DLC 2025

Dutch Lung Congress

RAI AMSTERDAM | 27 SEPT.

Van der Valk Hotel Utrecht

ABSTRACT BOOKLET

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Welcome to Dutch Lung Congress 2025

We are excited to welcome you to our special DLC 2025, associated with ERS in Amsterdam. This is a special moment to celebrate Dutch Respiratory Science (and collaborations with partners all over the world), as a prelude to the excitement of the coming few days as we see the showcase of respiratory science from across Europe and beyond. We hope you will take this opportunity to interact with colleagues and friends, old and new. This year the format for discussing our science is a little different, reflecting the shorter version of our meeting, but there should still be opportunities to highlight the exciting findings in the room. If you run out of time today for in depth discussions make an appointment to meet each other during the ERS meeting when your science is on display again and continue the discussion there. The excitement of exploring new/challenging concepts, and have robust scientific debates, with a multi-disciplinary group is one of the experiences DLC hopes to engender for all. Everyone here is striving to make DLC a safe, open and inviting environment for all; where everyone can engage with each other, regardless of who they are and where they come from. In our enthusiasm to discuss science, please remember to be respectful of each other's prior experiences and ensure it is a positive interaction for all.

The Dutch Lung Congress endeavours to bring together everyone interested in research related to pulmonary diseases in the Netherlands. We hope you enjoy the program the organizing committee have put together and will engage in dynamic discussions with all the presenters. I thank each and every member of the hard-working committee organizing the Dutch Lung Congress for their efforts that have culminated in the event we can now enjoy. If you cannot get to all the science today we will share a listing of all the Dutch presentations during ERS – take the opportunity to look up where you can have a second look at our great science.

This year we continue to celebrate early career scientists through the Chiesi Young Investigator Award Session. Be sure to join us for this exciting session when we will hear from presenters who submitted the top scoring abstracts. This session promises to be full of exciting science, both clinical and basic/translational, that will display the talent that constitutes the future strength for our field. You will, once again, have an opportunity to participate in selecting the most outstanding presentation in the Chiesi Young Investigator Award, as part of the public vote during this session.

We look forward to seeing you during the DLC and the great scientific (and other) discussions we are anticipating during our 2025 meeting.

On behalf of the DLC organizing Committee

Janette Burgess

Chair, DLC Organizing Committee

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Chiesi Young Investigator Presentations

O01 Towards personalized dosing intervals of biologics in severe asthma: current practice of interval extension in the Netherlands

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INTRODUCTION: Biologics in severe asthma (SA) are an effective but costly treatment. A personalised dosing strategy could improve cost-effectiveness.
AIMS AND OBJECTIVES: To explore real-world practice of dosing interval extensions for biologics in SA.
MATERIALS AND METHODS: A 28-question nationwide e-survey was conducted among Dutch pulmonologists prescribing biologics for SA. In addition, incidence and prevalence of dosing interval extension were investigated in the Dutch national SA registry RAPSODI.
RESULTS: Among 88 pulmonologists, 50 completed the questionnaire. Most respondents (72%) treat over 25 SA patients, while 88% have more than 2 years of prescribing experience of biologics. Dosing interval extensions were reported by 78% of respondents. Among the 39 physicians that apply dosing interval extensions, 32 (82%) apply it in dupilumab, 29 (74%) in omalizumab, 20 (51%) in mepolizumab, 18 (46%) in benralizumab, 4 (10%) in reslizumab and none in tezepelumab.Application of extensions was reported more frequently by clinicians treating more than 25 patients and those affiliated with the RAPSODI SA registry ($p <= 0.02$). Reasons for interval extension were good therapy response (95%) and costs (77%). More than one year of stable asthma before adjustment was required for 32 clinicians, commonly based on ACQ below 1.5 (90%), stable lung function (90%), no exacerbations (74%), and no OCS (69%), with 33% increasing inhaled corticosteroids dose beforehand. Of respondents, 62% found more than half of attempts successful, while higher ACQ (35.9%) and increase in exacerbations (28%) were main failure reasons. Most pulmonologists (92%) want to apply dosing interval extension more frequently, but key barriers were lack of evidence (62%) and experience (52%).Among 1603 SA patients that were included in the registry and treated with a biologic, 129 unique patients were identified that underwent dosing interval extension. The annual incidence of dosing interval extension increased from 0.7% in 2018 to 4.7% in 2024, while the prevalence of extended intervals increased to 8.1%.
CONCLUSION: A majority of 78% of included pulmonologists report that they perform dosing interval extension and real-world registry data show a prevalence of extended dosing intervals of 8% in 2024. Most clinicians wish to apply dosing interval extension more often and report lack of evidence and experience as key barriers. These findings highlight the need for evidence-based guidelines.

Impact Statement: Biologicals have significantly improved severe asthma care in recent years. A personalised dosing strategy could reduce costs, treatment burden and potential side effects. Our study is the first to report the current clinical practice of dosing interval extension using survey and real-world registry data. While the majority of pulmonologists perform dosing interval extension, it currently remains infrequent. Most pulmonologists want to apply it more frequently and report the lack of evidence and experience as key barriers.:

Funding: ZonMW:

Conflict of Interest/Disclosures: none

O02 Structural lung abnormalities in children and adults with cystic fibrosis after ETI using AI automated algorithms

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Background: Elexacaftor/Tezacaftor/Ivacaftor (ETI) is observed to have a positive impact on lung function and number of exacerbations in people with cystic fibrosis (PwCF).
Aim: This real-world study assessed structural lung changes pre- and post-ETI in pediatric and adult PwCF using LungQ (Thirona), an AI-based CT analysis platform.
Methods: Routine biennial chest CT scans from 205 PwCF (131 adults, 74 children) at Erasmus MC started on ETI were retrospectively collected and analyzed. Scans were processed with LungQ platform's PRAGMA-AI, Bronchus-Artery (BA), and Mucus Plugging (MP) algorithms. PRAGMA-AI quantified %Bronchiectasis (%BE), %Bronchial Wall Thickening (%BWT), and %Total Disease (%DIS). The BA algorithm measured bronchial dimensions respective to adjacent artery, which were used to compute BA ratios reflecting abnormalities of bronchial dilatation (Bout/A, Bin/A) and wall thickening (Bwt/A, Bwa/Boa). The MP algorithm detected airway-obstructing mucus plugs. Structural changes over time were assessed using linear mixed models.
Results: A total of 671 chest CTs were collected, with a median of 3 years before and after ETI. Of these, 654 (97%) were successfully processed. At baseline, children showed less structural damage than adults (median; %DIS: 4.06 vs. 7.78; Bwa/Boa: 0.48 vs. 0.52; mucus plugs: 0 vs. 49; $p<0.001$). Following ETI initiation, a strong significant improvements were seen in all outcomes between baseline scan and first post-ETI scan ($p<0.001$), except Bin/A ($p=0.15$). Comparing baseline with second post-ETI scan, improvements remained significant across all measures ($p<0.05$), except for Bin/A ($p=0.61$). In the pediatric cohort, significant reductions were observed between baseline and first post-ETI scan for %DIS ($p<0.002$), Bout/A ($p=0.013$), wall thickening measures (%BWT, Bwt/A, Bwa/Boa; $p<0.001$), and mucus plugging ($p=0.017$). In contrast, bronchial dilatation or bronchiectasis only showed a reducing trend (%BE $p=0.086$; Bin/A $p=0.352$). In adult cohort significant improvements post-ETI across all bronchial dilatation/bronchiectasis, bronchial wall thickening and mucus plugging outcomes ($p<0.01$ for all) was observed.
Conclusion: ETI led to sustained improvements in bronchial damage and mucus obstruction over 3 years, with greater effects in adults, though abnormalities did not fully normalize.

Impact Statement: Chest CT can be used to detect progression of structural lung disease CF patients, but for this it is essential that abnormalities are objectively and reliably quantified. This study shows that using an AI-based scoring algorithm bronchial wall thickening, widening and mucus plugging can be quantified and that all measures dramatically improve after initiation of a novel CFTR modulator therapy. Our data will be added to the European CF registry to facilitate other relevant real-life evidence studies:

Funding: Cystic fibrosis foundation (CFF), USA:

Conflict of Interest/Disclosures: none

O03 Inflammation diminishes muscle regeneration induced by mitochondrial impairment

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INTRODUCTION: Chronic obstructive pulmonary disease (COPD) is often accompanied by muscle weakness, reduced muscle mass, and mitochondrial dysfunction, partly due to the spillover of inflammatory and oxidative stress-related mediators from the lungs to skeletal muscle. Muscle-damaging insults such as mitochondrial dysfunction normally evoke a muscle regenerative response, though muscle regeneration appears blunted in COPD.
AIMS AND OBJECTIVES: With this study, we aim to investigate how mitochondrial dysfunction and systemic COPD-associated stressors inflammation and hypoxia affect skeletal muscle regeneration in COPD. To test this, we aim to (I) determine whether mitochondrial dysfunction triggers muscle regeneration and (II) evaluate the impact of inflammation (TNF-α) and hypoxia (4% O2) on this response. We hypothesize that the systemic disease factors inflammation and hypoxia impair muscle regeneration triggered by mitochondrial dysfunction.
MATERIALS AND METHODS: To test our hypothesis, we used Cre/LoxP-based mouse C2C12 skeletal muscle fusion reporter cell lines to assess muscle regeneration via conditional luciferase expression upon myoblast-myotube fusion. Naive or mitochondrially impaired myotubes (by pretreatment with mitochondrial uncoupler CCCP) were co-cultured with healthy myoblasts. Co-cultures were exposed to inflammatory marker TNF-α (10 ng/mL) and/or hypoxia (4% O2) and compared to vehicle and/or normoxia controls. Luciferase activity was determined as a measure of fusion.
RESULTS: CCCP-pretreatment of myotubes strongly increased fusion (3-fold vs. control; $p<0.001$). TNF-α reduced fusion in co-cultures with mitochondrially impaired (3-fold; $p=0.034$) as well as naive myotubes (3-fold; $p=0.062$). Hypoxia did not impact fusion in co-cultures with mitochondrially impaired myotubes, nor did it elicit an additional effect on fusion when combined with TNF-α vs TNF-α alone.
CONCLUSION: These results suggest that mitochondrial impairment triggers skeletal muscle regeneration, which is hindered by inflammation, but not by hypoxia. Future work will include more inflammatory cytokines (e.g. IL-1β and IL-6) and other COPD-related factors (e.g. glycocorticoids), as well as more physiologically relevant conditions such as conditioned medium from COPD-stressed lung cells and patient sera. This will help to further elucidate the mechanisms of progressing muscle dysfunction in patients with COPD.

Impact Statement: People with COPD often lose muscle mass and strength, which worsens survival. We found that impairment of muscle cell powerhouses (mitochondria)—commonly observed in COPD—can trigger muscle cell fusion, an early phase of repair. Using a muscle cell fusion-reporter cell model, we showed that inflammation, but not hypoxia, reduces muscle cell fusion induced by impaired mitochondria. These findings indicate that (systemic) inflammation may blunt muscle repair/buildup in COPD, which should be considered during, for example, pulmonary rehabilitation.:

Funding: This project was funded by ZonMW.:

Conflict of Interest/Disclosures: none

O04 Proteome Profiling Links Surfactant Proteins B and D to Interstitial Lung Abnormalities and its Progression

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Introduction: Interstitial Lung Abnormalities (ILA) are incidental radiological findings on chest CT scans that resemble radiologic patterns of interstitial lung disease (ILD) in asymptomatic individuals which may represent early-stage ILD. Up to 48% of ILAs progress to clinically significant ILD within five years, highlighting the need for reliable biomarkers to predict disease progression and elucidate underlying mechanisms. Recent studies have identified blood-based proteomic biomarkers associated with ILA; however, their validation, generalizability, and clinical implementation remain unclear.
Aims and Objectives: The study aims to identify plasma protein biomarkers that distinguish individuals with ILA from healthy controls, track changes in biomarker levels over time, and assess their association with radiographic progression.
Materials and methods: We retrospectively identified 201 individuals with ILA, based on Fleischner Society criteria (Hatabu, 2020), from the Dutch-Belgian lung cancer screening trial (NELSON) (de Koning et al., 2022). Plasma samples were available at baseline for 85 individuals and at 2-year follow-up for 47. Clinical data, including radiologic progression, was collected and compared to matched healthy controls. Plasma levels of 1500 different proteins were measured using SOMAscan assay at baseline and 2-year follow-up to identify biomarkers associated with ILA presence and progression.
Results: At baseline, 10 proteins were differentially expressed between participants with ILA cases and controls, with surfactant proteins SP-B and SP-D emerging as strongest biomarkers (Area under the curve (AUC) = 0.769). No significant proteomic differences were observed between progressive and non-progressive ILA cases or between fibrotic and non-fibrotic subtypes. However, among progressive ILA, SP-B levels increased significantly over time compared to those with stable disease.
Conclusion: In plasma, distinct proteomic signatures are present in individuals with ILA, with SP-B and SP-D emerging as strongest biomarkers for ILA detection. Longitudinal increases in SP-B may serve as a potential biomarker for ILA progression.

