression and anxiety symptoms. But there are not enough studies about psychological profile in BE pts.

**Aim:** The aim of study was to evaluate the mental status in stable BE pts.

**Material and Methods:** 22 pts with confirmed diagnosis of BE by high resolution computed tomography were included. All pts were clinically stable in previous two weeks. Anxiety and depression levels were evaluated by using hospital anxiety depression scale (HADS).

**Results:** The mean age of pts was 48.5±14.05 (32–72) years, 15 (68.2%) of them were women. In accordance with HADS 16 (72.7%) BE pts had psychological disorders. 13 (59.1%) pts showed symptoms of anxiety: 6 (27.3%) had clinical anxiety (CA) and 7 (31.8%) subclinical anxiety (SA). 8 (36.4%) pts showed symptoms of depression: 4 (18.2%) – clinical depression (CD) and 4 (18.2%) – subclinical depression (SD). Only 6 (27.3%) pts showed neither depression symptoms nor anxiety symptoms.

The number of pts without pathology is significantly less than with various mental status disorders ( $p=0.0055$ ).

There are no differences between the amount of pts without depression and anxiety ( $p=0.12$ ) and between number of pts with SD and SA ( $p=0.15$ ), and CD and CA ( $p=0.47$ ).

#### Conclusions:

1. Most of BE pts had psychological disorders.
2. More than half of them had anxiety and almost one third – depression.
3. It's important for clinicians to be aware of presence of depression and anxiety for complex correction of these conditions in BE pts.

### [P06] Using State-Trait Anxiety Inventory in Patients with Non-Cystic Fibrosis Bronchiectasis (BE)

Valeriia Dmytrychenko<sup>1</sup>; Kateryna Gashynova<sup>1</sup>; Kseniia Suska<sup>1</sup>

<sup>1</sup>State Institution "Dnipropetrovsk Medical Academy of the Ministry of Health of Ukraine", Department of Occupational Diseases and Clinical Immunology, Dnipro, Ukraine

**Background:** Mental disorders including anxiety are common comorbid conditions in patients (pts) with a chronic pulmonary diseases. But there are not enough data confirming the issue in pts with BE.

**Aim:** The aim of study was to assess anxiety in stable BE pts.

**Material and Methods:** Pts with BE confirmed by high resolution computed tomography. All pts who made the study sample were clinically stable in previous two weeks. Anxiety level was evaluated by State-Trait Anxiety Inventory (STAI) by 2 domains: State-Anxiety (SA) and Trait-Anxiety (TA).

**Results:** 21 BE pts were included (mean age –  $47.7 \pm 13.8$  (32–72) years, 14 (68.2%) – women).

We found that in accordance with STAI all pts had anxiety. The data of anxiety are presented in Table 1.

**Table 1: The data of anxiety in BE pts in accordance with STAI**

	Low level	Moderate level	Severe level
SA	4 (19.1%)	5 (23.8%)	12 (57.1%)
TA	1 (4.8%)	6 (28.6%)	14 (66.7%)
p	$p_{low} = 0.15$	$p_{moderate} = 0.73$	$p_{severe} = 0.53$

In 13 pts (61.9%) both domains were changed equally: 1 (4.8%) pts had low, 1 (4.8%) pts – moderate and 11 (52.4%) pts – severe anxiety.

Quantity of pts with severe level of anxiety significant higher then pts with low and moderate levels ( $p_{low-high} = 0.0006$ ;  $p_{moderate-high} = 0.0006$ ) in both domains.

#### Conclusions:

1. All BE pts had anxiety by STAI.
2. The number of pts with severe anxiety was significantly higher ( $p=0.0006$ ) than number of pts with low and moderate anxiety.
3. More than 60% of BE pts had similar anxiety level in both domains.
4. Clinicians need to be aware of the presence of anxiety for complex correction of these conditions in BE pts.

### [P07] Ultrastructural Changes of Pulmonary Interstitial Tissue in Case of Experimental Diabetes Mellitus

Yuliya Fedorchenko<sup>1</sup>

<sup>1</sup>Teaching Assistant of Pathophysiology Department of Ivano-Frankivsk Medical University, PhD student, MD, Ivano-Frankivsk, Ukraine

**Background:** Diabetes mellitus is one of the most significant problems of modern medicine nowadays which may lead to multiple dysfunctions including pulmonary interstitial tissue changes development.

**Objective:** To study dynamics of the submicroscopical changes of alveolar wall of interstitial tissue in case of experimental diabetes mellitus.

**Material and Methods:** The experiments were conducted on 20 mature white male rats weighing 170–210 g. Diabetes mellitus was induced by the single intraperitoneal injection of streptozotocin ("Sigma" manufacturer, USA) diluted in 0,1 M citrate buffer with pH 4,5 in dose 60 mg/kg of weight. Pulmonary tissue sample acquirement for electronic microscopic research was performed under thiopental narcosis after 14 and 42 weeks after streptozotocin injection. Pulmonary tissue samples were fixated in 2,5% solution of glutaraldehyde with the next co-fixation with 1% solution of osmium quadrioxide. After dehydration material was put in the epon-araldite. Ultrathin sections, acquired on the ultramicrotome "Tesla BS-490", were studied on the electronic microscope "PEM-125K".

**Results:** In 14 days after experiment initiation the conducted ultrastructural analysis revealed that fibroblasts' nuclei were incorrect in shape and had matrix of moderate electronic optical density. Chromatin granules were evenly spread among the nucleus area. Nucleoma had wavy contours and formed non-deep invaginations. Mitochondria were different in size with matrix of moderate electronic optical density. The Golgi apparatus was represented by the numerous small vesicles. Cisterns of the endoplasmatic reticulum were a little bit enlarged.

In case of experiment prolongation (to 42 days), changes in ultrastructural organization of interstitium were characterized by the development of moderate swelling in ground substance of connective tissue of alveolus. Fibroblasts with increased amount of collagen fibers were observed amongst swollen ground substance. Due to this interalveolar walls were thickened. Nuclei of many fibroblats had matrix of low electronic optical density and marginal displacement of chromatin granules. Nuclear membrane formed non-deep invaginations. Perinuclear space was enlarged. Mitochondria were enlarged in volume and contained solitary disoriented crystals. The Golgi apparatus consisted of enlarged cisterns and small vesicles. Cisterns of the granular endoplasmatic reticulum were enlarged, ribosomes quantity on the membranes was significantly decreased.

#### Conclusions:

1. Experimental diabetes mellitus is followed by changes of the ultrastructural organization of the pulmonary interstitial tissue.
2. Character and intensity of changes of pulmonary interstitial tissue depend on duration of the diabetes mellitus.

### [P08] Intrabrochial and Inhalational Amphotericin B for Treatment of Fungal Pneumonia with a Small Loculated Parapneumonic Effusion

Vanitha Gnanasoundran Sundarasamy<sup>1</sup>

<sup>1</sup>Vinayaka Missions Research foundation, Pondi, India

**Background:** Fungal pneumonia in immunocompromised patients is common. But the treatment of Fungal pneumonia is challenging because of the adverse effects of antifungal drugs. Here we report a case of Mucormycosis in a Diabetic patient with diabetic nephropathy treated with intrabronchial Antifungal drug-Amphotericin B and complete recovery of pneumonia without any adverse reaction.

**Method and Result:** Our patient of 60 years old presented with complaints of cough, dyspnea and chest pain for 1 week duration. No history of fever or expectoration present. The patient is a known Diabetic for 20 years. No other co-morbidities present. No history of any prior

respiratory infections present. In the Respiratory examination, there was decreased breath sound in the right lower chest. Blood examination was normal except for mild Leucocytosis of 12,000 and hyperglycemia with a random blood sugar of 244 mg/dl. Urine examination showed 2+protein (proteinuria) with 2+sugar suggestive of Diabetic Nephropathy with glycosuria. Radiological examination (Chest x-ray and Computed Tomography chest) showed right lower lobe consolidation with cavitation with small anteriorly loculated parapneumonic effusion. We proceeded further with Fiberoptic Bronchoscopy and the bronchial wash obtained was sent for Gram stain, Fungal smear, Acid-fast smear with bacterial and fungal culture and sensitivity. Also, the sample was sent for CBNAAT (cartridge-based nucleic acid amplification test), a special test for Tuberculosis. Then we did ultrasound-guided diagnostic tapping of loculated pleural effusion and it was sent for analysis. We got the report as mucormycosis from the microbiology department and there was no other organism detected in the smear or culture or CBNAAT. And the pleural fluid was exudative in nature.

Since intravenous antifungal drugs are notorious for nephrotoxicity, its administration would further aggravate the already existing nephropathy, it was planned to go ahead with intrabronchial administration of Amphotericin B. Three doses of 25 mg of the drug were given at weekly interval. Also, the inhalational method was used daily once for two weeks. Radiological improvement was seen with serial X-rays. X-ray taken at the end of three weeks was near normal. And the patient was asymptomatic with the blood sugar under control.

**Conclusion/Discussion:** In this era of increased incidence of immunosuppressant diseases, there is more incidence of fungal

infections. Antifungal drugs are known for their nephrotoxicity especially conventional forms of Amphotericin but not with the intravenous lipid formulations of the drug. But since the affordability of the patients is not high enough to buy the advanced antifungal drugs, treating physicians had to go for conventional form of the drug. In those circumstances, we have to go for less toxic better administrative routes like intrabronchial especially in a poor resource place. Also, the duration of the treatment





is reduced making less hospital in patient time and further hospital-acquired infection to the already immunocompromised patients.

**Conflict of Interest/Disclosure:** None

## [P09] Prevalence of Obstructive Sleep Apnea Among Asthmatics

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**Background:** Bronchial asthma is one of the most common diseases in the world affecting about 300 million individuals worldwide and therefore a substantial burden of disease. It is a heterogenous disease, usually characterized by chronic airway inflammation. Various pathophysiological mechanisms are related to the worsening of asthma symptoms and control, of them OSA is reported to be one of the important factor. There have been no studies in the literature for assessment of OSA in asthmatics alone without any other known predisposing factors. Therefore it would be of clinical significance to know the relation between OSA and bronchial asthma and their effect on one another, excluding all other known risk factors for OSA.

### Objectives:

- To know the prevalence of obstructive sleep apnoea among controlled and uncontrolled asthmatics.
- To know the relationship between severity of OSA and asthma control.

### Inclusion criteria

- Patients with at least 1 year diagnosis of bronchial asthma.
- Adults above the age of 18 years.
- Stable patients-those who were not in exacerbation.
- Asthma control according to 2015 GINA guidelines.
- Patients who had given written informed consent for the study.

### Exclusion criteria

- Current smoker or previous history of smoking (smoker >100 cigarettes in entire lifetime, ex-smoker-previously smoking but presently completely stopped).
- Obesity based on BMI>30 for men and women, neck circumference >17 inches for men and >15 inches for women.
- Other chronic lung diseases such as COPD, bronchiectasis etc.
- Patients with diabetes, hypertension and cardiac diseases.
- Patients with structural abnormalities known to cause OSA.

### Methods:

- Patients were divided into two groups based on their asthma control. Asthma control was assessed by GINA guidelines for asthma control along with pulmonary function test.
- Group A had patients with stable uncontrolled asthma and group B had patients with controlled asthma.
- 30 patients were taken in each group.
- Each patient in the study was subjected to polysomnography overnight.
- Patients having apnea/hypopnea index of more than 5/hour of sleep were diagnosed as OSA. Parameters were analysed and compared.

**Results:** The number of patients with OSA in the controlled group was 3 (10%) and in uncontrolled group was 13 (43.3%) with a total number of 16 patients (26.7%) ( $p=0.001$ ). The mean duration of symptoms with no OSA was 6.21 years, mild OSA was 17.90 years, moderate OSA was 13.50 years and for severe OSA was 18.71 years ( $p<0.001$ ).

**Conclusion:** OSA is significantly more prevalent in uncontrolled asthmatics compared to well controlled asthmatics. We found that severity of OSA was directly proportional to poor asthma control, severity of airflow obstruction and duration of asthma symptoms.

**Keywords:** Obstructive sleep apnea; Bronchial Asthma; Asthma control; Airflow Obstruction.

## [P10] Determine the Frequency of Polymorphisms of Gene of Xenobiotics Biotransformation System - Microsomal Epoxide Hydrolase in COPD and CHD Patients

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**Background:** Frequent exacerbations of COPD (2 or more per year) are an unfavorable prognostic sign. Revealing of COPD genetic markers, analysis of their association with the severity of clinical course and prognosis of the disease is an urgent task of pulmonology and clinical genetics.

**Aim:** The aim is to determine the frequency of gene polymorphisms of microsomal epoxide hydrolase EPHX1 (rs1051740) in groups of patients with COPD and coronary heart disease (CHD) with different COPD phenotypes.

**Materials and Methods:** The study was approved by a local ethics committee. All patients signed an informed consent form before carrying out of all study procedures. To identify the Tyr113His gene polymorphism of the EPHX1 (rs1051740) DNA was extracted from peripheral blood cells with the use of a standard method using a kit DNA-sorb-B (Amplisens, RF) according to the instructions. Genotyping was performed using allele-specific amplification with real-time detection of results and using a kit of reagents "SNP-Screen" (Sintol, RF) Amplification was performed using the device CFX96 Touch (Real-Time PCR Detection System, Bio-Rad). CFX Manager Software was used for allelic discrimination. Tests for the compliance of the obtained results with the Hardy-Weinberg equilibrium and the revealing of associations by use of the method of Pearson's  $\chi^2$  test were performed using the DeFinetti program of the Institute of Human Genetics (Munich, Germany). According to the study 232 patients were examined (153 men, 79 women), with an average age ( $M \pm SD$ ) of  $60.55 \pm 7.3$  years old and 12 healthy subjects without signs of cardiorespiratory pathology.

