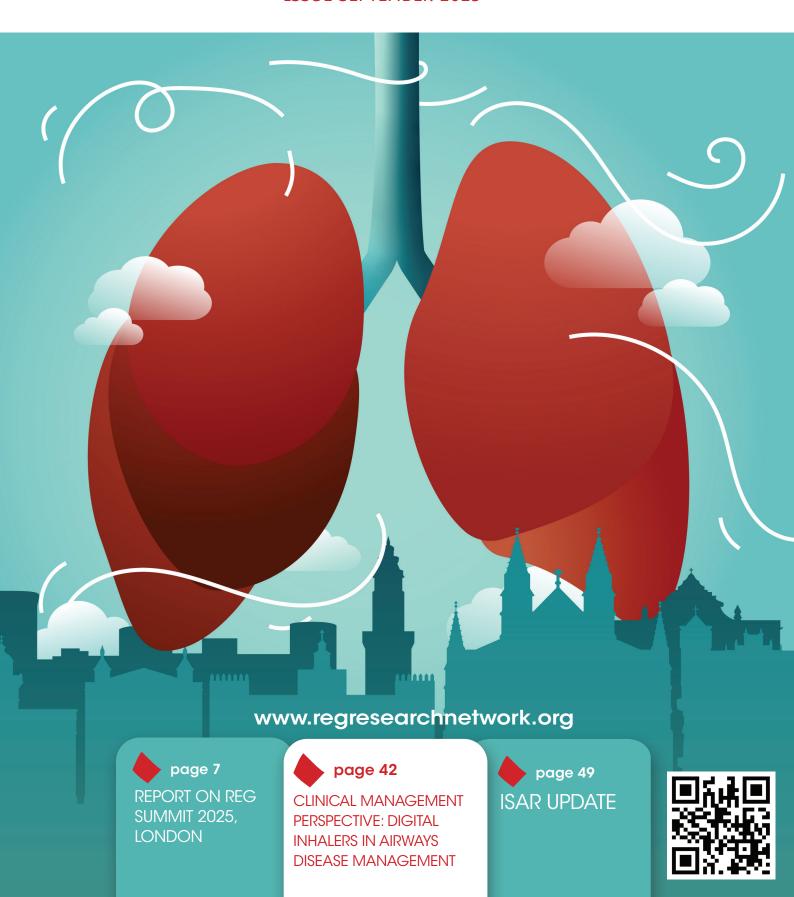


Respiratory Effectiveness Group

# in Real-life Respiratory Research

The Respiratory Effectiveness Group Newsletter ISSUE SEPTEMBER 2025







THE RESPIRATORY
EFFECTIVENESS
GROUP NEWSLETTER
ISSUE SEPTEMBER 2025

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Respiratory Effectiveness Group

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#### CELEBRATING RESPIRATORY EFFECTIVENESS RESEARCH

Here at REG we hope you all had a great summer and enjoyed some sort of summer holidays before our "back to school", as the new season appears frantic. Briefly, let me summarize a few new REG developments since the last Newsletter back in February, namely on EAACI, REG visibility, and a journal.

But first, we are soon looking forward to meeting you all in Amsterdam for another exciting ERS Annual International Congress, that will take place from 27 September to 1 October in Amsterdam, NL [https:// www.ersnet.org/congress-and-events/congress/1.The ERS Congress is the largest gathering of respiratory experts worldwide, typically attracting over 20,000 delegates from more than 100 countries, including GPs, pulmonologists, respiratory physicians, scientists, nurses, physiotherapists, psychologists, public health officers, and other healthcare professionals. The contribution of REG individuals in the official programme is again substantial, so there is little doubt that real-world research will be showcased and well framed there.