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Impact Statement: This research identifies key proteins in the blood, SP-B and SP-D, which are associated with radiologic abnormalities in the lungs of asymptomatic individuals that may reflect early interstitial (fibrotic) lung disease. Moreover, one biomarker, SP-B, may predict progression of these abnormalities. The identified markers may be used to diagnose lung fibrosis earlier (better monitoring) and also in the future to develop potential treatment strategies to prevent or limit disease progression thereby improving long-term health outcomes.:

Conflict of Interest/Disclosures: none

O05 Socioeconomic inequalities in severe asthma in the Netherlands: a geospatial analysis in a nationwide cohort

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Introduction: Emerging evidence shows that health disparities, such as poor housing or a low socioeconomic status, may contribute to an increased risk of severe asthma; however, research into social determinants of health remains challenging.
Aims and Objectives: The primary aim was to explore how socioeconomic disparities influence the risk of severe pediatric asthma and explore its geographical distribution across the Netherlands.
Materials and Methods: In this nationwide cohort study, all children aged 2-17 years living in the Netherlands between 2018-2022 were included. Severe asthma definitions were based upon individually linked data from non-public Dutch registry databases on asthma-related health expenditures including hospital and pediatric intensive care unit (PICU) admissions. Geospatial analysis was used to identify hot spots based on the regions with the highest counts of severe asthma. In addition, the impact of various socioeconomic variables (e.g. housing, migration background, socioeconomic status) on the primary outcome of severe asthma was assessed using a linear probability model.
Results: The total study population consisted of 4.538.020 children. Children from the lowest income class had twice the odds of severe asthma ($p<0.001$) and had a 2.6 times greater odds of being admitted to the PICU with severe acute asthma compared to the highest income class ($p<0.001$). Other socioeconomic disadvantage factors for severe asthma were living in a rental house (OR 2.0), having a lower socioeconomic status score based on income, education and employment history (OR 1.9) and having a migration background (OR 1.7).
Conclusion: We identified several disparities that were more prevalent in children with severe asthma and severe acute asthma at the PICU in the Netherlands, establishing the presence of a socioeconomic health gradient. Comprehensive assessment and mitigation of these determinants by using targeted interventions may improve health equity in pediatric severe asthma.

Impact Statement: In this study, we found that children growing up in a disadvantaged environment, such as having a low socioeconomic status or migration background, are more likely to have severe asthma. This is the first study to combine national data from all children in a country with geographical data, demonstrating how severe asthma and social disadvantages are distributed across the Netherlands. The results highlight the urgent need for government action to better support vulnerable patients and reduce inequality in asthma care.:

Funding: This study was supported by internal funding of Emma Children's Hospital and research support from the Dutch Foundation for Asthma Prevention (SAB 2025-010).:

Conflict of Interest/Disclosures: none

O06 Complementary predictors for asthma attack prediction in children: salivary microbiome, serum inflammatory mediators, and past attack history

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Introduction: Early identification of children at risk of asthma attacks is important for optimizing treatment strategies. Building upon existing literature, we hypothesized that salivary bacterial diversity and composition are associated with the risk of future asthma attacks in children.
Aims and Objectives: We aimed to integrate salivary microbiome and serum inflammatory mediator profiles with asthma attacks history to develop a comprehensive predictive model for future attacks.
Materials and Methods: This study contained a discovery (SysPharmPediA) and a replication phase (U-BIOPRED). School-aged children with asthma were classified into at risk and no-risk groups, based on the presence or absence of one or more severe attacks during one-year follow-up. Prediction models were developed using random forest on training set (70%) with data on past asthma attacks, microbiome composition, serum inflammatory mediator levels, and their combinations, then tested on the rest of the population (30%). Outcomes were replicated in a subset of children with severe asthma from U-BIOPRED.
Results: Complete data were available for 154 children (SysPharmPediA=121, U-BIOPRED=33). In discovery, the model based on past attacks resulted in an area under the receiving characteristic curve (AUROCC) ~ 0.7. Models including six salivary bacteria or six inflammatory mediators achieved similar results. Combined model incorporating seven features, past asthma attacks, Capnocytophaga, Corynebacterium and Cardiobacterium, TIMP-4, VEGF, and MIP-3β achieved highest accuracy with AUROCC ~ 0.87. The combined model in the U-BIOPRED limited to available inflammatory mediators (VEGF), and incorporating past asthma attacks, Capnocytophaga, Corynebacterium, Cardiobacterium, resultedin an AUROCC of 0.84.
Conclusion: Serum inflammatory mediators and salivary microbiome complement asthma attacks history for predicting future attacks. These results highlight the imperative for continued investigation into oral microbiota, and its interaction with immune system.

Impact Statement: This research shows that the types of bacteria found in children's saliva, along with immune system markers and past asthma history, can help predict future asthma attacks. Early identification of children at risk could lead to more personalized and effective treatment plans. In the future, it may be possible to reduce asthma attacks by safely changing the body's bacterial makeup through diet, supplements, or targeted therapies, potentially improving quality of life and care for children living with asthma.:

Funding: The SysPharmPediA consortium has been supported by ZonMW [project number: 9003035001], Ministry of Higher Education, Science and Innovation of the Republic of Slovenia (MVZI) [contract number C330-16-500106]; the German Ministry of Education and Research (BMBF) [project number FKZ 031 L0088]; Instituto de Salud Carlos III (ISCIII) through Strategic Action for Health Research (AES) and European Community (EC) within the Active and Assisted Living (AAL) Program framework [award numbers AC15/00015 and AC15/00058] under the frame of the ERACoSysMed JTC-1 Call. U-BIOPRED has received funding from the Innovative Medicines Initiative Joint Undertaking under FP7 Health grant agreement 115010, resources of which are composed of financial contributions from the European Union's Seventh Framework Programme (FP7/2007-2013) and European Federation of Pharmaceutical Industries and Associations companies' in-kind contributions (www.imi.europa.eu www.imi.europa.eu). M. I. Abdel-Aziz is supported by the Longfonds, Stichting Astma Bestrijding, and Amsterdam Public Health Institute in relation to this work.:

Conflict of Interest/Disclosures: JMB received an honorarium from Vitakruid. AHM is the PI of a public private consortium (P4O2 (Precision Medicine for More Oxygen)) sponsored by Health Holland

involving many private partners that contribute in cash and/or in kind (AbbVie. Boehringer Ingelheim, Breathomix, Clear, Fluidda, Ortec Logiqcare, Olive, Philips, Quantib-U, Smartfish, Clear, SODAQ, Thirona, Roche, TopMD, Novartis, RespiQ). She received unrestricted research grants from GSK and Boehringer Ingelheim and a Vertex Innovation Award grant from Vertex. She has received honoraria from Boehringer Ingelheim, GSK and Astra Zeneca. Others have no potential conflicts of interest to disclose.

Posters: Respiratory Health - impacts of exercise and exposure

P01 Respiratory health effects of occupational exposure to nanomaterials and ultrafine particles: a scoping review

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Background: Approximately 15–20% of respiratory diseases are work-related. Evidence suggests that exposure to the emerging occupational risks, such as nanomaterials and ultrafine particles (UFP) may impair respiratory function and increase disease burden.
Objective: To summarize evidence on respiratory health effects from occupational exposure to nanomaterials and UFP, identify common biomarkers, and highlight knowledge gaps needing further study.
Methods:A comprehensive search was conducted in MEDLINE, EMBASE, and Web of Science from inception to April 2024. Studies were eligible if they assessed health outcomes among workers exposed to nanomaterials or UFP in occupational settings. Of 6020 records screened, 66 met inclusion criteria; 43 reported respiratory outcomes.
Results: Most studies were cross-sectional (n=24), panel (n=12), longitudinal (n=1) studies. Common exposures included UFP and nanomaterials such as carbon nanotubes/fibers, titanium dioxide, and metal oxides. Workers showed impaired lung function (FEV_1, FVC, FEV_1/FVC, flow rates), local inflammatory responses (e.g., elevated IL-8, TNF-α, neutrophils, leukotrienes, KL-6), oxidative stress biomarkers (e.g., 8-OHdG, MDA, 8-isoprostane) and developed pulmonary diseases including silicosis, small airway remodeling, pulmonary fibrosis, and pleural effusions, with some studies reporting associations with irreversible lung damage or death.
Conclusion: Occupational exposure to nanomaterials and UFP is associated with impaired lung function and inflammation. This review highlights the need for longitudinal studies with detailed exposure assessment and standardized diagnostic tools to better understand causal pathways and inform occupational health policy.

Impact Statement: This research shows that workers exposed to nanomaterials and ultrafine particles may suffer lasting lung damage. By summarizing current scientific evidence, the study raises awareness of these often-overlooked workplace risks, highlights possible biological mechanisms behind the harm, and underscores the need for long-term health monitoring to better protect workers.:

Funding: This project was funded by LEXCES.

Conflict of Interest/Disclosures: We gratefully acknowledge Faridi S. van Etten–Jamaludin for her assistance with developing the search strategy. The authors declare no conflict of interest.

P02 Effect of endobronchial valve treatment on skeletal muscles, fatigue, and sleep in severe emphysema patients

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Introduction: Skeletal muscle dysfunction, fatigue, and poor sleep quality are common in severe emphysema patients. Endobronchial valve (EBV) treatment is a bronchoscopic procedure which improves pulmonary function, quality of life, and exercise capacity in these patients. However, its potential beneficial effects on skeletal muscle function, fatigue and sleep are unclear.
Aims and Objectives: Our aim was to investigate the effects of EBV treatment on skeletal muscles, fatigue and sleep.
Material and Methods: We conducted a prospective cohort study assessing the 2nd parasternal intercostal muscle thickening fraction, and quadriceps muscle thickness and rectus femoris cross-sectional area (RFCSA), both using ultrasound, limb muscle function using the 30-second sit-to-stand test, fatigue with the Checklist Individual Strength (CIS) fatigue subscale (score ≥36 indicating severe fatigue), and sleep quality with the Pittsburgh Sleep Quality Index (PSQI) at baseline and 6 months following EBV treatment.
Results: A total of twenty patients were included. At the six-month follow-up, significant improvements were observed in pulmonary function, quadriceps thickness and RFCSA in the nondominant leg, as well as in limb muscle function. Intercostal thickening fraction did not change following treatment. Fatigue decreased significantly, reducing severe fatigue prevalence from 70% to 25%. Sleep quality was generally poor and remained unchanged.
Conclusions: Our results show that quadriceps muscle size and function, as well as fatigue, significantly improve following EBV treatment in severe emphysema patients. However, BLVR seems to have no impact on intercostal thickening fraction and patient-reported sleep quality. This study highlights the beneficial extrapulmonary effects of EBV treatment in patients with severe emphysema, further supporting its clinical use.

Impact Statement: This study demonstrates that endobronchial valve treatment not only significantly improves pulmonary function, exercise capacity, and quality of life in patients with severe emphysema, but also provides meaningful extrapulmonary benefits, including increased skeletal muscle size and function, as well as reduced symptoms of fatigue. These findings provide additional evidence underscoring the clinical value of endobronchial valve treatment in this patient population.:

Conflict of Interest/Disclosures: DJS reports grants and consultancy paid to his institution from PulmonX USA, MoreAir USA, Nuvaira USA, PulmAir USA, FreeFlowMedical USA, and Apreo USA all outside the submitted work. EAMDtH and JEH have nothing to disclose.