**Results:** It is revealed that the frequency of alleles and genotypes according to Tyr113His gene of microsomal epoxide hydrolase EPHX1 in patients with COPD and coronary heart disease is: T-allele 54.8%, C-allele 45.2%, T/T 39.7%, T/C 35.8% and C/C 24.5%. It is revealed that the distribution of C/C, T/C, T/T genotypes according to Tyr113His gene of microsomal epoxide hydrolase EPHX1 in patients with COPD and CHD was not statistically different ( $P = 0.69$ ).

During the analysis of the distribution of the frequencies of C/C Tyr113His gene phenotypes of the microsomal epoxide hydrolase EPHX1 in patients with COPD with frequent and infrequent exacerbations and practically healthy individuals, it was revealed that the recessive homozygous phenotype, the so-called "slow" form of the enzyme, was observed more frequently in the group of patients with COPD with frequent exacerbations (31.4% vs. 9.2%,  $p < 0.05$ ), increasing the risk of developing of the disease with frequent exacerbations 3.2 times ( $OR = 1.54$ ; 95% CI 0.89–2.28).

We determined that T/C Tyr113His polymorphism was observed more frequently in healthy people (56.6%) than in patients with COPD (44.3%), and therefore it is a resistance factor for the development of the disease ( $OR = 0.61$ ; 95% CI 0.39–0.89). During the comparative analysis of the frequency distribution of the phenotype Tyr113His EPHX1 among patients with different stages of bronchial obstruction, significant differences were revealed. Thus, in patients with stage II according to GOLD, the production rate of heterozygous ("fast") form of the enzyme was 23.8%, while in patients with stage III and IV it was 11.6 and 8.9%, respectively. Thus, it was proved, the heterozygous variant of the enzyme is a protective factor, which reduces the risk of development of severe COPD 3.1 times ( $OR = 2.34$ ; 95% CI 1.20–4.55).

### [P11] Referral to Palliative Care, Assignment of End-of-Life Care Plan and Ceiling of Treatment Among Patients with COPD and Lung Cancer Respectively

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**Introduction:** In the terminal stage of any disease relief of symptom is the main target of treatment.

**Aim:** To investigate the use of i) end-of-life care plan, ii) ceiling of treatment, iii) referral to palliative care in chronic obstructive lung disease (COPD) and Lung Cancer (LC).

**Method:** Comparison of deceased patients, who in 2018 had been admitted to the Pulmonary Medicine Department of Aalborg University Hospital, Denmark (AaUH, DK) with the diagnosis of COPD or LC. Case records were searched for information on the above. COPD and LC patients were compared by binomial testing.

**Results:** In 2018, 97 admitted patients with COPD and LC died, 59 from COPD and 38 from LC. No statistically significant difference between groups were found in assignment of an end-of-life care plan ( $p=0,09$ ) and prescribed ceiling of treatment ( $p$ -value 0,05). Statistically significant difference was found in the referral to palliative care ( $p$ -value 0,027) among the patient groups with COPD and LC respectively.

**Conclusion:** Patients suffering from LC were significantly more frequently referred to palliative care.

### [P12] Return to Work and Detachment From the Workforce After Acute Exacerbation of Chronic Obstructive Pulmonary Disease. A Danish Epidemiologic Study

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**Background:** The existing literature on COPD patients return to work (RTW) after Acute Exacerbation of Chronic Obstructive Pulmonary Disease (AECOPD) is sparse, and the understanding of predisposing factors of early retirement is limited. The purpose of our study was, to examine RTW and permanent detachment from the workforce after AECOPD.

**Methods:** This is a nationwide epidemiologic cohort study using a register based follow-up design. Different Danish registries were available with information on admission diagnosis, public financial support, age and time of death. Inclusion criteria were admission to the hospital between 1999–2014 with a primary COPD diagnosis or a primary diagnosis of acute respiratory insufficiency/pneumonia with COPD as a secondary diagnosis in patients between age 35–64. Only 30 days survivors were included and the follow-up on patients began 4 weeks after admission to the hospital and ended after 5 years or when patients reached age 65.

**Results:** 24.687 COPD patients between age 35–64 were admitted to the hospital between 1999–2014. 1268 of these died within the first month and 18.162 patients were not a part of the workforce at the time of admission to the hospital leaving 5.257 patients included in the analysis. The median age of the population was 56 (IQR 51–60) and 52.8% were female. 4872 (92.68%) returned to work during follow-up and 3.706 (70.5%) had returned to work 4 weeks after AECOPD. The median time until RTW among the remaining 1166 (22.18%) was 9 weeks (IQR 6–17). Of the 385 (7.32%) that did not RTW, 39 (10.13%) were on permanent public support 4 weeks after admission to the hospital. 789 (15.01%) of patients had early permanent detachment from the

workforce during the entire follow-up period. The median time for permanent detachment from the workforce, excluding death, was 86 weeks (IQR 48–148).

**Conclusion:** The majority of patients RTW within the first month however 22.18% of the population had a delayed RTW with a median time of 9 weeks (IQR 6–18). Of the 385 (7.32%) patients that did not RTW only 39 (10.13%) left the workforce due to permanent detachment. However with 789 (15.01%) ending permanently detached from the workforce before the age of 64, vulnerable patients exist in the population. It would appear that the event in itself does not initiate the detachment but that the chronic predisposition in COPD patients will for 15.01% of the patients result in detachment in the following years.

This abstract therefore calls for increased attention to RTW in COPD patients with the aim of identifying predisposing factors that can help guide implementation of relevant intervention e.g. rehabilitation. However it is clear that, with regards to work retention, the cutoff of first hospitalization with AECOPD is already too late for the majority of the population. The identification of patients at risk and intervention to avoid detachment from the work force should therefore take place at an earlier stage of the disease and patients must be identified in the primary care sector.

### [P13] Economic Burden of Silica Exposure in Organised Sector Workers

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**Background:** Occupational exposure to crystalline silica has been described throughout history. Chronic silicosis develops slowly, usually appearing 10 to 30 years after first exposure. Silicosis related morbidity and mortality affects workers of all ages. Poor symptom perception and patient knowledge regarding the disease contributes to the under diagnosis. A majority of silicosis cases thus remain undiagnosed at early stages, leading to delay in treatment and rehabilitation. Loss of earning capacity is simple measure of morbidity which can be calculated using spirometry, oxygen saturation, chest radiograph and dyspnoea grade.

**Aims:** To evaluate the clinical, physiological and radiological parameters & its correlation with loss of earning capacity in patients with silicosis.

**Methods:** We did a retrospective observational study at Employee State Insurance -Post Graduation Institute of Medical Science and Research & Institute of Occupational Health and Environmental Research, Basaidarapur, New Delhi as a part of vapour, gas, dust and fumes (VGDF) study group. Our study sample was 26 male organised sector workers with silicosis referred to special medical board for evaluation of loss of earning capacity.

**Results:** Out of 26 study subjects only four were chronic smokers. None of the study population were aware about silica and its effects on health. The mean age of the patients included in the study was 46.92 years (SD 4.95 years) and mean FEV1 was 53.96% (SD 17.27%). All the patients had a profusion grade of >2/2 based on International Labour Organisation (ILO) radiograph classification. We have found statistically significant correlation between loss of earning capacity and years of exposure to silica dust ( $p = 0.041$ ). Also there was significant correlation between FVC% and FEV1% with loss of earning capacity ( $p < 0.0001$  in both instances). We found that there was no significant correlation between loss of earning capacity and symptoms score & activity score parts of St George's Respiratory Questionnaire ( $p = 0.180$ ,  $p = 0.712$  respectively). Interestingly, significant correlation was observed between impact score part of St George's Respiratory Questionnaire and loss of earning capacity

Correlations

		LOSS OF EARNING CAPACITY	EXPOSURE IN YEARS	SYMPTOMS SCORE	ACTIVITY SCORE	IMPACT SCORE	SGRQ SCORE	FVC%	FEV1%	6MWD(metres)
LOSS OF EARNING CAPACITY	Pearson Correlation	1	.403*	.271	.077	.486*	.381	-.893**	-.833**	-.376
	Sig. (2-tailed)		.041	.180	.710	.012	.055	.000	.000	.058
	N	26	26	26	26	26	26	26	26	26
EXPOSURE IN YEARS	Pearson Correlation	.403*	1	.214	.172	.121	.168	-.301	-.386	-.295
	Sig. (2-tailed)	.041		.293	.400	.557	.411	.136	.051	.143
	N	26	26	26	26	26	26	26	26	26
SYMPTOMS SCORE	Pearson Correlation	.271	.214	1	.654**	.728**	.833**	-.203	-.472*	-.216
	Sig. (2-tailed)	.180	.293		.000	.000	.000	.319	.015	.288
	N	26	26	26	26	26	26	26	26	26
ACTIVITY SCORE	Pearson Correlation	.077	.172	.654**	1	.673**	.835**	-.115	-.261	-.278
	Sig. (2-tailed)	.710	.400	.000		.000	.000	.576	.198	.169
	N	26	26	26	26	26	26	26	26	26
IMPACT SCORE	Pearson Correlation	.486*	.121	.728**	.673**	1	.959**	-.499**	-.600**	-.298
	Sig. (2-tailed)	.012	.557	.000	.000		.000	.010	.001	.140
	N	26	26	26	26	26	26	26	26	26
SGRQ SCORE	Pearson Correlation	.381	.168	.833**	.835**	.959**	1	-.387	-.544**	-.307
	Sig. (2-tailed)	.055	.411	.000	.000	.000		.051	.004	.127
	N	26	26	26	26	26	26	26	26	26
FVC%	Pearson Correlation	-.893**	-.301	-.203	-.115	-.499**	-.387	1	.832**	.338
	Sig. (2-tailed)	.000	.136	.319	.576	.010	.051		.000	.091
	N	26	26	26	26	26	26	26	26	26
FEV1%	Pearson Correlation	-.833**	-.386	-.472*	-.261	-.600**	-.544**	.832**	1	.475*
	Sig. (2-tailed)	.000	.051	.015	.198	.001	.004	.000		.014
	N	26	26	26	26	26	26	26	26	26
6MWD(metres)	Pearson Correlation	-.376	-.295	-.216	-.278	-.298	-.307	.338	.475*	1
	Sig. (2-tailed)	.058	.143	.288	.169	.140	.127	.091	.014	
	N	26	26	26	26	26	26	26	26	26

\*. Correlation is significant at the 0.05 level (2-tailed).

\*\* Correlation is significant at the 0.01 level (2-tailed).

( $p = 0.012$ ). However, there was no significant correlation between loss of earning capacity and overall St George's Respiratory Questionnaire scores along with six minute walk distance ( $p = 0.055$ ,  $p = 0.058$  respectively).

**Conclusion:** Unawareness and poor perception of symptoms among the workers exposed to silica dust at work place lead to delayed presentation and extensive functional limitation. This ultimately result in loss of earning capacity among these patients. So, improving awareness among people working in these industries through awareness programs and source control at work place limits exposure to these hazards. Since, use of personal protective gear is a last resort to prevent occupational exposure, regular screening of the workers may result in better outcome.

**Conflict of interest/Disclosure:** None

### [P14] Single Centre Observational Study of Pheno/Endotypes of Adult Severe Asthma Patients Attending Severe Asthma Clinic, India

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**Background:** No studies have reported prevalence of severe asthma and phenotypes in India. To understand pheno/endotypes of severe asthma for using biologicals/Bronchial Thermoplasty, we conducted a study in our severe asthma clinic.

**Aim:**

- To phenotype/endotype severe asthma patients attending severe asthma clinic in India.

**Methods:**

- After institutional ethical clearance, an observational study was done from June 2018 to May 2019. Hundred consecutively diagnosed adult severe asthma patients (retrospectively labeled as per GINA) were enrolled in study. Bronchiectasis, ACO, ABPA and smokers were excluded.
- Detailed chart reviews of demographic, clinical, lab tests (IgE total, AEC and Immunocap for aeroallergens), spirometry, skin prick test and FeNO were done. Patients were grouped into T<sub>H</sub>2 high eosinophilic

**Table 1: Demographics, Clinical, Physiological and pathophysiological features in 100 severe asthma cases**

Parameters	Group (TH2 eosinophilic)	Group (TH2 Overlap)	Group (TH2 low)	Group (TH2 atopic)	P values
No of Patients	4	53	5	38	
Onset (early)	0	18	2	15	0.05
(late)	4	35	3	23	
GINA step 4	0	14	1	6	0.03
step 5	4	39	4	32	0.05
ACT >19	4	0	0	7	0.04
<19	0	53	5	31	<0.001
IgE (U/mL)	17.4	412.3	21.5	422.4	<0.001
AEC (cu/mm)	572.5	455.3	202.4	193.2	<0.001
FeNO > 19	4	36	1	18	<0.001
< 19	0	17	4	20	
SPT (skin prick test)	4	46	2	35	0.02
Positive Immunocap Assay (atleast 1 aeroallergen)	4	36 (4 extra over SPT)	5	29	<0.001
Asp sp IgE (positive)	1	4	0	3	0.4
(negative)	3	49	5	35	
Mean FEV <sub>1</sub> (Post BD) % predicted	62	67	58	70	0.001
FEV <sub>1</sub> (reversibility) in %	19	15	10.2	15	0.03
BMI ≥30 (obesity)	0	16	1	9	0.03
≥35 (morbid)	0	3	0	1	0.4

(AEC >300) or Atopic (IgE>30 and allergen sensitization) or TH2 low (AEC<300 and no atopy) categories and assigned one out of four endotypes-TH2 Eosinophilic, TH2 Atopic, TH2 Overlap (both AEC>300 & atopy) and TH2 low.