Back to full REG business, we are happy to share we have just signed a Memorandum of Understanding with the European Academy of Allergy and Clinical Immunology (EAACI) that seals the extremely fine relationship of our two societies, confirms the participation of membership from both parties in our respective meetings, and the authorship of documents. As tokens discussed with Dr María José López, EAACI President, we are looking forward to meeting in the forthcoming EAACI Pediatric Allergy and Asthma Meeting (PAAM) 2025, that will take place on 23 - 25 October in Palma de Mallorca, Spain, showcasing the topic "Pediatric Allergy Matters: Inspiring Insights for Every Family" [https://eaaci.org/ events\_meetings/paam-2025/]; or at the 24th EAACI Immunology Winter School on Basic Immunology Research in Allergy and Clinical Immunology, that will take place 15 - 18 January 2026 in Sierra Nevada, Spain [https://eaaci.org/events\_allergy/immunology-winterschool-2026/]; and, we look forward to the progress of the landmark EAACI Guidelines on Environmental Science for Allergy and Asthma, that will give evidencebased recommendations for prevention and public health action to mitigate the impact of pollen exposure on respiratory allergy, also co-authored by significant REG members.

# EDITORIAL

# Joan B. Soriano **REG** President

As a scientific society, REG is exploring to have its own scientific journal. Few of you would disagree that this Newsletter has been sort of the embryo of one. We are browsing options within the many available publishers and business models, to tailor something new and ultimately useful, that fits an unmet niche within the growing respiratory arena, and helps the REG growth. Hopefully by the end of 2025 we will have exciting news to share.

On visibility, this President and REG as a whole were nicely spotted in the Lancet Respiratory Medicine August issue, focused on chronic respiratory burden worldwide, all available at <a href="https://www.thelancet.com/journals/lanres/article/">www.thelancet.com/journals/lanres/article/</a> PIIS2213-2600(25)00253-X/fulltext. Further on visibility and internationalization, we are also exploring the practicalities of small regional meetings to spread the word on real-life and comparative effectiveness research in respiratory medicine. These scientific meetings could help with local improvements to understanding of the optimum role of real-life data to inform meaningful clinical practice guidelines, drug licensing and post-marketing surveillance processes and improved patient care. Stay tuned.

Last, but indeed not least, our 2026 REG Annual Summit is shaping well. The Summit is our raison-d'être. Already mark in your calendars, and in bold letters, the dates 19 - 21 March 2026, to meet at Meliá Palma Marina hotel, in lovely Palma de Mallorca, Spain. Dr Alan Kaplan and his team at the Scientific Committee are delivering again a second-to-none program combining topics and speakers that cover broad topics in real-life respiratory research. Further info soon at www.regsummit2026.org. Our CEO Mr Michael Walker and his team are working hard to have the best mid-size respiratory meeting in the world, and combining scientific rigor within a friendly, business environment; and as a local, I will offer you my heart, lungs and soul to guarantee that you remember Mallorca for a long time, if not forever.

Please do not hesitate to contact Michael, myself, or anyone at the REG Board should you have comments or ideas to share. As the Dutch wisely say: "Werk hard, maar feest nog harder", that is "Work hard, party harder!". We will try in Amsterdam soon, then Palma... And thank you again.

#### Joan B. Soriano

President of REG

Pneumology Department

Hospital Universitario de la Princesa -

Universidad Autónoma de Madrid Madrid (SPAIN)



# REG TEAM UPDATE



Michael Walker REG CEO

The very successful REG Summit was held in central London from 20th to 22nd March, at the prestigious Royal College of Physicians. The stimulating scientific programme provided participants with valuable opportunities for in-depth discussions on the many issues and controversies that challenge everyday care of patients. More details about the meeting can be found in this issue.

On the day prior to the Summit meeting, REG Working Groups met to discuss and continue to develop their respective research projects. Our Working Groups continue to provide an important opportunity for our collaborators and supporters to connect, continue our active projects, or discuss new projects in development.

The last few months have also been focused on the various REG research projects that are in development with an update available in this edition. Here are two examples of our current projects in progress:

- Severe Asthma: A global evaluation of the economic impact of time to initiation of biologic treatment of severe asthma patients
- Predicting the Risk for First COPD Severe Exacerbation (PRECISE-X): To develop a risk model using common respiratory variables as indicators to help clinicians assess an individual's risk of a severe exacerbation at the time of diagnosis.