P03 Respiratory EMG and dyspnea during exercise in COPD patients

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Introduction: Exertional dyspnea is the main symptom of COPD. Based on the positive relationship between the levels of dyspnea (Borg score) and the electrical activity of respiratory muscles (electromyogram, EMG) during an incremental cardiopulmonary exercise test, it has been suggested that respiratory EMG can provide a physiological biomarker for dyspnea.
Aims and Objectives: This study aimed to characterize the relationship between dyspnea and EMG during exercises simulating daily activities.
Materials and Methods: Surface EMG was measured at 2 locations on the chest of 28 COPD patients while they were performing constant-work rate cycling tests and walking/cycling exercises that were part of their rehabilitation program. Simultaneously, the level of dyspnea was assessed using the Borg score at several timepoints throughout the exercise sessions, along with respiration rate (RR) and heart rate (HR). Patients completed each up to 10 such study visits during their 8-week stay at the rehabilitation center (CIRO, the Netherlands).
Results: In total, 1981 Borg-dyspnea scores with associated EMG measurements were recorded during 263 study visits. A linear mixed model was used to assess the relation of the Borg-dyspnea score with EMG while controlling for RR, HR, (type of) exercise, age and sex. Random effects for patient and visit were included to account for correlation in the measurements. EMG had a highly significant association with the Borg-dyspnea score ($p<0.0001$). Respiratory EMG and Borg-dyspnea score showed consistent positive correlations, of which the magnitude varied between patients.
Conclusion: These results indicate that respiratory EMG can provide a physiological biomarker for dyspnea during activities of daily living in COPD patients.

Impact Statement: The relationship between the electromyography (EMG) of respiratory muscles and level of dyspnea in COPD patients offers valuable insights for clinical practice. EMG can serve as a physiological biomarker for dyspnea, enhancing patient assessment and management. Monitoring EMG during exercise allows healthcare providers to better understand the level of dyspnea and adjust interventions accordingly. For example, pulmonary rehabilitation could be evaluated more effectively by tracking changes in EMG of respiratory muscles in addition to subjective scores for dyspnea.:

Funding: The study was funded by Medtronic.

Conflict of Interest/Disclosures: Geert Morren, Bart Gerritse, Gregory Hilleren and Fabio Pradella are Medtronic employees and shareholders.

P04 Body composition in patients with COPD: the extremes

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Introduction: Abnormal body composition is common in COPD and associated with morbidity and mortality. To date, body composition of COPD patients that have an extreme body mass index (BMI <18.5 kg/m2 or >30 kg/m2) and its clinical impact remain unknown.
Objectives and rationale: To examine body composition and its clinical impact in COPD patients with an extreme body mass index (BMI <18.5 kg/m² or >30 kg/m²).
Materials and methods: This analysis included 2936 COPD patients (52% women; age: 66 (60-72); FEV1: 44 (32-61) %pred) referred for pulmonary rehabilitation (PR) at Ciro. Patients were divided based on baseline BMI: underweight (UW <18.5 kg/m2), normal weight (NW 18.5-24.9 kg/m2), overweight (OW 25-29.9 kg/m2), obese 1 (OB1 30-34.9 kg/m2), obese 2 (OB2 35-39.9 kg/m2) and obese 3 (OB3 >39.9kg/m2). Fat-free mass index (FFMI) was derived from DXA. Low FFMI was based on age, gender and BMI-specific cutoff values by Franssen JAMDA 2014. Moreover, mMRC, SGRQ and FEV1 were assessed.
Results: The sample had a median BMI of 25.7 (21.9-29.8) kg/m2 and a FFMI of 16.3 (14.6-18.1) kg/m2. 7.4% of the patients were UW, 38.1% NW, 30.0% OW, 15.6% OB1, 6.4% OB2 and 2.6% OB3. FEV1 % predicted and SGRQ total score were not different between BMI-subgroups. In contrast, low FFMI varied between BMI-subgroups: 41%, 58%, 62%, 62%, 14% and 19% respectively. Fewer men were in the UW group than in NW, OW, and OB1. The percentage of males was higher in OW than in OB1 and OB2, and higher in OB1 than in OB2 and OB3. mMRC grades of 3/4 were more prevalent in UW (58%) and OB3 (77%) groups compared to all other BMI-subgroups (45.5%, 46.4%, 51.8% and 56.9%, respectively).
Conclusion: One-third of the COPD patients referred for PR had a BMI <18.5 or >30 kg/m2. Low FFMI was highly prevalent, even in overweight and obese patients and is not associated with FEV1 %predicted.

Impact Statement: This study reveals a high prevalence of extreme BMI (below 18.5 and above 30 kg/m2) in the COPD population, with low muscle mass common across all BMI groups. These findings emphasize that BMI alone is insufficient to assess nutritional or physical status in COPD. Routine evaluation of muscle mass is essential to identify at-risk individuals and to inform targeted interventions aimed at improving patient outcomes.

Funding: Longfonds

Conflict of Interest/Disclosures: none

P05 Impact of pulmonary rehabilitation on body composition in patients with COPD

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Introduction: Many COPD patients referred for pulmonary rehabilitation (PR) have abnormal body composition. Exercise training and dietary counselling are expected to positively impact lean mass (LM) and fat mass (FM) in these patients. To date, a detailed analysis of the impact of PR on LM and FM is lacking.
Aims and Objectives: To assess the effects of inpatient PR on body composition in patients with COPD.
Materials and Methods: 2936 patients (52% women; age: 66 (60-72) years, BMI 25.8 (22.5-29.6) kg/m2, FEV1: (44 (32-61) %pred) who completed an 8-week inpatient PR program in Ciro were analysed. Patients were grouped by baseline BMI: underweight (UW) <18.5; normal weight (NW) 18.5-24.9, overweight (OW) 25-29.9, obese (OB) 30-34.9, severely obese 35-39.9 (sOB) or morbidly obese (mOB) >39.9 kg/m2) and baseline fat-free mass index (FFMI; age-, sex- and BMI-specific cut-offs were used; Franssen et al. JAMDA 2014). LM and FM were measured by DXA before and after PR.
Results: Overall, in 47.6% of the patients the increase in FFMI exceeded the MCID (Jenkins et al. Pulmonology 2024) of 0.35 kg/m2. The largest median improvements in LM were found in UW, NW and OW (+1.6, +1.1 and +0.8 kg, respectively). Largest median reductions in FM were observed in OB, sOB and mOB (-2.0, -2.5, -3.2 kg, respectively), with preserved or even increased LM. Patients with low FFMI had a larger increase in LM within all BMI groups except for sOB and mOB when compared to normal FFMI.
Conclusion: Pulmonary rehabilitation, including exercise training and nutritional counselling results in improvements in body composition in COPD patients, irrespective of baseline body weight or composition.

Impact Statement: This study shows that pulmonary rehabilitation leads to improvements in body composition among patients with COPD, regardless of their baseline body weight or composition. These findings highlight the broad effectiveness of rehabilitation in enhancing muscle mass and physical health across diverse patient profiles. This underscores the value of pulmonary rehabilitation as a key intervention to improve clinical outcomes and functional status, independent of initial BMI or body composition.

Funding: Lung Foundation Netherlands / Longfonds (Grant #5.1.18.232).

Conflict of Interest/Disclosures: none

P06 Insight into oxygen deficit from phase relations between cardiopulmonary variables during intermittent exercise

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Background: At the start of exercise, individuals build up a certain level of O2 deficit, depending on their adaptation ability to the new physiological state. A greater O2 deficit represents slower V'O2 kinetics and is influenced by ventilation, diffusion, circulation and O¬2-consumption by the muscles, but the interaction and to what extent each system contributes remains unclear.
Aims and objectives: This study investigates the time-relations between periodic changes in physiological variables during intermittent exercise, expressed by gain and phase.
Methods: Ten healthy individuals performed four interval tests (6x1.5 minute of loaded or unloaded exercise). Measured were V'O2, V'CO2, tidal volume, breathing rate, heart rate and expiratory pressures. Tests were conducted in either supine or upright position and at moderate or high workload. The gain and phase relations between the measured parameters were calculated using MATLAB to assess their contribution to the O2 deficit.
Results: Phase differences (φdiff) showed that mixed-expiratory PO2 responds earlier than V'O2 to the increased workrate (φdiff=17°, p<0.001), HR responds a bit earlier (φdiff=6°, p=0.09), and mixed-expiratory PCO2, V'CO2 and total ventilation respond later than V'O2 (φdiff=-16°, p=0.002, φdiff=-22°, p<0.001 and φdiff=-25°, p=0.002). Across the different positions and workloads the gain and phase between most cardiopulmonary parameters remained stable.
Conclusion: Mixed-expiratory PO2 precedes an increase in HR and VO2, which can be the trigger of the primary cardial and ventilatory responses, opposed to the often described PCO2. Cardiopulmonary kinetics seem stable across different workloads and positions.

Impact Statement: Do you experience discomfort during exercising and don't want to experience this again, also not in the hospital. With our research we aim investigate the state of the lungs, blood circulation and muscles with a low level exercise test. Our physiological model helps us understand which system is impairing your exercise without you the need of a heavy exercise test in the hospital.

Conflict of Interest/Disclosures: none

Posters: Patterns of lung disease: Imaging & Omics

P07 Development of quantitative CT image analysis for NTM lung disease interventions

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Introduction: Evidence-based treatments for Nontuberculous mycobacteria (NTM) lung disease are urgently needed. A sensitive tool to quantify radiological abnormalities would be valuable.

Aims and Objectives: To develop quantitative CT image analysis for NTM lung disease interventions.

Materials and Methods: The prospective multi-center FORMaT study assessed Mycobacterium abscessus (Mabs) treatment in NTMpatients (n=41). Chest CTs were performed at baseline (n=37), 12 weeks (n=22), and 52 weeks (n=17). CTabnormalities were quantified using an adapted grid-based PRAGMA score (PRAGMA-NTM), identifyingatelectasis/consolidation, bronchiectasis, mucus plug/tree-in-bud, bronchial wall thickening, cavitation,ground-glass opacities, and emphysema/bullae. AI-based LungQ (Thirona) analyses were evaluated,including bronchus-artery (BA) ratio analysis (bronchial outer and inner diameter, bronchial wall thickness,artery diameter) and mucus plug (MP) analysis (number of mucus plugs). Additionally, Intervention group patients (n=26) were compared pre/post-treatment, while others (15 patients) were observed without intervention.
Results: At baseline (n=37), PRAGMA-NTM identified bronchiectasis (median 3.0%, range 0.3–10.2%), atelectasis/consolidation (1.3%, 0.2–12.6%), and mucus plug/tree-in-bud (0.9%, 0–9.7%) as most prevalent abnormalities. Cavitation was present in 6 (15%) patients. Mucus plug/tree-in-bud declined post-treatment (median at baseline 1.0%, 12 weeks 0.5%, 52 weeks 0.2%; p=0.007). The LungQ MP also showed a trend for reduced mucus plugs (at 12 weeks p=0.096), while BA ratios did not change post-intervention.
Discussion: This is the first structured CT analysis of Mabs NTM lung disease pre/post-treatment. Findings suggest mucus plugging is a key marker of active NTM disease and an early predictor of treatment response.

Impact Statement: Non-Tuberculous Mycobacterium (NTM) is a severe and difficult to treat infection in bronchiectasis patients and the incidence is rising Worldwide. There is an urgent need for sensitive outcomes measures to evaluate treatment success, to facilitate the search for effective and less toxic anti-NTM medications. We present an AI-assisted standardized chest CT score to detect NTM-specific abnormalities, that detect a signal after treatment.

Funding: Medical Research Future Fund (MRFF) Australia Cystic Fibrosis Foundation (CFF) USA

Conflict of Interest/Disclosures: Harm Tiddens is professor emeritus at Erasmus MC and the CMO of Thirona B.V. All other authors declare no conflicts of interest.