- Statistical Analysis done using SPSS 20 version with standard tests for categorical and continuous variable.

**Results:** Mean age of asthmatics was 45.8 ±16.9 years and 52 were males. Mean BMI = 26.4 kg/m<sup>2</sup>. Mean AEC = 368.9 ± 235.7/cumm (highest value in last 1 yr) and IgE = 402.6 ± 411.6 U/ml. Mean FeNO = 33 ± 25ppb. 79% severe asthma patients were in step 5 GINA with 89% had poor asthma symptom control and 1/3<sup>rd</sup> were obese. SPT + to atleast 1 aeroallergen in 87% cases. IgE Specific for aspergillus was positive in 8% of patients, however they did not fulfil the criteria for ABPA.

**Conclusion:** TH2 high overlap group (both eosinophils and atopy present) was the commonest (50%) phenotype in Indian severe asthmatics. Eosinophilic & TH2 low were seen in 4% & 5% respectively and atopic severe asthma in 38%. Overlap group of severe asthma in India would pose difficulties in choosing Anti IgE vs Anti IL 5 biologicals in real life.

**Reference:** Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2019. Available from: www.ginasthma.org

### [P15] Does Hospice Service Associated with Efficient Healthcare Costs Among Terminal Lung Cancer Patients? Hospital Charges Per Day by Lung Cancer Patients at their End of Life; A Retrospective Cohort Design of 2010–2018



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**Background:** Hospice palliative care is medical care aimed at improving the quality of life of terminal cancer patients and their families through comprehensive assessment and treatment of the physical, psychosocial and spiritual areas, including relief of pain and symptoms. The healthcare costs of cancer patients were markedly increased to show a “U” shape at the first stage of diagnosis and at the end of life. Especially during the last month of life, hospital charges are known to increase rapidly. Over the past decades, Cancer is the one leading cause of death in Korea, the latest statistics indicate that in 2016, there were 25,780 incident lung cancer cases (out of a total of 229,180 cancer cases; 69% male), 18,658 deaths (out of a total of 79,729 deaths; 74% male) in Korea. The share of hospice use among all deaths was 17.5% in 2016 and 20.0% in 2017, up from 7.3% in 2008. However, in 2011, the data lag far behind the United States (52.0%), the United Kingdom (46.6%), Canada (40.8%) and Taiwan, the same Asian country (39.0%). In July 2015, South Korea started applying national health insurance reimbursement to inpatient hospice, and it is now appropriate time to evaluate how hospice care associated with healthcare costs using national health insurance claims data among terminal lung cancer patients.

**Materials and Methods:** We used NHIS-NSC data during 2010–2018 which accounted for all patients’ health insurance claims. We transposed the dataset into a retrospective cohort design study that the unit of analysis is information of each lung cancer patient. Since September 2016, we have observed hospice user medical’s use for one year before death compaing non-sevice users. Furthermore, the differences in hospital charges and length of stay were checked according to one year, six months, three months, and one month before death. Finally, the

patients were identified according to the medical institution where they specialized for hospice services.

**Results:** The results showed that during year from 2016 to 2018, hospice users among lung cancer patients were 6,033 (23%, out of a total of 26,204). Hospice users were associated with lower hospital charges per day as they approached death than non-users (11% for 12 months before death, 15% for 6 months before death, 17% for 3 months before death, and 22% for 1 month before death). The gap between hospice specialized institution and general hospital is even greater (27% for 12 months before death, 31% for 6 months before death, 34% for 3 months before death, and 41% for 1 month before death).

**Discussion and Conclusion:** In this study, we found lower end-of-life healthcare associated hospital charges were found for the lung cancer inpatients who were admitted to hospitals with hospice care beds when nears death. This study suggests that health policy-makers and the National Health Insurance program need to consider expanding the use of hospice care beds within hospitals and hospice care facilities for end-of-life patients with lung cancer in South Korea, where very limited numbers of resources are currently available.

### [P16] Bronchial Challenge Testing Using Acetylcholine by Impulse Oscillometry

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**Background:** Currently, bronchial challenge test are widely used to diagnose bronchial hyperreactivity – a hyperreaction of the bronchi to various stimuli. The aim of study was appraisal of capabilities of the impulse oscillometry for making a diagnosis of bronchial obstruction using a pharmacological agent - acetylcholine.

**Materials and Methods:** This is a prospective, single center study including 11 healthy volunteers (8M/3F, mean ± SD age 25,8 ± 4,8 years) and 38 patients with bronchial asthma (BA) history in childhood without any BA symptoms in present time (35M/3F, mean ± SD age 24,2 ± 9,4 years) (Table 1).

A bronchial challenge test with acetylcholine included the parallel spirometry and impulse oscillometry (IO) measurement before and after inhalation acetylcholine chloride solution with different acetylcholine concentration. The study outcome were analyzed at each step after

**Table 1: Physical data of healthy volunteers and patients suffering from bronchial asthma in childhood (M±SD)**

Parameters	Healthy	BA
Age, yrs	25,8±4,8	24,2±9,4
Sex M/F	8/3	35/3
BMI	24,3±2,9	24,1±4,97
FEV1, %pred.	104,4±5,6	98,8±6,2

**Table 2: The per cent lung function parameters change from baseline (M±SD)**

Parameters	Healthy (n=11)	BA with positive test (n=30)	BA with negative test (n=8)
FEV1	11,4±3,3	26,4±5,4*	10,3±5,7
R5	31,4±20,5	78,3±51,5*	47,2±25,6
X5	104,1±112,7	184,9±183,4	42,0±33,4
Fres	75,4±70,2	118,7±88,9	45,5±28,3

\* - p < 0,05.

inhalation of 5 ml 0.9% NaCl and acetylcholine in a dose 100 mcg, 200 mcg, 500 mcg, 1000 mcg, 2000 mcg, 5000 and 10000 mcg. The obtained value of FEV1 after inhalation of 5 ml 0.9% NaCl was the baseline for calculating the intensity of changes in FEV1 and IO parameters.

Mann-Whitney test was used to compare differences between groups.

**Results:** The patients with BA history divided into 2 subgroups depending on the test result: 30 patients had a positive acetylcholine test - FEV1 falls more than 20% from baseline (28M/2F, mean  $\pm$  SD age 22,4  $\pm$  5,2 years); 7 persons had a negative acetylcholine test (7M/1F, mean  $\pm$  SD age 25,6  $\pm$  9,6 years). The most pronounced changes in IO parameters were changes of resistance at 5 Hz (R5), reactance at 5 Hz (X5), resonance frequency (Fres) (Table 2).

According to the impulse oscillometry, a significant difference between the healthy group and BA with positive test was obtained only for R5 change ( $p < 0,05$ ). FEV1 decline  $>20\%$  was matched by  $> 74\%$  R5 increase.

**Conclusions:** The R5 change was significantly different in healthy and BA with positive test. The parallel use spirometry and impulse oscillometry can increase the sensitivity of the test, which requires further accumulation of data.

### [P17] The Profile of Sarcoidosis in Greece: Clinical Characteristics, Extra-Pulmonary Manifestations, Long-Term Follow-Up

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**Introduction:** Sarcoidosis is a multisystem inflammatory disease of unknown etiology, which is characterized by granuloma formation. Clinical presentation, organ involvement, disease severity, and prognosis vary significantly according to region and population.

**Aim:** The aim of this study was to assess epidemiological and clinical characteristics, staging factors, and clinical course of the disease in Greek patients with sarcoidosis.

**Methods:** Data were collected and analysed retrospectively, between January 2002 and December 2019, from the Sarcoidosis Center of General Hospital of Chest Diseases in Athens. Demographics, stage at diagnosis, extra-pulmonary manifestations, symptoms, pulmonary function testing and current treatment were recorded.

**Results:** A total of 550 cases with pathologically confirmed sarcoidosis diagnosed between January 2002 and December 2019 were analysed. The mean age at diagnosis was 46 years (25 to 79 years), 58% were females and 42% were males. Lung involvement (91%) was the most common type of organ involvement. Approximately 48% of patients with pulmonary sarcoidosis had extra-thoracic manifestations. Most common were skin lesions 57%, followed by ocular involvement 16%, CNS 8.3%, cardiac 6.5%, joint 6.8% and hepatic involvement 5.7%. At the time of diagnosis, the majority of patients were in radiological stage II and stage I (43%–41%, respectively), 11% in stage III and 5% in stage IV. The most prevalent CT findings were pulmonary nodules in combination with hilar and mediastinal lymph nodes, (72%), traction bronchiectasis (9%) and ground glass (3%). The most common presenting symptoms included dry cough, dyspnoea with exertion, fatigue, chest discomfort and arthralgia. With respect to pulmonary function mean DLCO was 65% predicted and mean FCV was 76% predicted. Systemic treatment was administered in 46.7% of cases.

**Conclusion:** The epidemiological and clinical characteristics of this cohort of Greek patients with sarcoidosis were generally similar to those described in other Western Europe populations and in the US ACCESS study. However the mean age at diagnosis seems to be higher in Greece than other countries.

### [P18] Impact of Air Quality on Lung Function in Various Respiratory Disorders

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**Introduction:** Air pollution is a serious threat to the quality of life. The adverse effects of air pollution on the lung are well documented. However, the precise impact of Air quality on various respiratory disorders is yet to be understood. The present study aims to find the impact of air quality assessed in terms of lung function on various respiratory disorders.

**Methodology:** Pulmonary function tests (PFT) have been performed on various individuals twice in a year, first when the Air Quality Index (AQI) is satisfactory (AQI-78) and second on a day where the AQI is hazardous (AQI-526). The subsets include normal population (GROUP A), who underwent an annual mandatory health check, Individuals suffering from Bronchial Asthma (GROUP B), Chronic Obstructive Pulmonary Disease (COPD, GROUP C) and Interstitial Lung Disease (ILD, GROUP D). Individuals are recruited from each subset randomly and are subjected to PFT twice as mentioned. Individuals who had an exacerbation or hospitalization in the last 1 year, people using masks and air purifiers, active smokers, people with significant comorbidities like cardiac disease, Diabetes are excluded from the study. Comparison of fall in Forced Expiratory Volume at the end of the first second (FEV1), fall in Forced Vital Capacity (FVC) and variations in Post bronchodilator FEV1 values were made among each group.

**Statistical Analysis:** Continuous data is presented in the form of mean, median and interquartile range. Tests for normality were carried out before determining the statistical test to be applied for continuous data. The difference in mean between paired samples of non-parametric data is tested using Wilcoxon Signed rank test. The difference in mean between multiple groups is tested using ANOVA. A p-value  $<0.05$  was considered statistically significant. Statistical Analysis was carried out using IBM SPSS (Statistical Package for Social Sciences) version 22.0

**Results:** There is a significant fall in FEV1 noted in Asthma and COPD groups with a 'p' value of 0.023 and 0.005 respectively corresponding to the worsening air quality. There is also a significant improvement in post-bronchodilator FEV1 reversibility in COPD group ( $p=0.08$ ). However, the fall in FVC is not significant across the groups.

**Conclusion:** The present study is first of its kind to compare the lung function values across various spectra of respiratory ailments. Though the study has its own limitations in terms of smaller sample size and whether the duration of exposure and PFT are optimal to assess the impact, it has proved that people with obstructive airway diseases are affected most requiring close observation & follow up on this subset of people to prevent exacerbations during worsening air quality.

**Conflict of interest/Disclosures** – None

### [P19] Lung Function Changes in Young Patients with Pulmonary Tuberculosis and Undifferentiated Connective Tissue Disorders

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**Introduction:** Bad ecology, infection diseases and stress situations during the pregnancy lead to connective tissue disorders (CTD) which can be appear in all organs and systems. In the lungs CTD appear by thinning and ruptures of the interalveolar septa, underdevelopment of

**Table 1**

TB forms	1 group (%)	2 group (%)
Focus <10 mm	5,5	25
Tuberculoma	11	6
Infiltrates	41,5	42
Cavities	30,5	19
Disseminated	11,5	8

**Table 2**

Parameters	1 group mean	1 group 95%D	2 group mean	2 group 95%D	p<0,05
FEV1 %	92,33	84,41-100,24	106,39	98,74-114,04	0,014
VC %	97,75	90,72-104,77	111,44	102,12-120,76	0,02
RV %	133,81	123,82-143,8	121,4	110,36-132,43	0,04
RV/TLC %	122,76	114,9-130,62	106,48	93,90-119,05	0,01

elastic and muscle fibers in the small bronchi and bronchioles. These violations also change ventilation parameters.