A more detailed update of these activities can be found later in this issue. If you would like to know more about these or any of our other projects, please contact REG at enquiries@regresearchnetwork.org.

In this issue, you will find more insights into what REG means to our collaborators and supporters, an article on digital inhalers in airways disease management as part of the Clinical Management Perspectives series as well as an update on the tremendous work of the International Severe Asthma Registry (ISAR).

An important Save The Date Announcement: the next REG Summit will be held in Palma de Mallorca, Spain, from 19th to 21st March 2026, at the Meliá Palma Marina hotel, which is centrally located and a short ride from the airport. We hope everyone can join us for what promises to be a very exciting and special programme.

Lastly, I would like to acknowledge the support from our long-term supporters. Without their ongoing collaboration, much of the work of REG would not be possible. I hope others are encouraged by the activities of REG and the REG Working Group meetings and will consider collaborating with us later this year or planning to do so in 2026. We will continue to support and reach out to our partners as we work together in real-life research.



# Transforming Respiratory Care

Our ambition is to transform Respiratory and Immunology care for patients, moving beyond symptom control to disease modification, remission and, one day, cure.





# **CALL FOR NOMINATIONS FOR THE FIRST REG REAL-LIFE RESPIRATORY AWARD**

To celebrate the first decade of the Respiratory Effectiveness Group (REG), we are proud to launch the REG Real-Life Respiratory Award. This new annual recognition will honour an individual whose life-time achievements have made an outstanding contribution to lung health through real-life and comparative effectiveness research and advocacy in respiratory medicine.

#### Who is eligible?

We welcome nominations of individuals worldwide who have significantly advanced respiratory health in any of the following areas:

- Primary Care
- Chest Medicine
- · Allied Health Professions (e.g., Nurses, Physiotherapists, Pharmacists, Epidemiologists, Health Economists, Patient Advocates, and Healthcare Policymakers)
- Other disciplines with a strong and lasting dedication to lung health

The nominee should serve as a living tribute by significantly having helped with setting quality standards in the field of real-life research and improving our understanding of the optimum role of real-life data to inform meaningful clinical guidance, policy and decision-making for the benefit of improved patient care.

#### Candidates should have demonstrated:

- · Leadership in real-life or comparative effectiveness research
- Measurable impact on patient care, clinical guidance, or health policy
- · Innovation and excellence in using realworld data to improve outcomes

Both REG and non-REG collaborators may be nominated; there are no geographic restrictions (nominees are welcome from any country); self-nominations or posthumous nominations are not permitted.

#### The Award:

The recipient will receive:

- · A commemorative plaque
- Complimentary registration and travel support to attend the next REG **Annual Summit**
- An opportunity to deliver an honorary lecture at the REG Annual Summit
- Recognition across REG communications and website

#### **Procedures:**

Call for Nominations: A public call for nominations is being made through REG communication channels. Nominations can be submitted by email to any **REG Board member**.

Nomination deadline: Nominations close at midnight (CET) on Wednesday 3rd December 2025.

Conflict of Interest: REG Board members must declare any conflicts of interest with any nominee and will be recused from discussion or voting concerning that nominee. The REG Board will decide the awardee by openly discussing the merits of eligible candidates, and voting democratically and blindly, by absolute majority, or if not, by relative majority.

The decision of the REG Board will be final.

The first award ceremony will take place during the REG Summit in Palma de Mallorca, March 19 - 21 2026.

Let's celebrate more than a decade of real-world respiratory impact by honouring those who made it possible!





# **REG SUMMIT 2025**

The REG Summit 2025 was a tremendous success and attracted a wide audience from around the world. The event took place from 19th to 21st March. Close to 130 participants from 25 countries travelled to London for the meeting. The Summit included a Working Group Research Ideas brainstorming session, 12 exciting sessions on a wide and diverse range of key issues and topics in respiratory health, featuring talks and debates from esteemed speakers and guests. The Summit was accredited by the European Board for Accreditation in Pneumonology (EBAP) with 12 CME credits covering the whole program and the Summit was designated Compliant with provisions of the MedTech Europe Code.