P08 Prevalence of structural lung abnormalities in a large pediatric bronchopulmonary dysplasia cohort

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Background: Bronchopulmonary Dysplasia (BPD) is a common complication in very preterm-born children (<32 weeks (wks) gestational age (GA)). The prevalence of early life structural lung abnormalities in BPD remains unclear but may help assess disease severity and predict long-term outcomes.
Objective: To identify structural lung abnormalities in infants with BPD under 15 months of age using the PRAGMA-BPD score on high-resolution (HR) CT scans. Methods: A total of 302 children in a dynamic hospital-based severe BPD birth cohort in Rotterdam, the Netherlands, underwent an HR-CT during free breathing without sedation. The validated quantitative PRAGMA-BPD score was used to quantify hypo-attenuation (trapped air and hypo-perfusion), hyper attenuation (linear opacities, atelectasis, and consolidation), bronchial wall thickening, and normal lung/airways, expressed as % of total lung volume. The association of GA at birth categorized into tertiles (<25.4 wks/ 25.4-26.6 wks/ >26.6 wks) with PRAGMA-BPD scores was analyzed using non-parametric ANOVA.
Results: Hyper-attenuation was present in 283 (98%) patients (median: 4.8%, range: 0–87.3%), hypo attenuation in 273 (90%) patients (1.8%, 0–41.9%), and bronchial wall thickening in 266 patients (88%) (0.7%, 0–6.3%). Normal lung/airways was most frequently scored with a median of 91.0% and range 8.7%-99.5%. GA was associated with hyper-attenuation (p=0.002) and bronchial wall thickening (p=0.020) with the highest proportion of abnormalities in the children with GA <25.4 wks.
Conclusion: Structural lung abnormalities were detected in all infants with severe BPD and those with a lower GA had more hyper-attenuation and bronchial wall thickening

Impact Statement: This study reveals a high prevalence of structural lung abnormalities in infants with severe bronchopulmonary dysplasia (BPD), with nearly all patients exhibiting hyper-attenuation, hypo-attenuation, or bronchial wall thickening on high-resolution CT. The most severely affected were those born before 25.4 weeks gestation. These findings underscore the utility of quantitative CT scoring for early disease characterization, highlight the vulnerability of extremely preterm infants, and support its use in predicting long-term respiratory outcomes and guiding early interventions.

Conflict of Interest/Disclosures: none

P09 Complosome Unleashed: Tearing Down Barriers in Idiopathic Pulmonary Fibrosis

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Idiopathic Pulmonary Fibrosis (IPF) is a devastating disease characterized by progressive scarring of lung tissue and declining respiratory function. To investigate the cellular mechanisms underlying IPF, we developed a primary coculture transwell system that mimics the alveolar capillary niche by incorporating both epithelial and endothelial cells. Our study demonstrates that fibrotic features are more pronounced in coculture systems compared to monoculture, highlighting the importance of intercellular interactions in disease progression. A key finding is the loss of barrier integrity and increased permeability, which closely mirrors the pathological conditions observed in IPF patients.

Proteomic analysis revealed significant alterations in complement factor expression, revealing the critical role of the complosome in maintaining barrier integrity. By regulating complosome activity, we explored its impact on metabolic and functional crosstalk between epithelial and endothelial cells. These findings provide novel insights into the pathophysiology of IPF and offer potential therapeutic intervention targets

Impact Statement: This study sheds light on the cellular interactions driving Idiopathic Pulmonary Fibrosis (IPF) and identifies the complosome as a key player in maintaining lung barrier integrity. By understanding these mechanisms, we can develop targeted therapies to slow disease progression and improve patient outcomes, offering hope for those affected by this debilitating condition.

Funding: Boehringer Ingelheim Pharma GmbH & Co KG, Immunology & Respiratory Diseases Research, Biberach an der Riss, Germany

Conflict of Interest/Disclosures: AJF, JB, DS, KGK are employees of Boehringer Ingelheim Pharma GmbH & Co. KG.

P10 Volatile organic compounds in patients with primary ciliary dyskinesia with or without prophylactic azithromycin

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Introduction: In recent years many patients with primary ciliary dyskinesia (PCD) have started using azithromycin as maintenance therapy to prevent exacerbations. No data is available whether azithromycin influences the composition of volatile organic compounds (VOCs) in exhaled breath. Measurement of these VOC's is of interest since this technique might help to identify pathogens and (risk of) exacerbations in patients with PCD.
Materials and methods: In this analysis of a longitudinal, observational cohort of patients with PCD at the Amsterdam UMC we identified exhaled VOCs with gas chromatography-mass spectrometry. The most promising compounds to differentiate patients with and without azithromycin maintenance treatment were selected with sPLS-DA analysis. A composite model with these compounds was made and tested with logistic regression to determine optimal accuracy.
Results: In total 92 patients with PCD were included, of whom 24 received azithromycin maintenance therapy. The median age was 22.5 years in the group without and 18 years in the group with azithromycin use. There were significantly more Pseudomonas aeruginosa infections in the azithromycin usage group (29.9%) than in the group without azithromycin usage (8.5%) (p=0.03). The analysis identified ten compounds as most promising, of which three alkanes were selected for the composite model based on univariate significance and contribution to the accuracy of final model. The composite model showed an accuracy of 70% (95%CI 0.58-0.83), according to the area under the curve, with a sensitivity of 79%, specificity of 61%, positive predictive value of 41% and negative predictive value of 89%.
Conclusion: In this study we show that the composition of VOCs in exhaled breath differs between patients with PCD with and without azithromycin maintenance therapy. This highlights the need to correct for this therapy in future VOC research and can give new insights in the mechanism of action of azithromycin prophylaxis.

Impact Statement: This study addresses a largely unexplored aspect of Primary Ciliary Dyskinesia management by examining how azithromycin maintenance therapy may influence the profile of volatile organic compounds in exhaled breath. This underlines the importance of accounting azithromycin therapy in future VOC research and may offer new insights into its prophylactic mechanism.

Conflict of Interest/Disclosures: none

P11 Primary Ciliary Dyskinesia caused by DNAI1 mutations: diagnostic results and clinical phenotype

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Introduction: Primary ciliary dyskinesia (PCD) is a disease characterized by ciliary dysfunction in multiple organs. Impaired mucociliary clearance in the respiratory tract leads to accumulation of mucus increasing the susceptibility to infection and results in progressive lung function decline. Different mutations are known to cause PCD, such as mutations in the DNAI1 gene which are associated with a loss of dynein arms and immotile cilia. The specific features of this genotype are currently not well established.

Objectives: Our aim was to describe the baseline diagnostic results and clinical phenotype of patients with DNAI1 mutations.
Materials and Methods: All patients at the Amsterdam UMC with a clinical suspicion for PCD and two causative mutations in DNAI1 were included. Data was collected on genetics, high speed video microscopy (HSVM), transmission electron microscopy (TEM), lung function and microbiology.
Results: Fourteen patients were included. Genetic testing showed ten patients with a homozygote mutation and four with a compound heterozygote mutation in DNAI1. With TEM a strong decrease was seen in both outer (median remaining: 1.6, SD: 1.3) and inner dynein arms (median remaining: 1.4, SD: 1.5). At baseline HSVM showed heterogenic results. All patients had abnormal results, but some residual activity was present in most patients (77%). After cell culture complete immotile cilia were described with HSVM in most cases (n=7), where the others (n=2) had minimal movement. Clinical data of thirteen patients was available. Lung function did not decline in 62% of the patients over the last five years. On average the FEV1 percentage predicted increased with 2.59% per year (CI: -2.36% / 7.54%). None of the patients had a chronic infection with Pseudomonas aeruginosa at inclusion, but it was cultured at least once in 46% of patients. Median courses of antibiotic treatment for a pulmonary exacerbation was 0.90 (SD: 0.94) per year.
Conclusion: This study presents an overview of diagnostic results and clinical features in a population of patients with PCD due to DNAI1 mutations. Abnormal results of HSVM were more pronounced after cell culture. This cohort did not show signs of a severe phenotype, with some use of antibiotics and, in general, a stable lung function.

Impact Statement: This research helps to decide whether patients with primary ciliary dyskinesia suffer from a more severe form of the disease when it is caused by mutations in DNAI1.

Funding: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflict of Interest/Disclosures: none

P12 Different vascular protein profiles in systemic sclerosis with and without ILD

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Introduction: Interstitial lung disease (ILD) is a major cause of morbidity and mortality in patients with systemic sclerosis (SSc). Vascular remodeling is a central feature in SSc pathophysiology. Circulating vascular-related proteins may play a role in in pulmonary involvement in SSc-ILD due to endothelial-mesenchymal cross-talk.
Aims and Objectives: This study evaluates protein concentrations involved in vascular pathways in different SSc patient groups with and without ILD as to identify different protein concentration profiles.
Materials and Methods: We retrospectively analyzed serum from three gender- and anti-topoisomerase antibody-matched patient groups enrolled in a structured SSc healthcare program. Serum was collected at baseline. Clinical follow-up data were collected during 5 following years. Group 1 had no ILD at baseline and remained free of ILD. Group 2 had no ILD at baseline and developed ILD confirmed by HRCT. Group 3 had ILD at baseline. Serum samples were analyzed using proximity extension assay (PEA, Olink©) targeting a preset panel of 92 proteins involved in vascular biology. Protein expression levels were normalized and compared between groups using ANOVA and corrected for multiple testing.
Results: Age, gender, SSc-subtype and presence of ATA, CENP, U1RNP, RNP70 or RNA-polymerase III antibodies were equally distributed between groups. Mean duration of non-Raynaud phenomenon of all patients was 10.7, group 1 (n=22) 6.2, group 2 (n=23) 14.8 and group 3 (n=28) 11.1 months resp. (p=0.017). 15 proteins showed differential expression, of which TNFR2 (p=0.016), FABP4 (p=0.017) and GDF-15 (p=0.002) were significantly elevated in Group 2 vs. Group 1. TNFRSF14 (p= 0.017), TNFR2 (p=0.017), Gal-3 (p=0.011), FABP4 (p=0.006), GDF-15 (p=0.000), PSP-D (p=0.001), TNFSF13B (p=0.003),UPAR (p=0.008) and CCL15 (p=0.015) were significantly elevated in group 3 vs. group 1.
Conclusion: Proteins involved in endothelial activation, leukocyte adhesion and vascular remodeling show different expression between patients who remained free from ILD and patients who either suffer from ILD or developed ILD. Whether some of these proteins play a role in the pathobiology of interstitial disease in SSc or might serve as biomarkers will be topic of further research.

Impact Statement: The course of systemic sclerosis is often complicated with pulmonary involvement (interstitial lung disease, ILD), causing a high disease burden and increased risk of mortality. There is a great need for new biomarkers predicting ILD. Publications over the last decade emphasize the interaction between vascular (endothelial) cells and connective tissue potent cells (stem cells) in development of interstitial lung disease. Therefore we investigated several proteins involved in this interaction and compared levels with and without systemic sclerosis associated ILD.

Conflict of Interest/Disclosures: none

Posters: Lung cell biology and cross talk with other body systems

P13 Contact-compression induces inflammatory and remodeling responses in bronchial epithelial cells

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Introduction: Lung implantable devices, such as stents and valves used as treatment for diseases like lung cancer and COPD, apply continuous supraphysiological compressive stress to airway tissue, potentially triggering adverse effects such as chronic inflammation, granulation tissue hyperplasia and fibrosis at the implant site.
Aims and Objectives: In order to study and identify the biological responses underlying this process we developed an in vitro contact-compression model that applies variable compressive stress to bronchial epithelial cells.
Methods: Confluent layers of bronchial epithelial cells (16HBE) were subjected to compressive stress using agarose-embedded weights (3, 6, 9 and 15g). After 24hrs, cell viability (Calcein-AM/PI imaging, MTS, LDH and dsDNA release), inflammation, fibrosis and mechano-transduction were assessed using PCR, ELISA and immunofluorescent staining's.
Results: Max compressive stress slightly reduced cell viability, with a 10% increase in LDH release. Compression upregulated inflammation, CXCL8, TNF, IL1α and remodeling-related genes, EGR1, TNC, COL1A1, CTGF, while reducing TGFB1 and FN1 expression. These changes were reflected in protein levels with increased CXCL8, IL-1α, CTGF and reduced Fibronectin levels in supernatant upon compression. Compressed cells showed increased actin polymerization, mechanoreceptor alignment, and YAP translocation, reflecting a mechanotransducive response.
Conclusion: We developed a viable in vitro model to study contact-compression, showing biomechanical inflammatory and remodeling responses. With adjustable components, this model can be applied to further study tissue responses to lung implants.

Impact Statement: In this study, a novel laboratory model was developed to study how abnormal compressive forces affect airway epithelial cells. Devices like airwaystents help lungcancer patients breathe by pushing open tumor-blocked airways, applying pressure on the airway wall. However, this pressure can harm cells, cause inflammation, or lead to scarring, often requiring further treatment. Our model helps understand this process and generates ideas to prevent it, guiding the design of safer lung devices to help patients breathe easier for longer.