It was observed that young people with the connective tissue structure disabilities most often fall ill with tuberculosis (TB) than young people without CTD and have more severe TB forms.

We study the features of ventilation disorders in young patients with TB and CTD.

**Materials and Methods:** This is a prospective single center study including 60 verified TB patients from 18 to 45 years. They were divided for 2 groups:

1 group – 36 patients with proven manifestations of CTD

2 group – 24 patients without signs of CTD

The patients after lung resection were not included

Chest computer tomography, echocardiography, bronchoscopy, abdominal ultrasound and physical examinations were used to determine the presence of CTD.

Ventilation parameters we evaluated by spirometry, bodyplethysmography and respiratory muscle strength investigation.

The descriptive statistics and Mann-Whitney test were used.

**Results:** The most common TB pulmonary structure changes in both groups were infiltrates, but other patients with proven manifestations of CTD had more severe TB forms and only in this group we met generalization of TB infection (Table 1).

Patients with proven manifestations of CTD have tendency to obstructive remodeling of total lung capacity (decrease of vital capacity (VC), increase of residual volume (RV)) (Table 2).

Most patients with signs of CTD has reduced the respiratory muscles strength (isolated decrease in inspiratory muscles was found in 16%, expiration - 20%, decrease in strength of both types muscles - in 24%).

**Conclusion:** Ventilation disorders in young patients with TB and CTD had tendency to obstructive remodeling of total lung capacity and decrease of the respiratory muscles strength.

## [P20] Selection of Lung Transplant Candidates: Current Strategies and Issues

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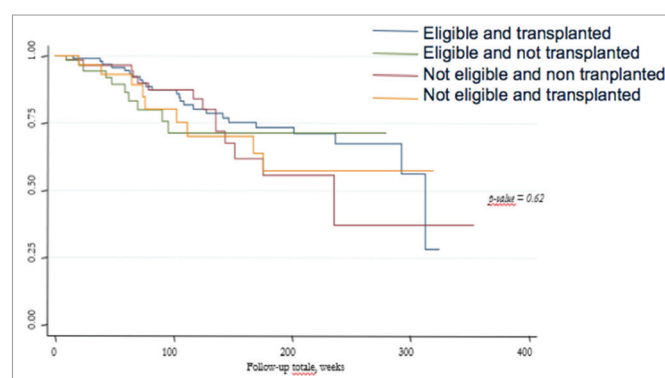
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**Introduction:** Lung transplant (LuTx) is nowadays considered a valuable option for end-stage lung disease, but an appropriate selection of candidates is essential to improve survival. However, currently available listing criteria for LuTx are based just on a consensus of expert opinion. The aim of this study is to evaluate the use of these criteria in our Centre and their possible relationship with survival.

**Methods:** This was a retrospective observational study on consecutive adult patients referred to our clinics for primary LuTx for any indication from January 2012 to June 2017. We analysed the prevalence of contraindications and listing criteria as stated in ISHLT (Orens 2006, Weill 2014) and SEPAR consensus. Population was divided into three groups, based on the bundle of listing criteria which was used: A) interstitial lung diseases, ILD (including idiopathic pulmonary fibrosis, IPF, and all other forms of ILDs), B) cystic fibrosis (CF) and bronchiectasis; C) COPD. Of note, no patient was referred because of pulmonary vascular diseases. A comparison was then performed between those who were listed and those who were not considered amenable to LuTx.

**Results:** 305 patients were evaluated in the study period, 179 (58.7%) males, median age 52 (32–66) years, 28.5% CF, 25.2% IPF, 16.4% ILDs not IPF, 10.5% connective tissue diseases, 12.1% COPD, 7.2% other indications. With regard to the general population, the contraindications with a significantly different prevalence between patients on waiting list (WL) and not listed were the absence of social support [OR 11.3 (1.4–89.4, p=0.02) and compliance [OR 21.6 (2.9–164), p=0.003]. For ILDs no single criteria proved significantly more frequent in listed patients. Conversely, criteria associated with an increased risk for listing were: for CF respiratory failure [OR 7.0 (1.4–34.3), p 0.02], and for COPD BODE > 7 [OR 12 (1.3–111.3), p 0.03]. Ineligible individuals (no criteria and/or due to contraindications) and transplanted patients showed a better survival than patients on WL but non yet transplanted, both for whole population and the different groups.

**Conclusions:** In our experience, placement on active WL is mainly based on multidisciplinary clinical decision more than on the strict application of listing criteria (Weill, JHLT 2015), with an improved survival both in patients not eligible for LuTx and patients transplanted. Absent social support and poor compliance were the only contraindications which significantly affected LuTx candidate selection. Based on our data, currently available listing criteria for ILDs did not prove a suitable tool for candidate selection; this was probably due to the great heterogeneity of these conditions and the possible need to identify specific criteria for IPF. CF patients with respiratory failure and COPD patients with a high BODE probably deserve faster listing decision.



## [P21] Effectiveness of Short-Term Pulmonary Rehabilitation Program for Overweight and Obese Patients with Asthma-COPD Overlap

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**Background:** Pulmonary rehabilitation (PR) is widely accepted as an effective treatment for patients with chronic respiratory disease, especially for COPD. However, the efficacy of PR has not yet been proven in patients with ACO and obesity.

**Aim:** The aim of the study was to evaluate the effectiveness of short-term pulmonary rehabilitation program in patients with ACO depending on their nutritional status.

**Materials and Methods:** Study included 30 ACO patients (mean age 63.87 ± 10.1 years) divided into three groups: normal body mass index (BMI 18,5–24,9), overweight, (BMI<25–29,9) and obese patients (BMI≥30). The BODE index (body mass index, forced expiratory volume in one second, dyspnea, and 6-min walk distance) and the CAT-test were evaluated before and after a 6-month PR program. Weight and body composition variables were measured with a segmental body composition monitor (BC-601 TanitaT, Japan).

**Results:** At baseline, obese and overweight patients had less severe airflow obstruction compared to normal BMI patients. After 6 months of PR, the BODE index decreased in each group reliably but was significantly lower in overweight patients (decreased by 44,7%) compared to obese and normal BMI patients. There was a decrease in dyspnea mMRC scale scores (from 1,89±0,16 to 1,23±0,10, p<0,05), improved exercise capacity 6-MWT scores (by 11,8%) and quality of life according to the CAT test (from 14,56±1,62 to 10,00±1,16; p<0.05). The BMI decreased more in obese group. The body fat percentage and visceral fat level decreased by 12,4% and 13,4%, respectively in obese patient and by 8% and 2,3% in the presence of obesity. FEV1 after the PR increased slightly (by 6% in overweight group, by 9,4% in obese group and by 4% in group with normal BMI).

**Conclusion:** An early use of pulmonary rehabilitation program significantly improved the quality of life and exercise tolerance in overweight and obese patients with ACO. The BODE index may serve as a criterion for evaluating short-term rehabilitation program in ACO patients with different nutritional status.

## [P22] Adipokines in Pathogenesis of Chronic Obstructive Pulmonary Disease Depending on Nutritional Status

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**Background:** Recent studies suggest an important role for leptin, adiponectin and resistin in respiratory immune responses and pathogenesis in patients with stable and exacerbation phases of chronic obstructive pulmonary disease. Zinc-Alpha 2-Glycoprotein (ZAG) has recently been implicated in the regulation of adipose tissue metabolism due to its negative correlation with obesity.

**Objective:** This study aimed to detect serum concentration of adipokines in acute exacerbation of COPD depending on nutritional status.

**Material and Methods:** The study involved 67 COPD patients with obesity, overweight, underweight and normal body mass index (BMI) and 22 healthy control group. Serum level of leptin, adiponectin, ZAG were measured using an enzyme-linked immunosorbent assay.

**Results:** Serum concentration of leptin in acute exacerbation of COPD were higher (10,64±1,81 in underweight patients to 54,91±5,92 in obesity

patients) compared with healthy control group (p<0.05). Adiponectin levels were significantly lower in COPD patients with obesity (4,81±0,41) and higher in underweight COPD patients (19,39±2,09), especially compared with patients with overweight and obesity (61,8% and 68,6%, p<0.05). Serum ZAG levels were significantly higher in underweight patients (84,12±10,00). Significant negative correlation between ZAG and BMI (r = -0,63, p<0,001), muscle mass (r = -0,38, p<0,01), fat mass (r = -0,52, p<0.001) and the level of visceral fat (r = -0,57, p<0,001) were detected.

**Conclusions:** Chronic obstructive pulmonary disease in exacerbation phases is characterized by an imbalance of adipokines, depending on the nutritional status of the patient and may suggest involved adipokines in the inflammatory process.

## [P23] Cardiac Dysfunction in Active Pulmonary Tuberculosis: Underestimated, Missed Routinely and Have Impact on Clinical Outcome! Prospective Study of 600 Cases in Tertiary Care Setting in India

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**Introduction:** Although cardiac involvement is extremely rare in tuberculosis, cardiac dysfunction is not uncommon.

**Methods:** Prospective observational and interventional study conducted in Pulmonary Medicine, MIMSR medical college, and Venkatesh chest Hospital, Latur India during July 2013 to December 2018. Included 600 case of active pulmonary tuberculosis confirmed microscopically or with Gene Xpert MTB/RIF documented MTB genome in respiratory specimens like sputum/induced sputum and bronchoscopy guided bronchial wash or bronchoalveolar lavage whenever necessary. Cases with known risk factor for cardiac disease and taking cardiac medicines, and cases with pericardial effusion were excluded from study. Disproportionate tachycardia and tachypnea with or without shock and hypoxemia were key entry point criteria in this study. Chest radiograph, pulse oximetry, ECG, Sputum examination, cardiac enzymes, serum cortisol and Echocardiography is done in all study cases during enrollment, at 2 months and 6 months of treatment with Anti-tuberculosis medicines. Statistical analysis were carried out by chi-square test.

**Observations and Analysis:** In 600 cases with active pulmonary TB, cardiac dysfunction were documented in 26% cases, females were 44%; and 56% cases were having age >65 years. Echocardiography abnormality were documented as global hypokinesia in 62% cases, depressed left ventricular systolic and diastolic function in 44% & 28% cases respectively, dilated right atrium and right ventricle in 32% cases, and pulmonary hypertension in 6% cases. Serum cortisol level is significantly lower in cases with cardiac dysfunction (p<0.00001). Hypoxemia has significant association with right and left heart dysfunction (p<0.00001). Cachexia, anemia and Hypoalbuminemia was documented to have significant association with cardiac dysfunction (p<0.00001). Treatment outcome shows significant improvement in cardiac function (p<0.00001) Coronary angiography is not showing significant coronary artery lesions and CT pulmonary angiography not showing pulmonary embolism.

**Conclusion:** Cardiac dysfunction in active pulmonary tuberculosis is underestimated and less evaluated routinely; disproportionate tachycardia and tachypnea with or without shock are clinical indicators to suspect early, especially in cases with risk factors like advanced pulmonary TB on chest radiograph, cachexia with BMI<18, advanced age, females, cases with anemia and hypoalbuminemia. Echocardiography showing 'Global hypokinesia' as a predominant cardiac dysfunction

in study cases; and right or left heart dysfunction depends on with or without hypoxemia respectively. Serum cortisol measurement will help in majority of cases and proportionate number of cases were having associated adrenal suppression.

### [P24] Halo Sign in Immunosuppressed Patients - A Systematic Review and Meta Analysis

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**Introduction:** Halo sign (HS) refers to the presence of ground glass opacity surrounding a nodule or mass in lung parenchyma.

#### Materials and Methods:

**Aim:** The aim of the systematic review was to report all the described etiologies of HS in immunocompromised subjects and to compute the diagnostic accuracies of HS in the background of immunosuppression. It was registered in PROSPERO (CRD42018094739) and reported as per PRISMA guidelines.

**Search strategy:** PubMed and EMBASE database were searched from 1982 till June 2018. Original articles, case reports and case series published in English language were included. The database was compiled in a reference package (Zotero) and subsequent analysis was done. Quadas (Quality assessment for studies of diagnostic accuracy) tool was used before quantitative analysis.

**Data extraction:** The reviewers independently extracted the data on a predesigned spreadsheet and any discrepancy was resolved after discussion.

**Data analysis:** Individual study estimates were charted and computed to get pooled estimates of diagnostic accuracies. Likelihood ratio model was used in the pooled estimate and represented in the forest plot. Heterogeneity was estimated with *I*<sup>2</sup> test statistic, including 95% CIs.

#### Results:

**Qualitative analysis:** A total of 168 studies were included. Total number of immunosuppressed patients were 4933; etiological diagnosis made in 1582 (32%) patients. Of these 1374, (86.9%) cases were due to IFI. Among IFI, IPA accounted for 75.4% (1036/1374) and mucormycosis for 3.2% (44/1374) of all cases. Non-mold fungal infections accounted for 1.96% (27/1374) of cases, most common was *Candida* (59.3%) followed by *Cryptococcus* (29.6%) and *PCP* (11.1%). In 19.1% (262/1374) cases, the IFI was uncharacterised. Viral pneumonia accounted for 3.4% (54/1582) of cases with RSV (51.85%) being most common followed by CMV pneumonia (20.37%). Bacterial pneumonia comprised 2% of all cases (32/1582). HS was described in other infectious and non-infectious pathologies.