The Scientific Programme included sessions on:

- Inhaler Session Propellants, planet, and the patient the real-life impact
- ILD/IPF Time taken from primary care referral to a specialist centre diagnosis of idiopathic pulmonary fibrosis
- Readers', authors', and editors' perspectives on observational research
- Early Career Travel Grant Winners Oral Presentation
- COPD & Bronchiectasis
- United Airways Disease
- Vaccine PRO/CONs discussing "Pneumococcal vaccine is the most important respiratory vaccine for our high-risk patients to receive" and "RSV is the most important respiratory vaccine for our high-risk patients to receive"
- Al/Digital in Respiratory Diseases
- •Asthma Session Expansion of biologic use in asthma: Where to?
- ISAR Registry Improving severe asthma care ISAR's research and quality improvement highlights
- Integrating RWE into Guidelines

All sessions are available to watch on demand. For more information, go to www.regsummit2025.org

Thanks to all the speakers, session chairs and meeting participants for making it such a great meeting.

Thank you also for the support from our sponsors: Platinum: Chiesi, Gold: Roche, Silver: Bristol Myers Squibb, Menarini and Teva, Sponsor: Adherium and Contributor: Verona Pharma

The REG Summit will return next year in Palma de Mallorca, Spain from 19 - 21 March 2026.

We look forward to seeing you there!









As a new initiative for the REG Summit 2025, Early Career Travel Grants were awarded to the best abstracts submitted by early career professionals. Designed to support early career professionals in the respiratory field, this initiative provides a unique opportunity for these emerging talents to attend the Summit, showcase their research to a targeted audience of medical professionals, and connect with leading experts, potential collaborators, and peers. To encourage and facilitate their participation, the REG Board offered Early Career Travel Grants, and winners presented their research in a special plenary session, as well as a poster throughout the meeting.

#### EARLY CAREER TRAVEL GRANT WINNERS I REG SUMMIT 2025

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PP01	Real-world long-term multicentric study of primary and secondary failure to biologicals in severe asthma Dr. Iria Veiga Teijeir, iriaveigat@hotmail.com, Lucus Augusti University Hospital, Spain
PP03	Significant all-cause mortality following interstitial lung disease inpatient admissions: what can we do?  Dr. Laura White, laurajanewhite@doctors.org.uk, Lancaster University, United Kingdom
PP05	Preliminary results of the Catalan registry of severe COPD patients (SPOCCAT): Differences between exacerbators and non exacerbators Dr. Cristina Aljama, cris.aljama94@gmail.com, Hospital Vall d'Hebron, Spain
PP08	Post-pandemic changes in respiratory mortality in Spain Dr. Adrián Peláez Laderas, apl00028@gmail.com, Centro Nacional de Investigaciones Cardiovasculares Carlos III (CNIC), Spain
PP09	Prevalence of respiratory viruses in stable and acute asthma: A systematic review and meta-analysis  Dr. Sachin Ananth, sachin.ananth14@imperial.ac.uk, National Heart & Lung Institute, Imperial College London, London, United Kingdom

PP11 Real-life impact of anti-IL5 therapy on exacerbation types in patients with obstructive lung disease

Prof. Lies Lahousse, lies.lahousse@ugent.be, Ghent University. Belgium



The meeting attracted abstract submissions which were presented as posters with authors from Belgium, Canada, Colombia, Greece, Italy, Mexico and Spain and UK.