Funding: This project was co-financed by the Ministry of Economic Affairs and Climate Policy by means of the PPP-allowance made available by the Top Sector Life Sciences and Health to stimulate public-private partnerships, with project code PPP2019-043. Additionally, co-financed by the Graduate School of Medical Sciences MD-PhD program of University Medical Center Groningen.

Conflict of Interest/Disclosures: Simon D. Pouwels and Dirk-Jan Slebos received funding from PulmonX Corp, USA. All other authors have nothing to disclose.

P14 Gut integrity and inflammation in COPD and exacerbations; the role of I-FABP

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Introduction: High plasma intestinal-fatty acid binding protein (I-FABP) levels reflect gut epithelial integrity loss. Its interplay with inflammation remains poorly understood in COPD and exacerbations of this disease (ECOPD).
Aim: Therefore, the aim of this study was to investigate the association between plasma I-FABP levels, inflammatory markers, and severity of COPD (including severity and frequency of ECOPD).
Methods: Data from the 2-year observational ICE-AGE study were analysed post hoc. Plasma I-FABP levels, and inflammatory parameters (e.g. IL-6, IL-8, monocytes, granulocytes and TNF-α) were assessed in patients with COPD and controls. Historic ECOPD frequency and severity were recorded at inclusion and monitored prospectively during the 2-year follow-up. Group comparisons were performed using the Mann-Whitney U and Kruskal-Wallis tests. Associations between variables were evaluated using Spearman rho.
Results: 205 patients with COPD (62 (57-67) years; 58% males; 50% (36-62%) FEV1 predicted) and 200 non-COPD controls (61 (57-64) years, 45% males) were included. The majority had ≥1 ECOPD in the previous year (77.3%) and during 2-year follow-up (86.3%). Plasma I-FABP levels were higher in patients with COPD vs non-COPD (1116.8 (840.4-1735.9)pg/mL vs 950.2 (707.4-1482.2)pg/mL, p=0.003). In patients with COPD, plasma I-FABP was positively associated with IL-8 (r=0.204, p=0.004) and TNF-α (r=0.181, p=0.017). Plasma I-FABP was not associated with ECOPD frequency and severity before or after inclusion.
Conclusion: Plasma I-FABP levels were higher and associated with systemic inflammation in COPD but not associated with ECOPD. This suggests that plasma I-FABP may reflect involvement of the gut-lung axis in patients with COPD.

Impact Statement: I-FABP is associated with systemic inflammation in COPD, but may not be a marker for ECOPD over a longitudinal time-scale.

Funding: The ICE-AGE study was funded by the Dutch Asthma Foundation and the Dutch Weijerhorst Foundation (3.2.09.049) and the current study was co-funded by AstraZeneca. Both institutes were not involved in this current study design, execution, analysis nor the compilation of the manuscript.

Conflict of Interest/Disclosures: none

P15 Comorbidities caused by occupational exposure to Chromium: the skin-lung axis

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Background: Hexavalent chromium (Cr(VI)) compounds are classified as both skin and respiratory sensitizers. Workers in industries such as electroplating, welding, painting, metalworking, and construction are exposed to high concentrations of Cr(VI). Occupational exposure has been linked to irreversible immune-related diseases, including contact dermatitis, occupational asthma, and rhinitis (1-4). This study aimed to investigate the association between airway symptoms and dermal disorders in patients referred for medical assessment under a national compensation program.
Method: Occupational exposure was assessed using a Job Exposure Matrix (JEM). Allergic sensitization was assessed using Skin Prick Test (SPT), where a positive result indicated allergic occupational asthma or rhinitis due to chromium exposure. Delayed-type hypersensitivity reactions were evaluated using a skin patch test, which is the golden standard diagnostic tool for contact dermatitis.
Results: A total of 37 allergy tests (12 SPTs and 25 patch tests) were conducted among 30 male participants. Five participants underwent only SPT, 18 underwent only skin prick test, and 7 received both tests. Overall, 4 tests (10.8%) were positive—2 (50%) from patch tests and 2 (50%) from skin prick tests. Among the workers assessed, 23 (76.7%) reported skin complaints, 17 (56.7%) reported asthmatic symptoms, and 22 (73.3%) reported rhinitis.
Conclusion: This study suggests a link between type IV hypersensitivity and respiratory symptoms in Cr(VI)-exposed workers, supporting the concept of a skin-lung axis for investigating underlying sensitization in both occupational settings and the general public.

Impact Statement: This study highlights a possible clinical link between skin allergies and breathing problems in workers exposed to chromium, a common industrial chemical. Understanding this connection can help improve workplace safety by encouraging better health monitoring and early detection of both skin and respiratory conditions in exposed workers.

Funding: this study was done in Amsterdam UMC.

Conflict of Interest/Disclosures: none

P16 Farm dust modifies rhinovirus-induced antiviral and inflammatory responses in airway epithelial cell cultures

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Introduction: Pre-school wheezing can be triggered by several respiratory viruses, among which rhinovirus (RV) is most commonly detected, and constitutes a major risk factor for asthma later in life. Children that grow-up on traditional cow farms develop less wheezing, allergies and asthma. This protective farm effect was further confirmed by studies using farm dust extract (FD) in experimental in vivo allergic airway models and in human primary bronchial epithelial cells (PBEC) infected with RV.
Aims and objectives/Materials and Methods: To further investigate the impact of FD on respiratory epithelial cell function in the context of RV infections, we performed RNA-sequencing on fully differentiated PBEC (n = 6 donor mixes; 3-4 donors/mix) that were treated with FD/vehicle for 6h, or pretreated for 24h with FD or vehicle and subsequently infected with RV-A16 (MOI 1) or mock for 24-48h in presence and in absence of FD.
Results: We observed that 6h-FD exposure slightly increased expression of genes that are associated with antiviral- and NF-κB-regulated responses. This was in contrast to the effects of FD on RV-infected cells at 24-48 hpi: FD attenuated the RV-induced expression of genes associated with antiviral responses, JAK-STAT signaling and pyroptosis (an inflammatory form of programmed cell death).
Conclusion: Collectively, this study showed that FD might promote antiviral and NF-κB-regulated gene expression in uninfected cells, whereas upon RV-infection these responses are attenuated by FD at 24 and 48 hpi. Whether this indicates that FD prepares epithelial cells for adequate responses to RV infection and downstream inflammation, requires further investigation.

Impact Statement: Rhinovirus infection in early childhood is a major risk factor for developing asthma. However, children that grow-up on traditional farms develop less childhood asthma. To investigate the mechanism underlying this “protective farm effect”, we exposed airway epithelial cells to farm dust (FD), before and after infection with rhinovirus. We observed that rhinovirus infection increases certain inflammatory gene expression profiles, which was inhibited by FD. This could imply that FD is protective through alleviating airway inflammation after rhinovirus infection.

Funding: This study was supported by a grant from the Lung Foundation Netherlands: AWWA grant # 12.0.17.001

Conflict of Interest/Disclosures: none

P17 Red Algae: A Natural Shield Against Air Pollution-Induced Airway Epithelial Responses in Respiratory Disease

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Marine algae-derived natural products are gaining attention for their therapeutic potential. Kappaphycus alvarezii, a red alga, is one of the important raw materials for carrageenan production, which has been widely used as an emulsifier in food, pharmaceutical and cosmetics industries. Those algae have been shown to display antioxidative stress and anti-inflammatory capacity. Oxidative stress and airway inflammation are processes that play a crucial role in respiratory diseases that are caused or aggravated by inhaled toxicants and air pollution, such as asthma and chronic obstructive pulmonary disease (COPD). Therefore, we propose that the use marine algae may act as a potential treatment strategy for respiratory diseases. In view of the pharmacological properties of the species, we aim to examine the antioxidant capacity and anti-inflammatory activity of K.alvarezii ethanol extract in airway epithelial cells, the cells that line the lungs, upon exposure to particulate matter, as the airway epithelium is in first contact to inhaled toxicants and plays a crucial role in respiratory diseases, activating inflammatory responses. The phytochemical profiling of K.alvarezii will be studied using Liquid Chromatography–Mass Spectrometry (LCMS). Beneficial effects of the extract will be studied on human airway epithelial cells upon exposure to particulate matter (PM) in vitro, assessing effects on e.g. oxidative stress responses (e.g. production of reactive oxygen species (ROS) by flow cytometry), cell viability (by an assay called MTT) and pro-inflammatory responses (e.g. release of inflammatory cell attractant CXCL8 by Western blotting and ELISA). Discovering anti-inflammatory properties in K. alvarezii could provide a promising alternative treatment for respiratory diseases linked to air pollution.

Keywords: Kappaphycus alvarezii; marine algae; anti-inflammation; air pollutants, respiratory diseases

Impact Statement: This research explores how a type of red seaweed, Kappaphycus alvarezii, might help protect our lungs from inflammation caused by air pollution. By studying its natural antioxidant and anti-inflammatory properties, we aim to find safer, plant-based treatments for respiratory diseases like asthma and COPD. If successful, this seaweed could offer a new way to fight pollution-related health problems using nature's own remedies.

Funding: The financial assistance provided by Sunway University (Post Graduate grant: PGSUREC2022/048), studentship and scholarship from both the Abel Tasman Talent Program (ATTP) sandwich PhD collaboration between Sunway University and University Medical Center Groningen, Netherlands are gratefully acknowledged

Conflict of Interest/Disclosures: none

P18 Impaired lung epithelial repair responses upon mitochondrial dysfunction

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Background: Mitochondrial dysfunction has been observed in lung epithelial cells in COPD. We hypothesise that these abnormalities not only result in increased pro-inflammatory activity, but also impaired epithelial regeneration either indirectly or directly due to e.g. cellular senescence/exhaustion of self-renewal capacity.
Aim: To assess the effect of mitochondrial dysfunction induced by Rotenone on lung epithelial regenerative responses.
Methods: Human alveolar A549 cells were treated with 50 or 200 nM of mitochondrial complex I inhibitor Rotenone to induce mitochondrial dysfunction, and mitochondria respiration was assessed using the Seahorse XF system. The effect of Rotenone (50, 200 nM) was also assessed in an A549 cell organoid model to allow self-renewal and organisation. After 7 days of culture, the size and number of organoids were quantified, and RNA was isolated for qPCR.
Results: Rotenone-induced mitochondrial dysfunction was confirmed by the reduction in mitochondrial respiration and altered expression of mitochondrial genes (e.g. TFAM). In the organoid model, we observed a significant increase in pro-inflammatory genes IL1B and CXCL8 and senescence marker CDKN1A, as well as a decreased LMNB1 gene expression upon Rotenone treatment. Furthermore, there was a significant reduction in both the number and size of organoids upon treatment.
Conclusion: Our data suggest that mitochondrial dysfunction induces cellular senescence and impaired lung epithelial regeneration. Restoring mitochondrial health may therefore be a therapeutic avenue to stop and reverse COPD-associated lung damage.

Impact Statement: This research shows that when the energy-producing parts of lung cells (mitochondria) stop working properly, the lungs lose their ability to repair themselves—a problem seen in diseases like COPD. Damaged mitochondria make cells inflamed and worn out. These findings suggest that protecting or restoring mitochondrial function could help the lungs heal better, offering hope for new treatments to slow or even reverse lung damage in people with chronic respiratory diseases.

Funding: ZonMw

Conflict of Interest/Disclosures: none

P19 Confocal, biochemical, and functional complementary approaches for investigating TGF-β1 induced epithelial-mesenchymal transition in A549 Cells

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Epithelial-mesenchymal transition (EMT) is important for different biological processes, including lung fibrosis. TGF-β1 is a key EMT inducer, triggering pathways that modify gene expression and cell morphology. To provide an integrated assessment of EMT, we measured cell morphology with the confocal Operetta CLS system and protein expression in the same samples. In addition, functional studies were performed using the xCelligence Real-Time Cell Analysis (RTCA), and gene expressions from the RTCA samples were analyzed with RT-qPCR.

After 24h of starvation, A549 cells were exposed for 3 days to TGF-β1 (0.01-100 ng/mL), with or without 1μM nintedanib (NTD) or SB-525334. Confocal analysis measured E-cadherin and α-SMA protein levels. RTCA studies evaluated cell index (CI) and E-cadherin/α-SMA gene expression.

In confocal studies, TGF-β1 increased cell length and α-SMA protein expression in a concentration-dependent manner and reduced cell roundness and E-cadherin. In functional studies, TGF-β1 reduced the CI and E-cadherin gene expression while increasing α-SMA gene expression. SB-525334 and NTD prevented all the effects of TGF-β11,2,3,4.