**Quantitative analysis:** In the quantitative analyses 14 studies were included. The diagnostic accuracies (sensitivity, specificity and Odd's ratio) were calculated in the subgroups of Invasive fungal infections (IFI), Invasive pulmonary aspergillosis (IPA), neutropenic subjects and those with antibiotic-resistant fever.

**IFI:** The pooled sensitivity of HS for IFI was 0.504 (95% CI: 0.393, 0.615); pooled specificity was 0.91 (95% CI: 0.755, 0.970) and odd's ratio was 6.613 (95% CI: 2.615, 16.724).

**IPA:** Both sensitivity and specificity of HS increased. The pooled sensitivity of CT Halo for IPA was 0.541 (95% CI: 0.397, 0.679); pooled specificity was 0.922 (95% CI: 0.731, 0.981) and OR (7.469, 95% CI: 2.218, 25.158).

**Neutropenic Patients:** The specificity increased to 0.939 (95% CI: 0.701, 0.990) in studies of neutropenic patients with IPA, without any change in sensitivity (0.561; 95% CI: 0.386, 0.722). The OR improved to 10.257 (95% CI: 2.381, 44.182).

**Neutropenic Patients with Antibiotic Resistant Fever:** There was a marginal increase in sensitivity (0.5918, 95% CI: 0.3541, 0.7932) without much change in the specificity (0.9374, 95% CI: 0.6595, 0.9914). OR

increased to 12.356 (95% CI: 2.249, 67.889).

**Differentiation Between IPA and Mucormycosis:** 6 studies were analysed to assess the ability of HS to differentiate IPA and Mucor (7–11,16) A 2x2 table was constructed and Chi-square test was applied. The HS could not reliably differentiate IPA from Mucormycosis (*p* = 0.449).

**Conclusion:** In immunosuppressed conditions the most frequent cause is invasive fungal infections (IPA being most common). In view of poor sensitivity (50%) it cannot be used as a screening test but has good specificity (91%). CT halo sign cannot differentiate between IPA and non-IPA fungal infections in this group.

### [P25] Nebulised Amphotericin B Versus Oral Itraconazole in Pulmonary Aspergilloma: A Parallel Group Randomized Controlled Trial

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**Background:** Pulmonary aspergilloma is a common problem in tuberculosis-endemic countries where the fungus colonizes the post-tubercular cavities resulting in myriad symptoms. While the definitive therapy is considered to be surgical, treatment with oral anti-fungals is often used as a temporizing measure as access to surgery may be delayed due to long waiting period, scarcity of trained personnel or inoperability of some patients due to poor lung function. In this trial, the effectiveness of daily oral itraconazole for 6 months was compared with nebulised amphotericin B given for a week. Here we present the interim analysis at 1 month of therapy.

#### Methodology:

**Hypothesis:** Nebulised amphotericin B given for treatment of pulmonary aspergilloma, as assessed by clinical resolution and radiological parameters, is non-inferior to daily oral itraconazole given for 6 months.

#### Objectives:

- 1) To compare the effectiveness of nebulised amphotericin B given for 7 days versus oral itraconazole given for 6 months, in reducing symptoms and size of the fungal ball at 1 and 6 months of therapy.
- 2) To compare the side-effects observed in patients receiving nebulised amphotericin B and oral itraconazole.

**Study design and duration:** It was a parallel group randomized controlled trial (RCT) with a non-inferiority design conducted over 2 years. It was registered in Clinical Trial Registry India (reference number CTRI2018/11/016266)

**Sample size:** The calculated sample size was 26, i.e. 13 in each arm.

#### Inclusion criteria:

- Patients having pulmonary aspergilloma on CT thorax with symptoms attributed to the fungal ball.
- Age more than 18 years.
- Patients not having concomitant respiratory infections like tuberculosis.

#### Exclusion criteria

- Patients having known hypersensitivity to azoles or amphotericin B.
- Patients not giving consent for receiving nebulised therapy or prolonged oral therapy.

**Results:** The two groups were age and sex matched and the mean age was 43±12 years with 92% being males. The most common symptoms were hemoptysis (96%), cough (85%) and weight loss (12%). The mean size of the fungal ball was 1.5 ± .4 cm in the largest axis with 90% located in the upper lobe. Fungal culture of bronchoalveolar lavage was positive most commonly for *Aspergillus fumigatus* (19%). At 1 month, there was no difference in clinical resolution and radiological parameters between



the itraconazole and amphotericin B arm. However, the amphotericin B treatment was more cost effective as it's cost was 6 times less than the itraconazole arm. There was no significant difference in the incidence of side-effects in the two arms. The most common side effect in the itraconazole group was gastric intolerance while it was cough in the amphotericin B group.

**Conclusion:** In patients with pulmonary aspergilloma, nebulised amphotericin B given is non-inferior to oral itraconazole in terms of clinical resolution and radiological parameters. Both the therapies were well tolerated but amphotericin B was more cost-effective.

## [P26] Potential New Biomarkers for Idiopathic Pulmonary Fibrosis

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This study was conducted to estimate oxidative stress status, inflammation markers - C reactive protein (CRP), serum amyloid A1 (SAA1), soluble programmed cell death-ligand 1 (sPD-L1) and also vitamin D and lipid status in idiopathic pulmonary fibrosis (IPF) patients, and to evaluate them as potential predictive and/or prognostic biomarkers for this disease. It was done in 30 IPF patients and 30 matched healthy controls (CG).

Our study found IPF patients upon an advanced oxidative stress compared to CG, evidenced by significantly higher level of advanced oxidation protein products (AOPP 54.7 vs. 34.2  $\mu\text{mol/L}$ ,  $P < 0.001$ ), pro-oxidant-antioxidant balance (PAB 131 vs. 75 U/L,  $P < 0.05$ ) and total oxidative status (TOS 21.4 vs. 7.4,  $P < 0.001$ ). IPF patients had decreased level of antioxidative potency, reflected by the significantly decreased total antioxidant status (TAS 1512 vs. 443  $\mu\text{mol/L}$ ,  $P < 0.01$ ) and total sulfhydryl groups (0.526 vs. 0.295 mmol/L,  $P < 0.01$ ). Paraoxonase 1 (PON1) was decreased, and malondialdehyde (MDA) and superoxide anion levels were increased in patients with more severe disease (stage II vs. I,  $P < 0.05$  for all). We found significant negative correlation between PON1 activity and O<sub>2</sub>-concentration (Spearman's  $\rho = -0.900$ ,  $P < 0.05$ ). Ischemia modified albumin was also significantly higher in patients with IPF than in CG. Concentration of 25 OH vitamin D in IPF patients was in the area of severe deficient values (11 nmol/L). We also found significantly increased CRP (10.8 vs. 0.5 mg/L,  $P < 0.01$ ) and SAA1 proteins in IPF patients (8.2 vs 3.72 mg/L,  $p < 0.05$ ), which are a positive reactants of the acute phase response. Our study found that concentrations of sPD-L1 in the serum were elevated in IPF patients and significantly higher compared with CG (297.5 ng/L vs. 89.9 ng/L).

Based on these results, we might suppose that IPF patients were in a state of a profound oxidative stress, which is, at least in part, the consequence of the inflammatory component of the IPF disease. sPD-L1 may have significant role in immune responses and prediction not only in tumours, but in IPF and other autoimmune disorders as well. It may be speculated that sPD-L1 should be evaluated as new prognostic or/and predictive biomarkers to aid potential treatment strategies including immunotherapy in the variety of diseases.

## [P27] Influence of Basic Treatment on the Exacerbation Rate and Medication Adherence in Patients with Bronchiectasis

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**Objective:** To evaluate the influence of basic treatment on the exacerbation rate, to evaluate the adherence to basic treatment and its association with exacerbations rate in patients with bronchiectasis.

**Material and Methods:** Patients with bronchiectasis who did not receive any basic treatment were enrolled into the analysis. Diagnosis of bronchiectasis was confirmed by HRCT. The number of exacerbations per year was calculated according to medical documentation. After that, basic treatment was prescribed to every patient. During the next year all exacerbations were recorded. To evaluate adherence to basic treatment, the *eight-item* Morisky Medication Adherence Scale (MMAS-8) was used.

**Results:** 18 patients (13 (72%) women) were selected for the investigation. Median age of patients was 48.05 years. Average number of exacerbations before basic treatment prescribing = 2.72 ( $\pm 2.01$ ). After one year of treatment average number of exacerbations significantly decreased (1.61 ( $\pm 1.33$ ),  $p = 0.009$ ). Average medication adherence was 5.16 ( $\pm 2.06$ ).

We analyzed association between the number of exacerbations per year in patients and their medication adherence. Correlation between adherence and exacerbation rate before treatment is moderate ( $r = 0.33$ ,  $p = 0.17$ ). And correlation between adherence and exacerbation rate after therapy prescribing is weak ( $r = 0.06$ ,  $p = 0.79$ ).

In accordance with number of exacerbations during previous year we divided patients into two groups. The first group – patients who had 0–1 exacerbation; second group – patients with 2 or more exacerbations. Average medication adherence was 4.16 ( $\pm 0.75$ ) in the first group and 5.66 ( $\pm 2.34$ ) in the second group ( $p = 0.07$ ). Average number of exacerbations in the first group before basic treatment prescribing was 0.66 ( $\pm 0.51$ ) and after treatment – 0.33 ( $\pm 0.51$ ),  $p = 0.47$ . Average number of exacerbations in the second group before basic treatment prescribing was 3.75 ( $\pm 1.76$ ); after basic treatment prescribing – 2.25 ( $\pm 1.14$ ),  $p = 0.02$ . There is no any correlation between medication adherence and exacerbation rate before and after one year of basic treatment prescription ( $p > 0.05$ ).

**Conclusion:** Basic treatment significantly reduces the rate of exacerbations in patients with bronchiectasis, in particular in patients with frequent exacerbations. Although statistic association between patient medication adherence and the number of exacerbation is low, doctors have to convince patients of importance of basic treatment.

## [P28] Second Generation hCFTR mRNA as an Effective Supplementation Therapy for Cystic Fibrosis

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The advancement in the field of *in vitro* transcribed mRNA and nano-carriers have made mRNA-based therapies suitable candidates for diseases associated with defective or deficient functional protein. Our group with others recently published that sequence engineering (SE) of mRNA can lead to better efficiency and lower immunogenicity of mRNA<sup>1</sup>. Cystic Fibrosis is a rare multiorgan, multifactorial, genetic disease with impaired respiratory

function and recurrent pneumonia being the main cause of mortality<sup>2</sup>. Our group previously presented expression of functional CFTR and strong improvement of lung function parameters including Forced Expired Volume (FEV in 0.1 sec for small rodents) in a CF knockout mouse model by delivering chemically modified hCFTR mRNA ((c)mRNA<sup>hCFTR</sup>)<sup>3</sup>.

Based on these findings a sequence engineered hCFTR template was cloned into pVAX. A120 for IVT mRNA production. Integrity of SE-mRNA<sup>hCFTR</sup> was analyzed using Agilent Bioanalyzer 2100 and expression of CFTR protein in CFBE41o- cells in 3D cultures was tested by flow cytometry using CF specific antibodies. Ability of SE-mRNA<sup>hCFTR</sup> to produce functional CFTR protein was shown by YFP assay<sup>3</sup>. For *in vivo* functionality, a CF knockout mouse model was utilized. Multiple doses of SE-mRNA<sup>hCFTR</sup> were administered via intravenous (i.v.) and intratracheal (i.t.) routes followed by measuring lung mechanics. Various body fluids such as saliva, bronchoalveolar lavage fluid (BALF), serum and organs (lungs) were collected to check for salivary chloride concentration, immunogenicity and CFTR protein level.

Transfection of CFBE41o- cells in 3D cultures with SE-mRNA<sup>hCFTR</sup> resulted in over 30 percent hCFTR positive cells. YFP assay confirmed significant functional protein expression ( $P \leq 0.01$ ). Multiple doses of SE-mRNA<sup>hCFTR</sup> in CF knockout mice improved FEV<sub>0.1</sub> up to 96% of wild type mouse value. The Chloride concentration in saliva reduced significantly ( $P \leq 0.01$ ) compared to the concentration in the saliva of untreated mice. Chemokine levels related to mRNA response (IL-12, IL-6, IFN- $\alpha$  and TNF- $\alpha$ ) remained low even after multiple doses of SE-mRNA<sup>hCFTR</sup>. The reduced immunogenicity and improved efficacy indicate the potential of sequence engineered mRNA for therapeutic applications. This emphasizes the value of mRNA-based therapy, bringing us a step closer to treating Cystic Fibrosis.

**Conflict of Interest:** M.S.D.K. holds a patent on RNA modification (EP2459231B1). M.S.D.K. and AKM A.H. hold a European patent on delivery of cmRNA<sup>hCFTR</sup> complexed with nanoparticles (17169561.2-1401).