**PP01** 

#### REAL-WORLD LONG-TERM MULTICENTRIC STUDY OF PRIMARY AND SECONDARY FAILURE TO BIOLOGICALS IN SEVERE ASTHMA

Iria Veiga Teijeiro, Laura Arias Zas, Luis Pérez de Llano

Lucus Augusti University Hospital, Lugo, Spain

Methods: This is a multicenter retrospective study of adult patients who received the same biologic for at least 24 months. Response was defined as no severe exacerbations in the preceding 12 months, Asthma Control Test (ACT) ≥20, and no need for maintenance oral corticosteroids (OCS). Failure was defined as the non-achievement of any of the objectives mentioned above. Sustained response (SR) was defined as an absence of failure during the entire follow-up period. PF was defined as no response at 12 months after biologic initiation. SF was defined as loss of response in patients who had achieved it at 12 months.

Results: A total of 315 patients were included, and 272 were finally analyzed. The mean follow-up was 46.1 ± 19.4 months. At 12 months, 175 patients showed a response and 97 showed PF. PF reverted (response was achieved) in 40% of patients at subsequent visits without switching the biologic (by changing inhaled therapy in 74%). Among the 175 patients who achieved a response at 12 months, 124 (70.8 %) experienced SR throughout the entire study period. Compared to patients with SR, those with SF (51, 29.1%) had lower FEV1 values after 12 months of biological therapy. SF reverted in 9 out of 25 (36%) of patients of cases where subsequent follow-up visits were available (inhaled therapy was changed in 41.6% of them) (Figure 1). Interestingly, FEV1 decreased by at least 100 mL from the value at the previous visit in 12 of 16 cases who did not recover response after SF.

Conclusion: This study illustrates that inhaled therapy should be optimized in patients with SA, even after starting biological treatment. Of the patients who show response at 12 months, the majority will maintain it over time, but 29% will lose their response. Lung function appears essential to achieve and maintain response over time.

**PP02** 

#### A REAL-WORLD STUDY ON THE EFFECTIVENESS OF TRIPLE INHALED THERAPY IN **SEVERE ASTHMA**

Laura Arias Zas, Iria Veiga Teijeiro, Luis Pérez de Llano

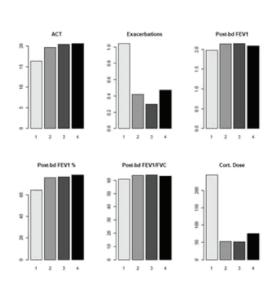
Lucus Augusti University Hospital, Lugo, Spain

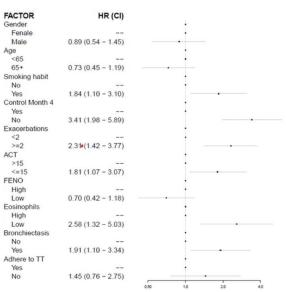
Introduction: The aim of this study was to evaluate the long-term effectiveness of TT in a real-world setting, to determine the extent to which it prevents the therapeutic escalation on the long-term, and to identify factors related to TT failure.

Methods: Observational, retrospective, multicenter study. Data were collected at three timepoints: the first at 24-32 weeks, the second as close as possible to 52 weeks, and at the last time the patient attended the clinic, if this occurred after 52 weeks (final visit). The follow-up period extended from the index date to the date on which the patient escalated his/her treatment or to the last recorded visit.  $\Pi$ was judged to be effective (primary outcome measure) if, at the last follow-up visit, the patient did not initiate oral corticosteroids (OCS), azithromycin, or a biologic, and asthma was controlled (defined as Asthma Control Test: ACT ≥ 20 and absence of severe exacerbations in the preceding 12 months).

Results: 390 patients were analyzed, median follow-up time 40.0 months (IQR: 14.0 - 72.0). Treatment was escalated in 83 (22.5%) patients and TT was effective in 54% at the final visit. Clinical remission (controlled asthma plus FEV1 ≥80%) was achieved in 20.6% of the sample. Severe exacerbations, OCS load, symptoms and FEV1 significantly improved at 52 weeks and at the final visit (Figure 1). Being a smoker or former smoker (HR 1.84; 95% CI: 1.10-3.10), lack of asthma control at week 16-24 (HR 3.41; 95% CI: 1.98-5.89), presence of bronchiectasis (HR 1.91; 95% CI: 1.10-3.34), ACT ≤15 (HR 1.81; 95% CI: 1.07-23.10) at baseline and ≥ 2 severe exacerbations in the 12 months prior to TT initiation (HR 2.01; 95% CI: 1.32-3.06) were associated with failure to achieve the main outcome measure at the final visit (Figure 2). FEV1 decline > 30 mL/yr was found in 25.3% of patients in whom TT was effective at the final visit.