Interestingly, on parameters related to loss of epithelial phenotype, TGF-β1 displayed higher potency, and SB-525334 was more active than NTD. On the contrary, on parameters related to the gain of mesenchymal phenotype, TGF-β1 displayed lower potency, and SB-525334 and NTD actions were similar.

In conclusion, integrating these complementary methods offers a robust model for EMT research and antifibrotic drug discovery.

References: 1PMID:34356903, 2 PMID:29166920, 3PMID:30636861, 4PMID: 28898237

Impact Statement: This study presents a robust, multiparametric model of EMT using A549 lung epithelial cells. By integrating confocal imaging, innovative real-time functional analysis (RTCA), and RT-qPCR, it quantitatively assesses both epithelial loss and mesenchymal gain induced by TGF-β1. The differential effects of antifibrotic agents nintedanib and SB-525334 are also explored. This approach strengthens the evaluation of EMT dynamics and drug responses, providing a valuable platform for antifibrotic drug screening and advancing mechanistic understanding in lung fibrosis research.

Funding: This research was supported by Chiesi Farmaceutici

Conflict of Interest/Disclosures: This research was funded by Chiesi Farmaceutici S.p.A., 43122 Parma, Italy. All other authors declare no competing interests

Posters: Clinical Management & Lifestyle

P20 Real-world effectiveness of antibiotics in addition to oral corticosteroids for managing asthma exacerbations in adults

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Introduction: Antibiotics are widely used to manage acute asthma exacerbations in clinical practice, despite little evidence of effectiveness and guidelines advising against their routine use.
Aims and objectives: To gain insight in the use of antibiotics for managing acute asthma exacerbations in adults in the Netherlands, and asses their effectiveness alongside oral corticosteroids.
Materials and methods: This retrospective cohort study included individuals from the Netherlands between 1994 and 2022 from the IADB.nl pharmacy dispensing database. Individuals had to be 16 to 45 years old, use inhaled asthma medication, and have a first recorded prednisone/prednisolone (OCS) dispense of ≥ 30 mg/day for 3 to 14 days. Patients were compared regarding treatment failure (a new dispense of OCS or antibiotics 15-30 days after initial dispense), based on whether or not they were dispensed antibiotics (AB) alongside their first recorded OCS dispense. Regression analyses with inverse probability of treatment weighting were used to adjust for various confounders.
Results: Of the 5401 individuals included, 38% received antibiotics alongside first-recorded OCS dispense, with a decreasing trend from 47% in 2009 to 24% in 2020. The odds ratio for treatment failure was 1.36 (95% CI: 0.81 – 2.16) for AB+OCS vs. OCS only. The hazard ratio for a new exacerbation within 31-365 days of follow-up was 1.20 (95% CI: 0.92 – 1.56) for AB+OCS vs. OCS only. The lack of beneficial effect of AB was consistent across subcohorts.
Conclusion: This study found no overall beneficial effect from adding AB to OCS treatment for managing acute asthma exacerbations. We suggest that antibiotics should not be used to treat acute asthma exacerbation unless there are clear signs of bacterial infection.

Impact Statement: This study highlights the unjustified prescription of antibiotics in the management of acute asthma exacerbations without clear signs of bacterial infection in the Netherlands. By raising awareness of this issue, we hope to contribute to further decreasing the unnecessary use of antibiotics in the treatment of acute asthma exacerbations.

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of Interest/Disclosures: JvB reports grants and/or consultancy fees from ALK Abello, Aardex, AstraZeneca, Chiesi, European Commission COST Action 19,132 “ENABLE”, GSK, Novartis, Pill Connect, Pfizer, Teva, Trudell Medical and Vertex, all outside the submitted work and paid to his institution (UMCG). He is Co-Chair and member of the European Respiratory Society Clinical Research Collaboration “CONNECT”. The authors report no other conflicts of interest in this work.

P21 Comparing Ecological Momentary Assessment and questionnaires for rating symptoms in patients with COPD

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Introduction: COPD is associated with respiratory and non-respiratory symptoms like fatigue and anxiety, which negatively impact quality of life. Traditional tools rely on retrospective reporting, introducing recall bias and missing symptom variability. Ecological Momentary Assessment (EMA) addresses these limitations by capturing real-time symptom data in natural environments.
Aims and Objectives: This study compares EMA symptom ratings with questionnaire scores in patients with COPD.
Materials and Methods: FAntasTIGUE study participants rated tiredness, dyspnea, anxiety, and energy on a 7-point Likert scale via 8 daily EMA questionnaires for 5 days. Tiredness was also assessed using the Checklist Individual Strength – subscale subjective Fatigue (CIS-Fatigue) and the Symptom Checklist Visual Analogue Scale (SCV). Dyspnea was measured using the modified Medical Research Council (mMRC) Dyspnea Scale, the Physical Activity Rating Scale - Dyspnea Questionnaire (PARS-D), and SCV. Anxiety was assessed using the Hospital Anxiety and Depression Scale (HADS) and SCV, while energy was measured using the COPD Assessment test (CAT). Spearman correlations and multilevel models analyzed associations between methods.
Results: Among 54 patients (67±7 years, FEV1% 53±20, 63% men), the EMA response rate was 76.1%. EMA scores correlated moderately to strongly with corresponding questionnaire scores (rs = 0.49 – 0.78, all p≤0.05). Higher EMA scores corresponded with higher questionnaire scores (all p≤0.05).
Conclusion: EMA is a valid and complementary tool for assessing symptoms in patients with COPD. By capturing real-time variability, it enhances understanding of symptom burden and supports personalized management.

Impact Statement: This research shows that tracking symptoms in real time using a smartphone—through a method called Ecological Momentary Assessment (EMA)—can be just as accurate as traditional questionnaires. Unlike those questionnaires, EMA also reveals how symptoms like fatigue and breathlessness change throughout the day. For people with chronic obstructive pulmonary disease (COPD), this helps doctors better understand what patients experience in their daily lives, allowing for care that's more personalized and responsive to their needs.

Funding: This project is supported by grant 4.1.16.085 of Lung Foundation Netherlands, Leusden, the Netherlands; AstraZeneca Netherlands; Boehringer Ingelheim Netherlands; and Stichting Astma Bestrijding, Amsterdam, The Netherlands.

Conflict of Interest/Disclosures: MVH and YMJG report research grant 4.1.16.085 from Lung Foundation Netherlands. MSYT reports research grant from Lung Foundation Netherlands. RTMS reports payment from GSK for lectures and from PENTAX Medical. EWMAB reports research grants from The Dutch Research Council (NWO) and The Netherlands Organization for Health Research and Development (ZonMw). DJAJ reports research grants from Dutch Foundation for Asthma Prevention and the Netherlands Respiratory Society (award), payment from Chiesi, Abbot and AstraZeneca (all

paid to the institution). MAS reports research grants from Lung Foundation Netherlands, Dutch Foundation for Asthma Prevention, AstraZeneca, TEVA, Boehringer Ingelheim and Chiesi. BP, ZE, QD, CB, JBP, EW, MAGS, JHV, SH-W, and AWV declare that they have no competing interests.

P22 Activin Type II Receptor Blockade Impacts Muscle Wasting in Glucocorticoid-Treated Exacerbations of COPD

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Introduction: COPD is often accompanied by muscle wasting. Muscle wasting intensifies during exacerbations of COPD (ECOPD), partially driven by glucocorticoids (GCs) given as standard-of-care treatment
Aim and Objective: As GC-driven wasting partially relies on myostatin signaling, we hypothesized that blocking its receptor (with CDD866) would attenuate muscle wasting in GC-treated ECOPD.
Materials and Methods: Emphysema ('COPD') was induced in male C57BL/6J mice by intratracheal elastase followed by vehicle or lipopolysaccharide (LPS) instillation to evoke pulmonary inflammation, mimicking ECOPD. Dexamethasone (GC) was injected daily ('GC-ECOPD') and CDD866 (CDD, provided by Versanis Bio) once with the first GC dose. µCT scans were made weekly to confirm development of emphysema, and before and 48h after LPS to measure muscle volume. Excised hindlimb muscles were weighed and used for gene expression analyses.
Results: Compared to control, body weight change of GC-ECOPD was lower (-6.4%, $p<0.001$) whereas body weight change of GC-ECOPD/CDD866 was not. GC-ECOPD was not different from GC-ECOPD/CDD866. Muscle weight was reduced in GC-ECOPD compared to control (-6.7%, $p<0.01$), but not in GC-ECOPD/CDD866. GC-ECOPD muscle weight was not different from GC-ECOPD/CDD866. Preliminary analysis of right hindlimb muscle volume change showed no significant difference of GC-ECOPD or GC-ECOPD/CDD866 compared to control (-6.6% and +0.7% respectively, compared to -1.8%). Compared to GC-ECOPD, muscle volume change of GC-ECOPD/CDD866 was significantly higher (+0.7% vs -6.6%, $p<0.05$). Atrogene expression was not increased in GC-ECOPD compared to control but tended to decrease in GC-ECOPD/CDD866 compared to GC-ECOPD (Atrogin-1: $p=0.053$; MuRF1: 0.076).
Conclusion: In conclusion, in this model of GC-ECOPD, CDD866 significantly increased hindlimb muscle volume and tended to reduce atrogene expression. These findings warrant further investigation of myostatin signaling blockade as an approach to prevent or restore GC-treated ECOPD-associated muscle wasting, thereby increasing the therapeutic efficacy of GCs.

Impact Statement: People with COPD often lose muscle mass and function during exacerbations, especially when treated with glucocorticoids like prednisolone as common practice. Muscle loss reduces mobility and quality of life and increases mortality. In our preclinical COPD mouse model, blocking the myostatin signaling pathway involved in muscle breakdown partly preserved muscle mass during a glucocorticoid-treated exacerbation. This pathway therefore poses a novel therapeutic target to minimize exacerbation-mediated muscle wasting in COPD.

Conflict of Interest/Disclosures: none

P23 COPD management and optimisation opportunities in Dutch primary care using the COPDOptimiser

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Introduction: The COPDOptimiser, a class IIa medical device, supports healthcare providers in COPD consultations based on the GOLD recommendations. This study assessed alignment of current COPD management with 2024 GOLD recommendations and opportunities for optimisation.
Methods: COPDOptimiser is used during routine consultations in the Netherlands by primary care nurses in patients with COPD. COPDOptimiser input and output are collected during these consultations. Data from patients enrolled between October-December 2024 were analysed.
Results: Sixteen primary care practices recruited 68 patients with COPD (mean age 70.3 (±8.7 SD) years; 57% male). Of these, 30% had experienced an exacerbation in the past year; 22% did not use a maintenance inhaler, 31% used a single bronchodilator, and 15% were on triple therapy. The data shows that in 65% of the cases, the COPDOptimiser recommended a change in current (inhaled) pharmacotherapy. In 49% of the cases, a referral to pulmonary rehabilitation was recommended. Vaccination was recommended for 30% (Influenza), 36% (pneumococcal), and 41% (Covid) of the patients.
Discussion: In the majority of patients, multiple opportunities for treatment optimisation (and, thus, potential outcome improvement) were identified, highlighting that validated tools like the COPDOptimiser could aid and educate healthcare providers and support delivery of evidence-based COPD management in primary care.

Impact Statement: Implementation of the COPDOptimiser will support healthcare professionals in providing optimal care for their patients with COPD by providing individualized GOLD-guided management suggestions. By implementing this novel tool in routine clinical practice and evaluating the GOLD-guided management suggestions, we will be able to describe the modifiable factors which can be optimized in current COPD care in Dutch primary care. Next, we will collect further information on the barriers and facilitators for broader implementation.