## [P29] Diagnosis of Tuberculosis (TB) Through an Electronic Nose

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**Background/Aims:** One third of TB suspects has difficulty to collect an adequate quality sputum sample. Therefore, a non-sputum based test would be a tremendous asset. Due to infections, the host metabolism changes and produces distinct volatile organic compounds (VOCs). In addition, *Mycobacterium tuberculosis* (MTB) also produces several VOCs. These VOCs can be detected from the breath. Breath tests have several advantages, which are non-invasive, potentially point-of-care, easy-to-perform, fast, and convenient. A gas chromatography combined with mass spectrometry (GC/MS) was used to analyse specific VOCs in breath specimens, but it requires complex equipment, operation skills, and a well-conditioned environment; moreover, different studies report different VOCs. The electronic-nose has an array of sensors that identifies a pattern of VOCs without considering the specific composition of VOCs. We investigated the potency of a hand-held electronic-nose to diagnose pulmonary tuberculosis (PTB) among those suspected of PTB. We also measured the time needed to generate the results of breath test. To our knowledge, this is the first study testing the electronic-nose to diagnose PTB among patients with suspected TB.

**Methods:** We recruited patients with suspected PTB and healthy controls in Yogyakarta, Indonesia. The participants breathed through an electronic nose for 5 minutes. Patients with suspected PTB were classified into active PTB, probably active PTB, probably no PTB, and no

PTB based on sputum-smear-microscopy, culture, chest-radiography, and follow-up for 1.5–2.5 years. After building a breath model based on active PTB, no PTB, and healthy controls (Calibration phase), we validated the model in all patients with suspected PTB (Validation phase). We evaluated several variables that may associate with the breath prints, which were age, sex, body mass index, co-morbidities, smoking status, use of antibiotics, consumption of alcohol, flu symptoms, stress, food and drink intake. In each variable, one stratum's Receiver Operating Characteristic (ROC)-curve indicating sensitivity and specificity of the breath test was compared with another stratum's ROC-curve. An association between the variable and sensitivity - specificity of the breath test was shown by differences between Area-under-the-Curve between strata ( $p < 0.05$ ). Statistical analysis was performed using STATA (version 15 SE; Stata Corporation, College Station, TX, USA).

**Results:** We enrolled 400 participants; 73 were excluded due to extra-pulmonary TB, incomplete data, previous TB, and cancer. Calibration phase involved 182 subjects, and Validation phase involved 287 subjects. Sensitivity was 85% (95%CI: 75–92%) and specificity was 55% (95%CI: 44–65%) in calibration phase. In validation phase, sensitivity was 78% (95%CI: 70–85%), and specificity was 42% (95%CI: 34–50%). The test was significantly less sensitive and specific for men than for women. The analysis time with electronic-nose took approximately two weeks as the data needed to be sent to the device producer.

**Conclusions:** Among patients with suspected TB, the electronic-nose showed modest sensitivity and low specificity. To improve the sensitivity, a larger calibration group needs to be involved. To give real-time measurements, the pattern recognition technique algorithm should be fully trained. With its portable form, the electronic-nose could be used for TB screening in remote rural areas.

**Conflict of Interest:** A.S. and T.S.W. report grant from the e-Nose company (support to conduct a study with the equipment of this company).

## [P30] Non Cystic Fibrosis Bronchiectasis: Results of Bronchiectasis Severity Index and Quality of Life in an Indian population

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**Introduction:** The Bronchiectasis Severity Index (BSI) uses a combination of clinical, radiological and microbiological features and is a strong predictor of morbidity and mortality for patients with non-CF bronchiectasis. There is extreme paucity of data from the Indian subcontinent regarding the utility of BSI and its association with various aspects of bronchiectasis. Our study is a first ever attempt to look at the utility of BSI in an Indian cohort.

**Aims and Objectives:** To assess the association of Bronchiectasis Severity Index with various aspects (i.e., aetiology, Quality of Life, etc.) in patients with non CF Bronchiectasis in an Indian Population.

**Materials and Methods:** This was a prospective analytical study comprising of consenting adult patients with non-cystic fibrosis bronchiectasis, diagnosed on a CT scan of thorax, attending the outpatient department of a tertiary care hospital. These patients were subjected to a pre-set questionnaire and BSI was calculated for these patients. Data was recorded and submitted for multivariate analysis. QoL data was collected using QOL-B questionnaire.

**Results:** A total of 173 patients were recruited in the study and 71 (41%) had post infective bronchiectasis, 56 (33%) post tubercular and 15 (8.67%) had idiopathic bronchiectasis. 45 (26%) patients had Mild BSI (1–4), 81 (47%) had moderate (5–9) and 47 (27%) had severe BSI (9–12). Aetiology wise distribution of BSI is as follows:

AETIOLOGY	MILD BSI (n=45)		MODERATE BSI (n=81)		SEVERE BSI (n=47)	
	No.	%	No.	%	No.	%
Post Infective	12	26.67%	35	43.21%	24	51.06%
Post Tuberculosis	20	44.44%	22	27.16%	14	29.79%
Idiopathic	4	8.89%	10	12.35%	1	2.13%
COPD/Asthma/ ABPA	8	17.78%	9	11.11%	6	12.77%
Others	1	2.22%	5	6.17%	2	4.26%

Mean BSI in patients with Post infective aetiology was 7.66, 6.25 in post tubercular bronchiectasis and 5.87 in idiopathic bronchiectasis. While prior history of exacerbations showed significant correlation with BSI score, interestingly, no significant correlation was seen between BSI and FEV1 ( $p=0.144$ ). Quality of life data was collected for 21 patients and a significant negative correlation was observed between severity of BSI and QoL vitality ( $p=0.03711$ ), QoL emotional ( $p=0.03711$ ) and QoL treatment burden scores ( $p=0.035$ ).

**Conclusion:** This is a first ever attempt in an Indian population to look at Bronchiectasis severity Index and to determine the severity according to different aetiologies. In our cohort, post infective bronchiectasis was seen as the most common aetiology of bronchiectasis. At the same time, this group of patients tend to have more severe bronchiectasis, as observed by higher mean BSI in this group. Our study gives a detailed insight of severity of bronchiectasis in an Indian population and an attempt shall be made to further validate the score in our population. There are certain aspects of BSI that correlate well with the severity of bronchiectasis while some, such as FEV1 don't. It would be essential to re look at the index in our population with a larger cohort and studies like EMBARC India registry shall be prudent in coming to a conclusion. QoL was seen to correlate well with severity of bronchiectasis, however, a larger population is needed to study the quality of life and disease burden in Non Cystic Fibrosis Bronchiectasis patients in the Indian population.

### [P31] Familial Pulmonary Alveolar Microlithiasis: A Case Series with an Emphasis on Management of PAM

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**Introduction:** Limited data exists regarding the burden and management of rare diseases like pulmonary alveolar microlithiasis (PAM) from developing countries. PAM is an orphan disease and few reports of familial PAM exist around the world. Improved access to lung transplantation in India in recent times has proved to be an advantage in the management of these patients.

**Methods:** We present a case series of Pulmonary Alveolar Microlithiasis, affecting two siblings in a family with the elder sibling ending up with bilateral lung transplantation and the younger sibling diagnosed as a part of familial screening.

**Cases:** Our first patient is a 25-year-old male presenting with recurrent spontaneous pneumothorax. Over 2 years of follow up, he became progressively dyspnoeic and oxygen dependent. The patient underwent bilateral lung transplantation and has returned to pre-disease lifestyle with no complications till recent follow up at 10 months post transplantation. The second patient is a sibling of the patient and is likely suffering from a less severe genetic variant of PAM. She has radiological features suggestive of PAM and is asymptomatic with mild restriction on spirometry and is currently under follow up. We plan to list her for transplant if she deteriorates clinically.

**Conclusion:** Our cases exhibit the heterogeneity in presentation and clinical course along with a familial predisposition of PAM in our population. It should also be emphasized that increased awareness and early referral to lung transplantation in presence of recurrent infections and pneumothorax is definitely lifesaving. Familial screening and family planning in these individuals should also be stressed upon in such cases.

### [P32] Utility of BAL Galactomannan Testing: A Prospective Analytical Study

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**Introduction:** Galactomannan (GM) is a component of Aspergillus cell wall. The usefulness of GM levels in body fluids is still unclear. We evaluated the utility of Bronchoalveolar Lavage (BAL) GM testing in patients with suspected pulmonary Aspergillosis.

**Aims and Objectives:** To assess the utility of BAL Galactomannan assay in diagnosis of pulmonary Aspergillus infections.

**Methods:** 90 consecutive patients with suspicion of pulmonary Aspergillosis, based on pre-defined clinic-radiological parameters, were included in our study. BAL samples obtained via fibre optic bronchoscopy were tested for routine microbiology and Galactomannan (GM). Data was collected and multivariate analysis done.

**Results:** 50 patients (55.56%) were found to have BAL GM >0.8, a cut off considered as positive. 13 samples were fungal smear/fungal culture positive for Aspergillus spp. and BAL GM was positive in 11 of these samples (84.62%;  $p=0.04794$ ) with a mean GM of 1.65. 39 patients with negative fungal smear/culture but BAL GM positive (mean GM=0.97) were also prescribed systemic anti-fungal drugs and clinico-radiological improvement was seen in these patients. BAL GM was positive in 18 of 20 patients with bronchiectasis (90%;  $p=0.0011$ ) and in up to 65% patients with asthma or COPD. Smoking history or biomass fuel exposure also showed a trend towards positivity with BAL GM value.

**Conclusion:** In patients with suspicion of pulmonary Aspergillosis, BAL galactomannan level was found to be a better marker than fungal smear/culture. While microbiological and histopathological evidences are gold standard to diagnose fungal infections, our study shows that in patients with negative fungal smear or culture, BAL Galactomannan can be conclusive for diagnosis.

### [P33] H1N1 influenza: Changing Patterns Since the First Pandemic

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**Introduction:** In 2018–19, a substantial number of patients were affected by H1N1 influenza in Eastern India. We intend to present the clinico-radiological features of the 2019 epidemic.

**Methodology:** 45 consecutive patients suspected to have H1N1 viral influenza based on clinico-radiological findings were recruited in the study. Throat swab samples were collected and tested H1N1 PCR. The patients were divided into 2 groups based on H1N1 positivity. Clinico-radiological & laboratory parameters were collected and submitted for analysis.

**Results:** 19 patients were tested H1N1 positive in this cohort of patients. These patients were significantly younger (mean age: 46.7 years) as compared to their H1N1 negative counterparts (mean age: 56.5;  $p=0.04$ ). H1N1 positive patients sought health services earlier, at mean 4.84 days after the onset of symptoms, as compared to 8.8 days in H1N1 negative group ( $p=0.004$ ) and also had shorter hospital stay. Fewer patients had co-morbidities in the positive group (57.8% vs 76.9%), with underlying chronic lung condition being the most common co-morbidity in both the

groups. Respiratory failure, requiring ventilation support, was less common in H1N1 positive group (36.8%) with 2 deaths occurring in this group. Consolidation and ground glass appearance were the most common radiological findings but these findings were similar in the two groups.

**Conclusions:** Our study shows that in the 2018–19 influenza epidemic in the Indian subcontinent, younger patients with fewer co-morbidities were more affected. These patients presented to health services earlier and tend to have a shorter hospital stay. Younger age of affection might encourage physicians to consider vaccination, as opposed to the age of 50 years as suggested by current guidelines.

### [P34] Development in $p\text{CO}_2$ Over 12 Months in Chronic Hypercapnic Patients Treated with High Flow Nasal Cannula- Post Hoc Analysis From a Randomized Controlled Trial



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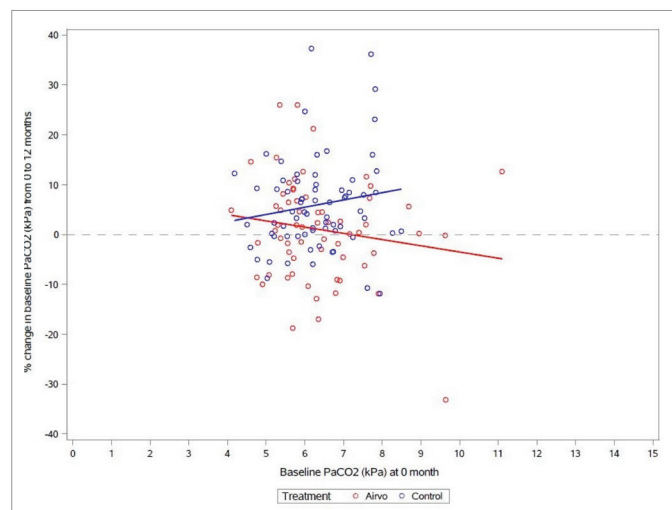
**Background:** There is increasing evidence that high flow nasal cannula (HFNC) in chronic hypoxic patients. For patients with stable hypercapnia with  $p\text{CO}_2 > 7.0$  kPa treatment with long term non-invasive ventilation (LT-NIV) is recommended.

**Aim:** To investigate development in  $p\text{CO}_2$  levels in patients with chronic hypoxic and hypercapnic failure in patients treated with HFNC and controls over a 12-month period.

**Methods:** In a post hoc analysis of a prospective randomized controlled trial of chronic hypoxic patients in long term oxygen treatment, half of the included patients randomized to HFNC, patients with stable hypercapnia defined as  $p\text{CO}_2 > 6.0$  kPa were identified and included. Patients were compared at baseline with paired t-test. Change in  $p\text{CO}_2$  was investigated with comparison of means.