Conclusion: IT is effective in most patients in a real-life setting, avoiding therapeutic escalation in a high proportion of them and achieving long-term control in about half. Patients with bronchiectasis, smokers or former smokers, and those with greater clinical severity at TT initiation have a lower chance of long-term benefit. Failure to achieve a response at 4-6 months makes a subsequent response unlikely.





#### SIGNIFICANT ALL-CAUSE MORTALITY FOLLOWING INTERSTITIAL LUNG DISEASE INPATIENT **ADMISSIONS: WHAT CAN WE DO?**

**PP03** 

Laura White<sup>1</sup>, Jonathan Shaw<sup>4</sup>, Bethan Powell<sup>5</sup>, Nyan May Kyi<sup>3</sup>, Rebecca Huang<sup>6</sup>, Emma Hardy<sup>6</sup>, Gareth Hughes<sup>7</sup>, Dilanka Tilakaratne<sup>7</sup>, Conal Hayton<sup>8</sup>, Georges Ng Man Kwong<sup>3</sup>, Amy Gadoud<sup>1</sup>, Timothy Gatheral<sup>1</sup>

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Introduction: Patients with interstitial lung disease (ILD) are admitted to hospital frequently and are at risk of hospitalisation due to respiratory decompensation. A proportion of ILD-related admissions occur secondary to an Acute Exacerbation of Interstitial Lung Disease (AE-ILD) – defined by <30-day clinical deterioration and radiologically new bilateral ground-glass changes on computed tomography. We sought to determine the impact of ILD-related admissions on all-cause mortality in a real-world retrospective dataset from across the North West of England.

Methods: We undertook a multi-centre retrospective observational study of ICD-10 coded primary admissions for interstitial lung disease patients ≥18 years old between 01.01.2017 and 31.12.2019 across seven NHS trusts (encompassing ten secondary and tertiary centres) in the North West of England, with data from four NHS trusts completed and presented here. The primary outcome was time to death from admission. AE-ILD was identified by review of clinical notes and defined by <30-day progression of symptoms not caused by cardiac, thrombotic or pneumothorax events. Further data on patient demographics, admission investigation results, treatments and mortality were collected from coding and inpatient records.

Results: 519 admission events met inclusion criteria. 38 (7.3%) were excluded from analysis due to insufficient data to determine AE-ILD status. Overall all-cause inpatient mortality was 16.5% and 90-day all-cause mortality 39.1%. 227/478 (47.5%) admissions met clinical AE-ILD criteria with AE-ILD inpatient mortality 24.7% and 90-day all-cause mortality 51.1%. Mean survival following AE-ILD admission was significantly lower than admissions for other ILD-related pathology (406.56 days (95% CI 319.24 – 493.82) vs 769.55 days (95% CI 654.04 – 885.96) p <0.001). AE-ILD remained associated with increased risk of all-cause mortality in multivariate cox regression analysis (HR 1.31, p = 0.018), as was IPF diagnosis (HR 1.58, p = 0.031), pre-admission oxygen use (HR 2.09, p < 0.001) and increasing Charlson Comorbidity Index (HR 1.15, p <0.001). Overall, 11.9% of patients had formal palliative care reviews.

Conclusion: Hospitalisation events related to ILD, especially in AE-ILD, show significant inpatient and post-admission mortality. Collaboration is required to build larger datasets in both ILD and AE-ILD to develop and validate mortality modelling predictors. Early identification of those at increased risk of all-cause mortality will allow patients timely access to palliative care services, and represent important considerations for researchers in future studies.