Funding: This study was supported by a sponsorship from AstraZeneca

Conflict of Interest/Disclosures: Professor Kocks reports grants, personal fees and non-financial support from AstraZeneca, grants, personal fees and non-financial support from Boehringer Ingelheim, grants and personal fees from Chiesi Pharmaceuticals, grants, personal fees and non-financial support from GSK, grants and personal fees from Novartis, grants from MundiPharma, grants from TEVA, outside the submitted work. IvG, EH, were employed by General Practitioners Research Institute (GPRI) at the time of the study. In the past four years (2022-2025), GPRI conducted investigator- and sponsor-initiated research funded by non-commercial organizations, academic institutes, and pharmaceutical companies (including ALK-Albello, AstraZeneca, Boehringer Ingelheim, Chiesi, Eli Lilly, GSK, Mundipharma, Novartis, Teva, and Valneva)

P24 Improving breathlessness diagnostics in primary care: the "Breathlessness Diagnostics in a Box" (BiaB) multi-country stepped-wedge RCT

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Introduction and methods: Breathlessness is common and often multifactorial. We are conducting the multi-country stepped-wedge cluster RCT "Yellow Box – Breathlessness Diagnostics in a Box (BiaB)" to evaluate its impact on time to diagnosis in routine primary care.
Methods: The BiaB box includes an oscillometer/spirometer (ALDS), 4-patch 12-lead ECG, point-of-care NT-proBNP & D-dimer, pulse oximeter, and an iPad with BiaB app providing integrated interpretation. The study is ongoing in NL, ES, and PT, with a usual care period followed by an intervention period using BiaB. We analysed inclusion reasons, demographics, and test results to date.
Results: 277 patients have been included (900 expected) (mean age 62.7±15.9 years, 50.4% male). Of these, 63.8% had new-onset breathlessness; 36.2% had worsening or unexplained symptoms in existing disease. Data from 65 intervention patients show abnormal results in the BiaB box tests in the following proportions: 43% for lung function tests (oscillometry ± spirometry), 76% for ECG, 14% for NT-proBNP, 37% for the PHQ-4 questionnaire, and 32% for oxygen saturation. Patients could have more than one abnormal result.
Conclusion: Early findings show BiaB often detects relevant abnormalities, supporting its potential to expedite diagnosis. Diagnostic outcome and treatment changes are expected this summer.

Impact Statement: Breathlessness is a symptom in various conditions and a common reason for consulting a general practitioner. There is a lack of quick and easy tests that can be used in primary care to diagnose the cause of breathlessness. Therefore, we have developed BiaB, an easy and quick tool intended to support healthcare professionals with fast execution of diagnostic procedures required to diagnose the cause(s) of breathlessness. We will now investigate implementation of BiaB in primary care.

Funding: This study is financially supported by AstraZeneca.

Conflict of Interest/Disclosures: Professor Kocks reports grants, personal fees and non-financial support from AstraZeneca, grants, personal fees and non-financial support from Boehringer Ingelheim, grants and personal fees from Chiesi Pharmaceuticals, grants, personal fees and non-financial support from GSK, grants and personal fees from Novartis, grants from MundiPharma, grants from TEVA, outside the submitted work. IvG, ML, GP, EH, were employed by General Practitioners Research Institute (GPRI) at the time of the study. In the past four years (2022-2025), GPRI conducted investigator- and sponsor-initiated research funded by non-commercial organizations, academic institutes, and pharmaceutical companies (including ALK-Albello, AstraZeneca, Boehringer Ingelheim, Chiesi, Eli Lilly, GSK, Mundipharma, Novartis, Teva, and Valneva)

P25 Assessing lifestyle goal setting in patients with COPD

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Introduction: Healthy lifestyle changes can reduce symptoms and slow disease progression in patients with COPD. Understanding patient willingness to engage in lifestyle goal setting and the factors influencing this process could help tailor more effective approaches to support long-term behavior change.
Aims and Objectives: This study investigated patients' willingness to set lifestyle goals during personalized counseling and differences in general characteristics between goal- and non-goal-setters.
Materials and Methods: As part of an ongoing RCT (NCT03807310), patients received monthly phone calls from researchers offering lifestyle counseling on diet and physical activity, using a motivational interviewing approach. Data were analyzed for a subset of patients, who had completed the trial on 12 February 2025. Standardized counseling notes, drafted by the researchers, were used to assess the willingness to set lifestyle goals over 12 months of counseling (yes/no), and baseline trial data for patient characterization.
Results: Data from 103 patients, including 29 trial dropouts (mean age: 68.3±6.5 years, BMI: 26.3±4.9, FEV1: 56.6±17.9% predicted, 61.2% male), were analyzed. Overall, 65% were willing to set lifestyle goals. No differences in sex, age, BMI or FEV1 were observed between goal- and non-goal-setters.
Conclusion: The majority of patients with COPD were willing to set lifestyle goals during personalized counseling, while common demographic and physiological factors did not explain willingness for lifestyle changes. Further research will explore reasons for unwillingness, additional differences between goal- and non-goal-setters in physiological, motivational, and lifestyle characteristics, and the type, adjustment, and achievement of goals over time.

Impact Statement: This research shows that most people with COPD are willing to set lifestyle goals when supported through personalized counseling. Understanding what helps or hinders goal-setting can lead to better support for long-term lifestyle changes. These insights may help healthcare providers design more effective, tailored programs to improve quality of life and slow disease progression for individuals living with COPD.

Funding: The NUTRECOVER trial was supported by a LSH-TKI Lung Foundation grant (10.2.16.119, 2017: ‘Food for thought and active lifestyle in COPD’)

Conflict of Interest/Disclosures: Ardy van Helvoort is employed by Danone Research & Innovation, Utrecht, Netherlands.

The presenting author has no, real or perceived, conflict(s) of interest that relate to this abstract.

P26 The effect of eosinophilia on pulmonary rehabilitation outcomes in COPD

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Introduction: Pulmonary rehabilitation (PR) reduces symptoms and exacerbations in COPD. Eosinophilia is a biomarker in COPD, but its effect on PR outcomes is unknown.
Aim: To evaluate the effect of eosinophilia on PR-induced change in CCQ and annualized exacerbation rate in COPD.
Methods: From the Radboudumc PR database, data was extracted from COPD patients who had completed a 10-week PR program (Jan 2017-Feb 2023) and 1-year follow-up, and who had available blood eosinophil count at pre-PR assessment. We extracted age, gender and FEV1 (pre-PR), CCQ score (pre-PR and at PR conclusion) and self-reported number of prednisolone/antibiotic courses and hospitalizations for exacerbation in the previous year (pre-PR and at 1-year follow-up). Eosinophilia was defined as blood eosinophils ≥300/µL. Baseline characteristics were compared with the appropriate statistics. Repeated measures ANOVA was performed with interaction time*eosinophilia to analyze change in CCQ, change in number of prednisolone/antibiotic courses, and change in number of hospitalizations for exacerbation. P<0.05 was considered significant.
Results: Data were available of n=244 COPD patients (55% female). At pre-PR assessment, mean (SD) age was 62 (8) years, FEV1 43 (16) %predicted, CCQ 2,7 (0,9), and blood eosinophil count 200 (220)/µL. Patients reported a mean(SD) number of prednisolone/antibiotic courses of 2,11 (1,91) and 0,73 (1,23) hospitalizations for exacerbations in the year preceding PR. Forty-six patients (19%) had eosinophilia. Age, gender, FEV1, CCQ and number of prednisolone/antibiotic courses and number of hospitalizations for exacerbation in the year preceding PR were comparable between patients with and without eosinophilia (all p>0.05). ANOVA showed a significant overall effect of PR on CCQ (mean difference -0.74, 95%CI -0.60 -- -0.88; p<0.001), number of prednisolone/antibiotic courses (-0.33, -0.66 -- -0.00; p=0,048), and number of hospitalizations for exacerbation (-0.24, -0.44 -- -0.04; p=0.020), but neither of these analyses revealed an interaction of time*eosinophilia (all p>0.05).
Conclusion: These results suggest that PR is equally effective in COPD patients with and without eosinophilia in terms of CCQ improvement and reduction in annualized moderate and severe exacerbation rate.

Impact Statement: In light of the anticipated approval of biologics for eosinophilic COPD, our data indicate that pulmonary rehabilitation remains highly relevant to consider as a means to improve symptoms and decrease exacerbations.

Conflict of Interest/Disclosures: BVDB reports consulting, presentation, and travel fees/support by AstraZeneca B.V., Chiesi Pharmaceuticals B.V., Sanofi B.V., Boehringer Ingelheim bv, and Genzyme Europe B.V. All payments were made directly to his institution, and all were outside the scope of the current study.

JBP reports no conflict of interest.

BR reports travel support from Chiesi Pharmaceuticals B.V. All payments were made directly to his institution, and all were outside the scope of the current study.

P27 Effect of methotrexate and prednisone on intermediate monocytes in pulmonary sarcoidosis

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Introduction: In sarcoidosis, the inflammatory subset of CD14+/CD16+ intermediate monocytes (IM) have been found to correlate with disease severity and prognosis. We assessed the percentage of IM in patients with pulmonary sarcoidosis during their treatment with either methotrexate (MTX) or prednisone as exploratory endpoint of the PREMDETH trial.
Method: Monocytes were measured by FACS in whole blood and IM were identified. Mann-Whitney U tests were used to test for differences between groups.
Results: During treatment with MTX there was no change in percentage of IM over the course of 24 weeks. In patients treated with prednisone percentage of IM decreased significantly resulting in a median change of -61% at 4 weeks, -50% at 16 weeks and -42% at 24 weeks ($p < 0.001$, < 0.001 and 0.001). At 4, 16 and 24 weeks mean percentage of IM was significantly different between MTX and prednisone.
Conclusion: While prednisone and MTX are both anti-inflammatory drugs and equipotent in improving FVC after 24 weeks of treatment of patients with pulmonary sarcoidosis during the PREDMETH trial, there is a difference in levels of circulating IM between both drugs. Our data suggests that compared to prednisone, the anti-inflammatory effect of MTX in patients with sarcoidosis does not involve an effect on the IM monocytes in the peripheral circulation.

Impact Statement: Monocytes are key players in sarcoidosis and are affected by first, second and third line treatments. Every insight in how monocytes and their subpopulations are affected by the different treatment options and what the monocyte profile looks like before treatment brings us one step closer to personalized treatment for patients with sarcoidosis. Not only leading to a faster relief of burden of disease but also less side effects from ineffective treatment.

Funding: Longfonds and St. Antonius Onderzoeksfonds

Conflict of Interest/Disclosures: none

Posters: Modelling complex lung biology to understand disease

P28 The Effects of Nandrolone on Muscle Wasting in a Mouse Model of Glucocorticoid-Treated Exacerbations of COPD

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Introduction: COPD is often accompanied by muscle wasting. This muscle wasting intensifies during exacerbations of COPD (ECOPD), which is partially driven by glucocorticoids (GCs) that are given as standard-of-care treatment.
Aim and objective: We hypothesized that the anabolic steroid nandrolone, which stimulates muscle growth, would attenuate muscle wasting in the context of GC-treated ECOPD.
Materials and Methods: Emphysema ('COPD') was induced in male C57BL/6J mice by intratracheal elastase followed by vehicle or LPS instillation to evoke pulmonary inflammation, mimicking ECOPD. Dexamethasone (GC) was injected daily ('GC-ECOPD') and nandrolone decanoate (ND) once with the first GC dose. µCT scans were made weekly to confirm development of emphysema, and before and 48h after LPS to measure muscle volume. Excised hindlimb muscles were weighed and used for gene expression analyses.
Results: Compared to control, body weight of GC-ECOPD was reduced (-6.4%, $p<0.001$) whereas GC-ECOPD/ND was not (-3.2%, $p=0.076$). GC-ECOPD was not different from GC-ECOPD/ND ($p=0.072$). Muscle weight was reduced in GC-ECOPD and GC-ECOPD/ND compared to control (-6.7%, $p<0.001$ and -4.4%, $p<0.05$, respectively). Compared to control, preliminary analysis of (right hindlimb) muscle volume change showed no significant differences for GC-ECOPD or GC-ECOPD/ND (-6.6%, $p=0.057$ and -5.0% respectively, compared to -1.8%). Atrogene expression (Atrogin-1 and MuRF1) was not affected.
Conclusion: In conclusion, in this model of GC-ECOPD, co-treatment with ND did not significantly attenuate loss of body weight, muscle weight or right hindlimb muscle volume. Further and additional analyses of the collected CT scans and tissues will be performed and might reveal underlying processes that provide more information on the effects of nandrolone in this mouse model of GC-treated ECOPD.

Impact Statement: People with COPD often lose muscle mass and function during exacerbations, especially when treated with glucocorticoids like prednisolone as common practice. This research explores whether the well-known anabolic steroid nandrolone protects against muscle wasting during an glucocorticoid-treated exacerbation in a COPD mouse model. Preliminary data so far did not show any beneficial effect, but this need to be verified by more accurate muscle volume data obtained by CT scans and additional tests on tissues obtained in this study.