**Results:**  $p\text{CO}_2$  was  $> 6.0$  kPa in 53 patients treated with HFNC and 63 controls. Of those 31 HFNC patients and 43 controls remained in study for 12 months and were included. HFNC was used a mean of 6.9 hours/day. HFNC treated had a mean  $p\text{CO}_2$  of 7.3 kPa, controls 7.2 kPa at baseline ( $p=0.71$ ) also comparable concerning age, sex, BMI, exacerbations one-year pre study, FEV<sub>1</sub> and number of active smokers, differing in MRC-score ( $p=0.04$ ). Per cent changes in  $p\text{CO}_2$  per patient is

**Figure 1: Per cent change in  $p\text{CO}_2$  from baseline to 12 months in the individual patients, treated with HFNC (Airvo) and controls**



demonstrated in Figure 1. In average HFNC treated patients decreased  $p\text{CO}_2$  with 1.3%, controls increased 7.0% ( $p=0.004$ ).

**Conclusion:**  $p\text{CO}_2$  decreased in hypercapnic HFNC treated patients with mean  $p\text{CO}_2$ -levels within recommendations for LT-NIV, development of means significantly different from controls.

### [P35] Modifiable and Non-Modifiable Predictors of Frequent Exacerbations in Adults with Non-Cystic Fibrosis Bronchiectasis

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**Background:** Exacerbations of Bronchiectasis (B) are associated with accelerated lung function decline and deterioration in quality of life, management which imposes a significant economic burden on the healthcare system.

**Aim:** The aim of the study was to determine modifiable and non-modifiable predictors of B exacerbations.

**Materials and Methods:** 47 patients with B in stable phase were divided into two groups due to the number of exacerbations per previous year: G1 —  $\geq 3$  exacerbations per year ( $n=24$ ) and G2 —  $< 3$  exacerbations per year ( $n=23$ ). Body mass index (BMI) was calculated by the conventional formula. Duration of the disease from the moment the diagnosis is confirmed and frequency of exacerbations during the previous year were detected in medical source documentation. Smoking status was self-reported. Dyspnea was assessed using Modified Medical Research Council Dyspnea Scale. Microbiological detection of sputum samples were conducted by conventional bacteriological methods. Respiratory function was measured by computed spirometry. The number of lung lobes involved was calculated by analysis of high resolution computed tomography. Methods of descriptive, parametric and non-parametric statistics were used to process the results.

**Results: Non-modifiable factors:** median age in G1 — 58 (42.5;64.5) years, in G2 — 44 (36;62) years,  $p=0.2$ ; quantity of males in G1 — 6 (25%), in G2 — 6 (26.1%),  $p=0.39$ ; median confirmed disease duration in G1 — 6 (0.37;12.5) years, in G2 — 0.42 (0.08;2) years,  $p=0.01$ ; median quantity of involved lobes in G1 — 3 (2;3.5), in G2 — 2 (1;3),  $p=0.054$ .

**Modifiable factors:** Mean BMI in G1 — 25.7 (4.8)  $\text{kg}/\text{m}^2$ , in G2 — 22.9 (3.6)  $\text{kg}/\text{m}^2$ ,  $p=0.03$ ; quantity of patients with BMI  $< 18.5$   $\text{kg}/\text{m}^2$  in G1 — 3 (12.5%), in G2 — 2 (8.7%),  $p=0.08$ ; quantity of patients with BMI  $\geq 25$   $\text{kg}/\text{m}^2$  in G1 — 16 (66.7%), in G2 — 5 (21.7%),  $p=0.01$ ; quantity of never smoked patients in G1—20 (83.3%), in G2 — 16 (69.6%),  $p=0.88$ ; median mMRC scores in G1 — 1 (1;2), in G2—1 (1;1),  $p=0.01$ ; median  $\text{SpO}_2$  in G1 — 95 (94;96)%, in G2 — 96 (96;97)%,  $p=0.01$ ; mean FEV<sub>1</sub> predicted in G1 — 72 (30.1)%, in G2 — 91.7 (22.4)%,  $p=0.0003$ ; number of patients with *Pseudomonas aeruginosa* sputum colonization in G1 — 7 (29.2%), in G2 — 4 (17.4%),  $p=0.914$ ; number of patients with sputum colonisation with other organisms in G1—10 (41.7%), in G2—10 (43.5%),  $p=0.269$ .

**Conclusions:**

1. Disease duration was confirmed as significant non-modifiable factor affecting frequency of exacerbations, in turn, age, sex and quantity of involved lobes did not show a statistically significant effect on the number of exacerbations.
2. We found out that overweight even more than underweight can be an independent predictor of more frequent exacerbations in patients with B. The presence of signs of airway obstruction, a decrease in blood oxygen saturation and shortness of breath are also modifiable factors leading to more frequent exacerbations. In turn, smoking and

colonization of sputum by bacteria did not show a direct statistically significant effect on the number of exacerbations.

- Based on the results obtained, we can assume the need for diagnosis and correction of airway obstruction, determination of the effectiveness of oxygen therapy, as well as normalization of body weight in all patients with B.

### [P36] Factors Influencing Preferences for Medical Decision-Making in Asian COPD Patients

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**Introduction:** Chronic Obstructive Pulmonary Disease (COPD) is a chronic lung disease with high burden of care and has been identified as a healthcare priority in Singapore. Because of the potential for imminent deterioration, patients are often confronted with complex decisions such as mechanical ventilation or Intensive Care Unit care, where the trade-offs are unclear. There are uncertainties about the prognosis, interplay of personal emotions, and opinions from caregivers who themselves are struggling with the diagnosis. Without awareness of the common struggles and priorities of a COPD patient, it is not possible to provide patient-centered care and empower them in medical decision-making. Data to support a framework for such conversations is limited in an Asian context. To fill this gap in medical literature, we conducted a qualitative study on how COPD patients in Singapore make decisions about medical care, exploring (1) health literacy, (2) lifestyle impacts of COPD, (3) patient's values and coping strategies, and (4) consideration factors in medical decision-making.

**Methods:** Semi-structured interviews were conducted on COPD patients from both inpatient and outpatient settings in Singapore General Hospital from July–December 2019. Patients were recruited, with accompanying caregivers, if they had a confirmed diagnosis of COPD (FEV1/FVC<70%). Patients were excluded if they have other active functional status limiting medical conditions. Interviews were audio-recorded and transcribed verbatim in the natural language. Transcripts were coded by two independent members of the research team. Themes were qualitatively extracted using NVivo. Demographic and clinical data were retrieved from the electronic patient records.

**Results:** Data collection is ongoing and will continue until data saturation. Our preliminary data of 12 male patients (Median age=72±12; 83% Chinese, 8% Malay, 8% Indian; Disease severity: 9% Gold A, 8% Gold B, 8% Gold C, 75% Gold D) revealed low health literacy despite receiving COPD specialist services and COPD patient education counselling by a nurse-clinician. COPD symptoms resulted in inability to perform activities of daily living (ADLs), work and hobbies, negative mood, and frequent hospital admissions. Patients learned to cope by accepting death as unavoidable, having realistic expectations about their health, positive thinking, counting their blessings, practicing self-care, and avoiding negative thinking. Other common coping strategies included relying on medications, seeking medical attention early, physiotherapy, smoking cessation and taking rest breaks.

Finance, function, relationships and work were important to patients. When patients make medical decisions, they commonly considered family, the impending death, ADL function, financial burdens, trust in healthcare providers, age and religion. Common treatment goals were to get well, avoid suffering and retain ADL function. Treatment preferences included accepting all treatments, denying specific interventions or letting their family decide. Many patients refused to discuss treatment preferences with family in advance for fear of burdening them. Discomfort from disease, inability to anticipate the future and lack of control over treatment outcomes dissuaded patients from planning for

future medical care.

**Conclusion:** COPD patients face disease-specific impacts, and have developed coping strategies and mindsets aligned with their personal values. These guide treatment goals and preferences. The issues brought up can be used to frame physician's discussions with patients and to design tools to facilitate medical decision-making.

### [P37] Alteration of Serum Potassium Levels in Patients of Acute Bronchial Asthma on Sequential Nebulized Salbutamol Therapy

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**Background:** Nebulized Salbutamol is the mainstay in the management of Acute bronchial asthma. Nebulized Salbutamol is known to cause decrease in Serum Potassium Level which has metabolic and cardiac consequences.

**Objective:** To assess serum potassium level in the patients on sequential nebulized salbutamol therapy and its cardiac effect.

**Method:** The study includes 30 patients of acute bronchial asthma. Out of total 30 patients, 17 were of 10–20 years of age, 7 of 21–30 years and 6 of 31–40 years. The mean age of the patients (n=30) was 22.43 years 14 patients were male and 16 female. Out of 16 females, 68.75% patients were of 10–20 years of age group. All the patients were treated with 4 doses of nebulized salbutamol (2.5 mg per dose). There was a progressive improvement in the disease. There was a progressive decrease in serum potassium (K<sup>+</sup>) level and the decrease became significant at 4 hrs in all the patients. In 10–20 years age group the K<sup>+</sup> decreased from basal 4.30±0.07 mEq/L to 4.02±0.07 mEq/L at 4 hrs (p less than 0.05), 3.84±0.07 mEq/L at 8 hrs (p less than 0.001) and 3.62±0.06 mEq/L at 12 hrs (p less than 0.001). In 21–30 years age group, it decreased from basal 4.62±0.09 mEq/L to 4.30±0.06 mEq/L 8 hrs (p less than 0.01). Similarly 31–40 years age group showed a decrease from 4.51±0.15 mEq/L at zero hr to 3.67±0.14 mEq/L at 12 hrs (p less than 0.01). No cardiac adverse effect was detected in the study.

**Conclusion:** The nebulized salbutamol produces a significant fall in the Potassium Concentration which has the potential for cardiac adverse effects. In our study, we have not found any cardiac adverse effect, in spite of the significant decrease in K<sup>+</sup> level.

### [P38] Utility of Intrapleural Streptokinase in the Management of Different Etiologies of Loculated Pleural Effusion

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**Background:** Intra-pleural instillation of fibrinolytic agents (Streptokinase) is being increasingly used for management of loculated pleural effusions and empyema thoracis. It resolves fibrin strands of loculated Pleural Fluids by converting the intrinsic plasminogen to its active plasmin form thus lysing the fibrin strands.

**Objective:** The present study was carried out to describe the role of streptokinase on outcome of patients with pleural fluids with multiple loculations having different etiologies.

**Methods:** The study includes 20 patients of pleural fluids, of which 10 patients were suggestive of tubercular effusion. 6 patients were Para pneumonic effusions and 4 patients were of proven malignant pleural effusion. All the patients had multiple loculations. ICTD done in all the patients before instillation of Streptokinase. All had pleural fluid pH < 7.2, as observed by gas analysis, high LDH and sugar < 60 mg/dl. 2.5 lakhs units of streptokinase dissolved in 100 ml normal saline was injected intrapleurally for three successive days via ICTD and Tube was clamped

for 6 hours post instillation.

**Results:** In all the patients of loculated tubercular and complicated parapneumonic effusion showed rapid resolution of loculation as evidenced by decrease in number of loculations on USG and CXR showed a favorable expansion with rapid increase in amount of drain in next few days of streptokinase.

The instillation of streptokinase was not so successful in loculated hemorrhagic malignant pleural effusion.

**Conclusion:** In the present study the best result were observed in loculated tubercular pleural fluid followed by loculated parapneumonic effusions. Loculated malignant pleural effusions have least response.

### [P39] Perception of Non-Tuberculous Mycobacterial Lung Disease Among Italian Pulmonologists

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**Introduction:** Non-tuberculous mycobacteria (NTM) can cause progressive inflammatory lung damage, a condition termed NTM lung disease (NTM-LD). NTM-LD often worsens underlying structural lung disease, impairs quality of life, health care resource utilization and increases mortality. Bronchiectasis is one of the strongest risk factors for development of NTM-LD.

**Rationale:** The objective of this study was to measure current perception of risk of NTM infection, disease severity and understanding of NTM at the molecular level among Italian pulmonologists treating adult non-CF bronchiectasis patients (NCFB).

**Methods:** An online survey with 60 Italian physicians who spend at least 80% of their time in hospital setting and treated at least 10 adult NCFB patients in the previous 12 months was conducted in Jan 2019.

**Results:** 85% of respondents considered adult NCFB patients to be at particular risk of contracting NTM, with 91% believing the risk for NTM infection is greater in patients with NCFB vs. patients with moderate-severe grade COPD. The respondents estimated that on average 23% of patients with NCFB contract NTM over the course of their disease. Patients with NCFB were perceived to have an average risk for contracting NTM, and less risk compared with *Pseudomonas aeruginosa*, *Haemophilus influenzae*, *Streptococcus pneumoniae*, *Staphylococcus aureus*, and *Influenza*. A large majority of respondents (79%) agreed or strongly agreed that NTM-LD when left untreated or inappropriately managed can lead to severe consequences, including progressive worsening of respiratory function, increased morbidity, and more frequent hospitalizations. 10% of physicians did not agree that NTM-LD has a significant impact on mortality risk. 70% and 74% of respondents agreed that NTM can form biofilms within human lung tissue and that the macrophages are an important reservoir of NTM in a host, respectively.