# PP04

# DEVELOPMENT AND VALIDATION OF PRECISE-X, A RISK PREDICTION MODEL FOR THE FIRST SEVERE COPD EXACERBATION

<u>Mohsen Sadatsafavi</u><sup>1</sup>, Marc Miravitles<sup>2</sup>, Hamid Tavakoli<sup>6</sup>, Joseph Emil Amegadzie<sup>3</sup>, Jenni Quint<sup>4</sup>, Bernardino Alcazar Navarrete<sup>5</sup>

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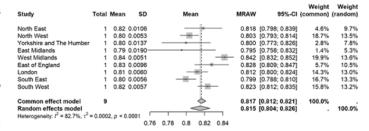
**Background:** Severe exacerbations of Chronic Obstructive Pulmonary Disease (ECOPDs) are associated with significant morbidity and mortality. Current guidelines emphasise using ECOPD history to guide preventive treatments but offer limited guidance for stratifying the risk of a first severe ECOPD. PRECISE-X aimed to develop and validate an individualised risk prediction model for the first severe ECOPD using variables routinely captured in electronic medical records.

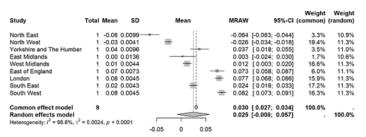
**Methods:** We created a cohort of newly diagnosed COPD patients in UK's Clinical Practice Research Datalink (2004–2022) to develop a risk prediction model for the first severe ECOPD during the next 5 years (primary outcome) and the next 12 months (secondary outcome). Candidate predictors were identified through clinical expertise and data-driven variable selection. Internal-external validation was performed across practice regions to evaluate the out-of-sample performance of the model in terms of discrimination (c-statistic), calibration, and net benefit.

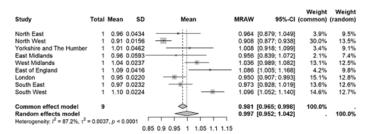
Results: The study included 219,015 patients (mean age 66.0; 42.4% female). The predicted 5-year risk

of a first severe ECOPD was 29.5%. The final model included four mandatory predictors (sex, age, MRC dyspnoea score, and forced expiratory volume in one second) and 22 optional predictors. In internal-external cross-validation, the average out-of-sample c-statistic was 0.815 (95%Cl 0.804–0.826) for 5-year prediction and 0.767 (95%Cl 0.757–0.776) for 1-year prediction (Figure). The model demonstrated good calibration across regions and showed positive net benefit across the entire plausible range of risk thresholds.

**Conclusion:** The risk of a first severe COPD exacerbation can be predicted with high accuracy using routine clinical data, addressing a critical gap in COPD management.







#### PRELIMINARY RESULTS OF THE CATALAN REGISTRY OF SEVERE COPD PATIENTS (SPOCCAT): DIFFERENCES BETWEEN EXACERBATORS AND NON EXACERBATORS

Cristina Aljama Vizcarra<sup>1</sup>, Roser Costa<sup>2</sup>, Jessica González<sup>3</sup>, Elena Miguel<sup>4</sup>, Annie Navarro<sup>5</sup>, Noelia Pablos<sup>5</sup>, Miriam Barrecheguren<sup>1</sup>, Galo Granados<sup>1</sup>, Núria Rodriguez<sup>6</sup>, Eduardo Vélez<sup>7</sup>, Artur Juan<sup>8</sup>, Sergi Pascual<sup>9</sup>, Dan Sánchez<sup>10</sup>, Daniel Monserrate<sup>11</sup>, Marc Miravitlles1

**PP05** 

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Introduction: This work analyzes the differences between exacerbating and non-exacerbating severe COPD patients in the SPOCCAT registry to try to identify areas of possible intervention.

Methods: Prospective multicenter registry of patients with severe COPD (FEV1(%) <50%) from 18 hospitals in Catalonia. At the baseline visit, socio-demographic characteristics, comorbidities, underlying treatment, symptoms, number and type of exacerbations in the previous year, quality of life, physical activity, analytical results, lung function and chest CT are collected. Those patients who presented one or more moderate and/or severe exacerbations were considered within the exacerbator group.