Conflict of Interest/Disclosures: none

P29 Breathing-related stresses alter fibrogenesis in a human lung fibrosis-on-chip model

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Introduction: Mechanical forces, such as breathing motions, are increasingly recognized for their role in lung cell fate and repair. In fibrotic disease, stiffened niches are formed due to tissue remodelling and respond differently to breathing-related forces. It is currently incompletely understood if (changes in) breathing-related stretch play a role in fibrosis development. Relevant models are needed to integrate complex biology while controllably capturing these mechanical forces. Aims and objectives: Here, we established a fibrosis lung-on-chip to assess the effects of changes in breathing-related stresses on fibrogenesis.
Material and methods: Co-cultures were generated with human primary bronchial epithelial cells (PBECs, top channel) and human primary lung microvascular endothelial cells (bottom channel) in a commercial organ-on-chip platform. Once PBEC were differentiated for one week at the air-liquid interface, chip cultures were exposed to airflow and cyclic stretch (5% strain, 0.25 Hz) to mimic breathing for an additional week. Next, part of the chip cultures were exposed to a combination of pro-fibrotic compounds (fibrotic cocktail, FC). Simultaneously, chips were switched to no stretch (0%), maintained stretch (5%) or increased stretch (12%) for 3 days. Expression of pro-fibrotic genes was assessed by qPCR, inflammatory cytokine production by ELISA, and protein expression by IF.
Results: Our preliminary results show that FC exposure increased expression of fibrosis-related genes (e.g. FN1, COL1A1) in the maintained and 0% chip cultures. Exposure to 12% stretch suppressed fibrotic (FN1/COL1A1) responses to FC, and inflammatory responses (IL-8) at baseline, but not in response to FC (n=1-2).
Conclusion: Breathing-related stresses constitute an important factor in response to pro-fibrotic stimuli.

Impact Statement: Our preliminary data gives new insights into how physical forces, such as the stretching during breathing, may influence the development of lung scarring (lung fibrosis). Using an advanced platform that mimics real lung function, our study suggests that changes in breathing stretch motions can affect how the lungs respond to stimuli that cause fibrosis. These findings show the importance of mechanical forces in lung disease, which could help to find new treatment strategies for lung fibrosis in the future.

Funding: This study was supported by ZonMw (grant #10430132230002).

Conflict of Interest/Disclosures: none

P30 A perfused muscle-on-chip platform to study muscle impairments in COPD

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INTRODUCTION: Skeletal muscle (SKM) is known to engage in inter-organ crosstalk. As SKM impairments in COPD arise together with lung pathology, it is plausible that SKM impairments arise after interactions with diseased lung tissue. However, platforms for studying the direct impact of lung cells on SKM are inadequate, as they lack any perfusion (flow) of culture medium and do not support the connection of multiple organ cultures.
AIMS AND OBJECTIVES: We aimed to develop a novel perfused muscle-on-chip (MoC) suitable for culture and differentiation of SKM cells, which can be connected with lung-on-chips to study their interactions. To achieve this, we aimed to I) select suitable MoC materials (plastics), geometry and medium flow rate; and II) validate muscle culture and differentiation of muscle cells on these MoCs on a biochemical level.
METHODS: Five candidate plastics were assessed for biological compatibility with murine C2C12 myocytes under static conditions using brightfield microscopy. MoC dimensions and perfusion conditions were determined with computer simulations to mimic physiologically relevant shear stress. Based on these parameters, we designed two final MoC prototypes, which we then biologically validated by culturing and differentiating C2C12 myocytes under flow conditions and evaluated their differentiation capacity by brightfield imaging, immunofluorescent staining of myosin heavy chains (MyHC) and expression levels of myogenic and proliferation genes on day 0 vs day 6 of differentiation.
RESULTS: Brightfield microscopy revealed the best myotube formation on polystyrene under static conditions, which was therefore selected as the base material for the MoC designs. An oxygen-permeable and an oxygen-impermeable MoC were then designed based on computer simulations. Equal myotube formation and MyHC staining were observed in cells differentiated in both MoCs under a flowrate of 10 µL/minute and mRNA expression of myogenic genes increased from day 0 to day 6 of differentiation, while the mRNA expression of proliferation markers decreased as expected.
CONCLUSION: These data show that our novel perfused MoC platforms are suitable for C2C12 myocyte culture and differentiation. This approach offers a novel platform to study inter-organ crosstalk in COPD and may help uncover new mechanisms and therapeutic targets for muscle dysfunction in COPD.

Impact Statement: Muscle weakness in COPD may be mediated by signals from diseased lungs, but laboratory models to study this possible interaction are lacking. We developed a new muscle-on-chip that supports physiologically relevant muscle cell growth and differentiation. Our muscle-on-chip can connect to lung-on-chip models, allowing direct study of lung–muscle interactions. Our new muscle-on-chip will guide the development of new therapies for muscle weakness in COPD, while reducing animal research.

Funding: This project is part of the P4O2 consortium and co-funded by the PPP Allowance made available by Health~Holland, Top Sector Life Sciences & Health (LSHM20104; LSHM20068).

Conflict of Interest/Disclosures: none

P31 Extracellular matrix mechanical modulation of lung mesenchymal stromal cells improves the capacity for supporting tissue repair in COPD

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Introduction: In COPD, disruption of the extracellular matrix (ECM) compromises lung tissue mechanical properties and contributes to disease progression by impairing structural support and inducing cytoskeletal changes, which can impede mitochondrial function and affect cellular behaviour. Lung-resident mesenchymal stromal cells (LMSCs) maintain lung homeostasis by supporting alveolar epithelial repair through mitochondrial transfer and growth factor secretion, such as hepatocyte growth factor (HGF), which is impaired in COPD.
Aims and Objectives: We hypothesized that altering the ECM mechanical cues could restore disrupted LMSC-ECM interactions in COPD, thereby improving the regenerative function of LMSCs..
Materials and Methods: Collagen-derived gelatin methacrylate (GelMA) hydrogels were crosslinked with 0.5 mg/ml or 1 mg/ml lithium phenyl-2,4,6-trimethylbenzoylphosphinate (LAP), providing 2 mechanical environments (GelMA 0.5 and GelMA 1) representing the stiffness range in healthy lung tissue. LMSCs from COPD patients and controls were cultured on plastic or GelMA hydrogels. HGF expression, cell morphology, cellular composition and mitochondrial function were evaluated.
Results: HGF mRNA and protein levels were lower in COPD compared to control LMSCs cultured on plastic. Culture on GelMA 0.5, increased HGF levels for both COPD and control. COPD-derived LMSCs displayed impaired mitochondrial function and altered mitochondrial distribution. Culturing on GelMA restored mitochondrial function in COPD-derived LMSCs to levels comparable to controls. It also improved mitochondrial morphology, showing well-defined cristae and reduced swelling, similar to that observed in control LMSCs.
Conclusion: This study suggests that modulating the ECM mechanical microenvironment has the potential to restore the reparative properties of LMSCs in COPD and could thus be a promising strategy to enhance tissue regeneration in COPD.

Impact Statement: This research shows that adjusting the stiffness of the environment around lung stem cells can help restore their natural ability to repair damaged tissue in COPD. By mimicking healthy lung conditions, the study improved stem cell function and energy production, suggesting a promising new approach to support lung regeneration in people with COPD.

Funding: Longfonds

Conflict of Interest/Disclosures: Rousselot provided the hydrogel used in this study.

P32 Long-term airway alterations in prematurity-related lung disease: insights from a preclinical ovine model

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Introduction: Prematurity is associated with adverse lung outcomes, and emerging evidence indicates that prematurity-related lung disease (PRLD) is a distinct clinical entity. However, its pathophysiology across lifespan remains largely unknown.
Aims: We aimed to elucidate the pathophysiology of PRLD using a preclinical ovine model comprising prematurity, antenatal inflammation, and neonatal oxygen therapy.
Material and Methods: Ovine fetuses were intra-amniotically exposed to lipopolysaccharide (LPS 5mg) or saline (control) at 125d gestation. At 132d gestation (30-32w human gestation) fetuses were delivered preterm, ventilated for 48h and subsequently hand-reared until adulthood (1y). Longitudinal lung function and provocation test were correlated with MRI and postmortem tissue analysis at 1y and compared to term born controls.
Results: LPS-exposed lambs required higher and longer oxygen support and had more respiratory events up to 2m of age. At adulthood, airway hyperreactivity in ventilated preterm lambs was accompanied by smooth muscle hypertrophy and epithelial remodeling of bronchioles, which was not aggravated by LPS-exposure. Moreover, all preterm animals had a reduced number of bronchioles and formation of inducible bronchus-associated lymphoid tissue, but no differences in immune cells in bronchioalveolar lavage fluid were observed compared to term born controls at 1y.
Conclusion: While antenatal inflammation negatively impacts lung function around birth, long term structural and functional airway alterations were primarily driven by prematurity and mechanical ventilation, providing mechanistic insights into PRLD and creating opportunities to develop new diagnostics and therapies for PRLD.

Impact Statement: This study in a clinically relevant large animal model shows that prematurity and perinatal events including antenatal inflammation and mechanical ventilation cause persistent structural and functional pulmonary abnormalities. This study reveals that the mechanisms underlying adverse pulmonary outcomes following preterm birth are distinct from classical respiratory conditions, emphasizing PRLD as distinct and mechanistically defined disease entity. The established clinical phenotype in our ovine model creates a unique platform to advance insights into PRLD pathophysiology and subsequent development of targeted therapy.

Funding: This work was financially supported by the Dutch Lung Foundation (Grant no. 6.1.16.088 to NLR, and TGAMW).

Conflict of Interest/Disclosures: none

P33 AT2R agonists buloxibutid (Compound 21) and NAc inhibit fibrogenesis in human precision cut lung slices ex vivo

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Introduction: Buloxibutid, also known as Compound 21 (C21), is an angiotensin type 2 receptor AT2R agonist in early clinical trials for IPF, having shown antifibrotic efficacy in a bleomycin mouse model (PMID 29636695; 2018).
Aims and Objectives: To compare C21 with an experimental AT2R agonist NAc and the IPF drug pirfenidone (PFD), using human precision cut lung slices (hPCLS).
Materials and Methods: Matched hPCLS from agarose-inflated lungs were left untreated or stimulated with fibrotic cocktail (FC = TGFβ1, TNFα, LPA, PDGF; PMID 28314802; 2017) ± C21 (10μM), NAc (10μM) or PFD (500μM). In situ fibrosis was assessed after 120h by Masson's trichrome staining. Secreted cytokines and extracellular matrix proteins were measured by ELISA in hPCLS-conditioned media collected at 48h and 120h respectively.
Results: FC did not induce collagen deposition in hPCLS but increased secretion of both procollagen 1α1 (ng/mL: vehicle 40±12; FC 209±28, n=21, $p<0.01$, paired t-test) and fibronectin (□g/mL: vehicle 1.6±0.2; FC 4.4±0.3, n=15, $p<0.01$). C21 and NAc, but not PFD, significantly reduced secretion of both matrix proteins ($p<0.05$, one-way ANOVA, n=17, 14). Both AT2R agonists performed as well as PFD in inhibiting FC-induced IL-6 and IL-8 secretion ($p<0.05$, one-way ANOVA, n=5).
Conclusion: Fibrogenesis and inflammation can be modelled ex vivo in hPCLS using a cocktail of IPF-relevant mediators. C21 and NAc, at a 50-fold lower concentration than PFD, significantly reduced secretion of fibrogenic and inflammatory markers. Future studies to establish reversal of fibrosis by AT2R agonists in hPCLS from IPF lung would address a major limitation of current therapy and further support clinical translation of this novel drug class for IPF.

Impact Statement: IPF is an incurable disease, with the current treatment pirfenidone limited in both efficacy and tolerability. Buloxibutid (C21), a first-in-class AT2R agonist, inhibits and reverses fibrosis in pre-clinical PF models, and has progressed to Phase 2b human trials. This is the first translational study using ex vivo human lung slices to demonstrate inhibition of fibrogenesis by both C21 and the more highly selective AT2R agonist NAc with superior efficacy to pirfenidone, supporting AT2R as a novel therapeutic target for IPF.

Funding: Australian Government Research Training Program scholarship; Lung Foundation of Australia David Wilson PhD scholarship

Conflict of Interest/Disclosures: none