**Conclusion:** The results indicate that Italian pulmonologists treating adult patients with NCFB agree that bronchiectasis is associated with the risk of contracting NTM. The vast majority of respondents perceived that NTM lung disease can lead to severe health consequences, although some physicians do not agree that NTM-LD leads to significant increase in mortality. A majority of respondents were also aware of the biofilm formation by NTM and the role of macrophages as a reservoir for NTM.

### [P40] Comorbidities in Patients with COPD-OSA Overlap Syndrome Compared with Gender-, Age- and BMI- Matched Patients with OSA Alone

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**Introduction:** Patients with chronic obstructive pulmonary (COPD) and obstructive sleep apnea (OSA) usually demonstrate several comorbidities.

**Aim:** The aim of this study was to investigate the prevalence of comorbidities in COPD-OSA overlap syndrome (OS) and patients with OSA alone and to explore potential differences between these two groups.

**Patients-Methods:** Consecutive OS patients (n=165, 138 males, AHI>5/h and FEV<sub>1</sub>/FVC<0.7) and OSA patients (n=165, 139 males, AHI>5/h and FEV<sub>1</sub>/FVC>0.7); matched in terms of gender, age, BMI, and smoking history; diagnosed with polysomnography and pulmonary function testing, were included.

**Results:** As mentioned, the two groups were matched in terms of age (p=0.221), BMI (p=0.496), neck circumference (p=0.922). No difference was observed in ESS values (p=0.988), AHI (p=0.346), ODI (p=0.668) and minimum sleep oxyhaemoglobin saturation (p=0.100). Compared to OSA patients, OS patients had lower average sleep oxyhaemoglobin (p=0.008), higher sleep time with oxygen saturation<90% (p=0.002), lower levels of FEV<sub>1</sub>% (p<0.001), FVC% (p<0.001) and PaO<sub>2</sub> (p<0.001) values. OS was characterized by a higher prevalence of total comorbidities [2 (1–3) vs 2 (1–2), p=0.033] and particularly cardiovascular disease (CVD) i.e. coronary artery disease, heart failure, cerebrovascular and peripheral artery disease (p=0.016) than OSA. No differences were observed in prevalence of arterial hypertension (p=0.571), diabetes mellitus (p=0.27), dyslipidemia (p=0.469), atrial fibrillation (p=0.114), depression (p=0.455), gastroesophageal reflux (p=0.777), osteoporosis (p=0.652), thyroid disease (p=0.345), and hyperuricemia (p=0.521).

**Conclusions:** In OS patients both nocturnal hypoxia and impaired breathing function in awake are more overt, while a higher burden of comorbidities is observed. The latter is attributed to the increased number of CVD in comparison to sex-, age- and BMI-matched patients with OSA.

### [P41] Acute Exacerbation of COPD: Factors Predicting Re-Hospitalization

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**Introduction:** The aim of the study was to develop the prognostic model for prediction of re-hospitalisation due to acute exacerbations of COPD (AE COPD).

**Material and methods:** Retrospective analysis was done for the case-records of patients hospitalized due to AE COPD during three years at the Pulmonology department in the city clinical hospital #6 (Dnipro, Ukraine). The anthropometric parameters, medical history, physical examination data, complaints, chest x-ray, ECG, post-bronchodilator spirometry tests, blood analyses results, oxygen saturation were evaluated. The procedure basing on a probabilistic Bayes method and sequential analysis of Vald was used in order to predict the integrated effect of the parameters on the probability of re-hospitalization due to AE COPD. The study has been approved by institutional ethics committee.

**Results:** 162 case-records were included into the analysis. Diagnostic significance of pre-selected parameters was confirmed to determine the risk of multiple hospitalizations for patients with AE COPD. The obtained data allowed us to identify five major and eight additional criteria of hospital re-admission due to AE COPD. The major criteria included: BMI < 19, diabetes mellitus, blood eosinophilia > 5 %, serum C-reactive protein >

13 mg/l, total protein > 80 g/l. The list of additional criteria included active smoking, a presence of any comorbidity, increased respiratory rate > 20 per minute, the presence of dyspnea, involving of additional muscles in breathing; decline of respiratory function below the critical values (FEV1/FVC < 45% predicted, FEV1 < 45% predicted, FVC < 80% predicted).

**Conclusion:** The presence of at least two major or one major and three additional criteria make the probability of re-hospitalization due to AE COPD significant. The proposed model could be helpful for the practitioners in quick and easy prediction of repeated AE COPD and in the case of high-risk of re-hospitalizations it may be the background for the more aggressive medical intervention.

## [P42] Renal function in patients with chronic obstructive pulmonary disease

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**Introduction:** The involvement of the kidneys in the pathological process in pulmonary diseases to a certain extent depends on the fact that the basement membrane of the capillaries of the renal glomeruli and pulmonary alveoli has a similar antigenic structure, which promotes the formation of antibodies and their cross-reactions, as well as a high sensitivity of the epithelium of the renal tubules to hypoxemia.

Purpose. Investigate the functional state of the kidneys in patients with COPD, depending on the degree of bronchial obstruction.

**Materials and Methods:** 16 patients with COPD, stage II, III, categories B and C (GOLD 2019) aged from 37 to 70 (mean age 57.4 (7.3) years) were examined. Exclusion criteria from the study: congenital anomalies of the kidneys, the presence of pyelonephritis, glomerulonephritis, diabetes mellitus and cancer. The patients were divided into two groups according to the spirogram: group I (n = 9) included patients with FEV1 ≥ 30% and <50%, and group II (n = 7) - patients with FEV1 ≥ 50% and <70%. Albumin and creatinine of urine, albumin creatinine ratio (ACR) in urine, blood creatinine were determined, and glomerular filtration rate (GFR) was calculated. The obtained results were subjected to statistical data processing (STATISTICA 6.1 program) with the determination of mean values (M), standard deviation (SD) or median (Me), upper and lower quartiles ([25% -75%]).

**Results:** Urine albumin in group I patients was 3 [2; 3] mg, in II- 1.6 [0.7; 1.2] mg (p = 0.5), blood creatinine in group I is 90.6 [86.5; 90.3] mg / l, in group II - 94.2 [90.7; 93.2] mg / l (p = 0.1), albumin-creatinine ratio in the urine in group I 1.5 [0.7; 1.25] mg / g, in II - 1.7 [1.5; 1.65] mg / g (p = 0.18), urine creatinine in group I - 1432 [1310; 1411] mg / l, in group II- 1441 [1320; 1421] mg / l, (p = 0.08), GFR in group I-76 [68; 75.5] ml / min, in group II - 86 [81; 81.5] ml / min (p = 0.02).

### Conclusion:

1. In patients with COPD stage II and III, signs of damage to the renal parenchyma with a significant decrease in GFR were found.
2. Reduction of GFR depends on the degree of broncho-obstruction and is found in patients with COPD with a decrease in FEV1 <50%.

## [P43] Simple inactivation of mycobacteria samples for safe transport and laboratory preparation using cobas Microbial Inactivation Solution

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**Background:** As NAATs are increasingly used to diagnose tuberculosis, inactivation of mycobacterium for safe laboratory handling is essential. This study was conducted to determine the mycobacterial inactivation efficacy of the cobas® Microbial Inactivation Solution (MIS).

**Design/methods:** To verify inactivation of *Mycobacterium tuberculosis* (MTB) complex organisms, culture panels of two MTB strains (MTB-H37rv; MTB-CDC268) were prepared at microBIOMix GmbH, UKR. Cultures were grown to ~1E+08 CFU/mL then diluted to test concentrations (5E+07 CFU/mL; 2E+06 CFU/mL) in sterile PBS and shipped to three sites: Institute of Clinical Microbiology and Hygiene (IMHR), Roche Diagnostics (RDI) and Lucerne Cantonal Hospital (LUKS).

At each site, 0.4 mL of sample was inactivated according to manufacturer's instructions and then centrifuged. The bacterial pellet was resuspended in 0.5mL PBS and inoculated into liquid or solid culture and followed for up to 8 weeks post inactivation and inoculation. Negative (PBS buffer) and positive (treated with PBS only) controls were included. Five replicates of samples treated with MIS and two replicates each of the positive and negative controls were included. Liquid cultures were performed at IMHR and RDI. Solid cultures were performed at LUKS. Liquid culture was done using the (MGIT) BACTECTM MGITM-320 Mycobacterial Detection System (Becton Dickinson) and solid culture was done using Lowenstein-Jensen slants.

**Results:** All replicates of MTB cultures of both strains and both concentrations were fully inactivated and showed no culture growth eight weeks post inoculation (Table 1). One culture was not interpretable due to contamination by rapid growing nontuberculosis-mycobacteria.

**Conclusion:** pre-analytic treatment by MIS is effective in reducing MTB infectivity.

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*Author Disclosures:* AK, PL, SGM and DK are Roche employees.

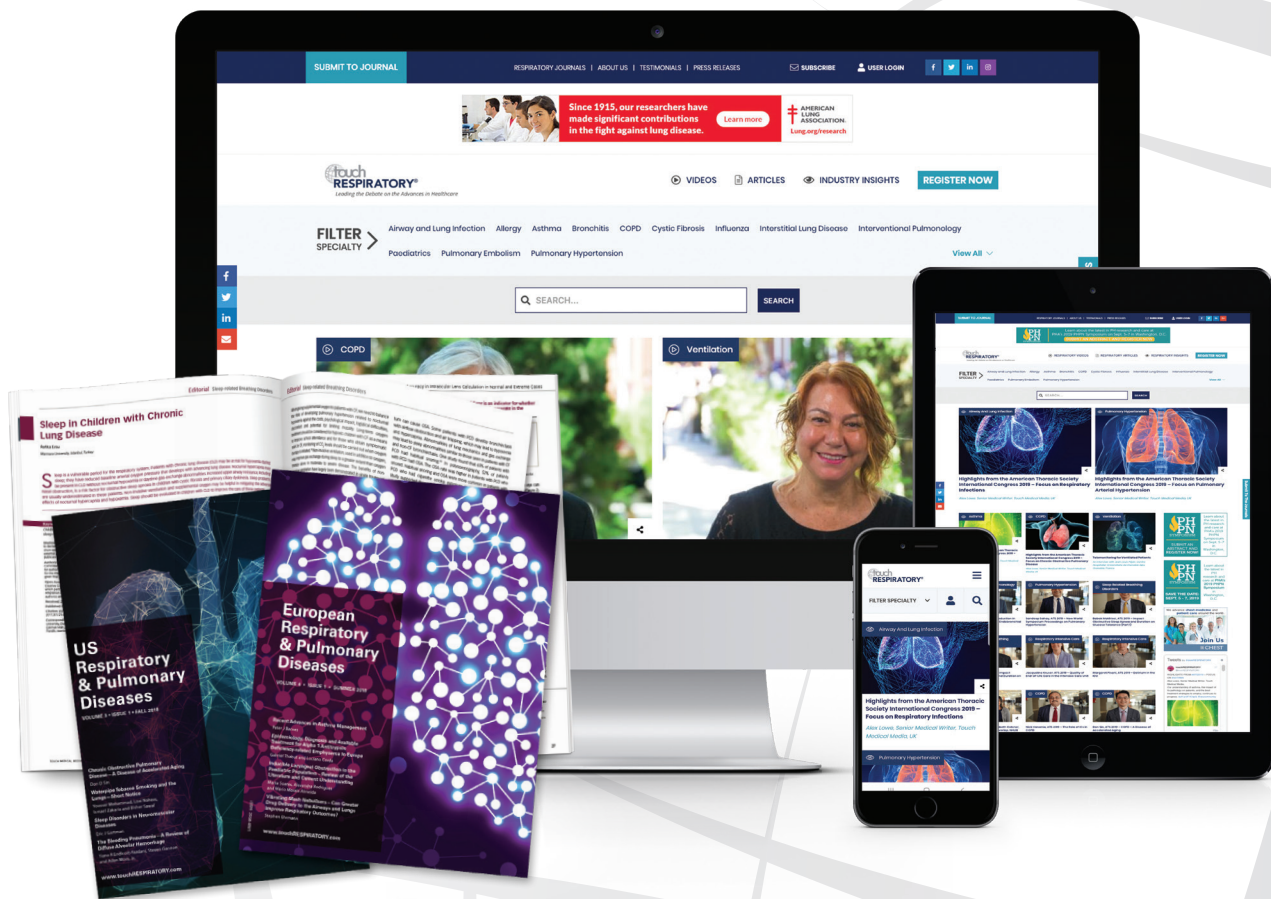
**Table 1**

Culture Isolate	Bacterial Load	Testing Site	Culture Type	Duration of culture (weeks)	Positive Results (%)
MTB (CDC 268)	5E+07 CFU/ml	RDI	Liquid	8	0/15 (0%)
		LUKS	Solid	8	0/15 (0%)
		IMHR	Liquid	8	0/15 (0%)
	2E+06 CFU/ml	RDI	Liquid	8	0/15 (0%)
		LUKS	Solid	8	0/15 (0%)
		IMHR	Liquid	8	0/15 (0%)
MTB (H37rv)		RDI	Liquid	8	0/15 (0%)
		LUKS	Solid	8	0/15 (0%)
		IMHR	Liquid	8	0/15 (0%)
		RDI	Liquid	8	0/15 (0%)
		LUKS	Solid	8	0/15 (0%)
		IMHR	Liquid	8	n/a*

\*Invalidated due to contamination by non-mycobacteria

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