Results: In the SPOCCAT registry, 317 patients were included, 78% were men with a mean age of 68.4 years and 20% were active smokers. The mean FEV1(%) was 35.6%, with a mean (SD) eosinophil count of 230/µL (SD: 270). 20% had bronchiectasis and 5% had chronic bronchial infection. Regarding treatment, 86% were treated with inhaled corticosteroids, 21% with home oxygen therapy and 7% with noninvasive mechanical ventilation. In the previous year, 181 patients (57%) had presented moderate and/or severe exacerbations, 89 (28%) required hospital admission. Of those hospitalized, 80% did not have moderate exacerbations in the previous year. When comparing exacerbators versus nonexacerbators, significant differences were observed in the prevalence of anxiety (30% vs. 18%, p=0.018), depression (24% vs. 14%, p=0.045), level of physical activity (mean of 35 vs. 44 minutes daily, p=0.05), use of a single inhaled device (63% vs. 78%, p=0.009), use of pMDI (71% vs. 51%, p=0.01), pCO2 levels (44 vs. 41 mmHg, p=0.006) and hematocrit (47% vs. 45%, p=0.031). No significant differences were found in lung function, radiological or echocardiographic findings.

Conclusion: More than half of the patients with severe COPD in the SPOCCAT registry have had exacerbations in the previous year, half of them severe. Exacerbators have greater psychiatric comorbidity and less physical activity, as well as a greater use of inhalers and pMDIs. Strategies to address psychiatric comorbidity and promote physical activity should be considered, as well as optimising inhaled therapy in patients with severe COPD.

**PP06** 

#### DIGITAL SMART INHALER MONITORING IN CHILDREN AND YOUNG PEOPLE WITH HIGH-**RISK ASTHMA IN UK PRIMARY CARE**

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Background: Children and young people (CYP) with asthma in the UK have the highest rate of severe asthma attacks of any high-income country in Europe. A major obstacle to good asthma outcomes is poor adherence to preventer medication (ICS) and over-reliance on short-acting beta-2 agonists (SABA). We aimed to discover whether a smart inhaler-enabled care pathway in high-risk CYP with asthma is acceptable to CYP/parents and feasible within primary care.

Methods: Prospective cohort study (Nov-23-Dec-24) in Leicestershire primary care. CYP (5-16yrs) on the practice asthma register with high-risk asthma (attack in previous year and/or high SABA prescriptions) were invited to attend an asthma review at their practice. Spirometry, FeNO and asthma control were assessed at baseline. CYPs were given a digital smart inhaler (Hailie, Adherium (NZ) Limited) linked via Blue-tooth to the app on their/their parent's smart phone. Telephone follow-up at 3-months was conducted and face-to-face follow-up at 6-months is in progress.

Results: 72 children were recruited; mean age 9.0 (SD 3.1) years, 43 (60%) boys. 58 (81%) were from White ethnic backgrounds, and 45% from the most deprived areas of Leicester/Leicestershire. 68 (94%) were prescribed an ICS inhaler at baseline. FeNO at baseline was available for 40 (55%) CYP, median 39.5ppb (range 5-130ppb). Baseline spirometry was available for 62 (86%), median FEV1%predicted 82% (range 68-123%). The mean asthma control score increased from 19.6 (SD 3.6) at baseline to 23.5 (SD 3.1) at 3 months follow up.

Conclusions: Digital smart inhaler monitoring of high-risk children with asthma in primary care is feasible and acceptable to CYP and their carers. Digital smart inhaler monitoring was associated with a substantial improvement in asthma control at 3-months follow-up.

#### LAMA WITHDRAWAL EFFECTS ON COPD EXACERBATIONS: A REAL-WORLD CHALLENGE OF LOW TREATMENT ADHERENCE

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**PP07** 

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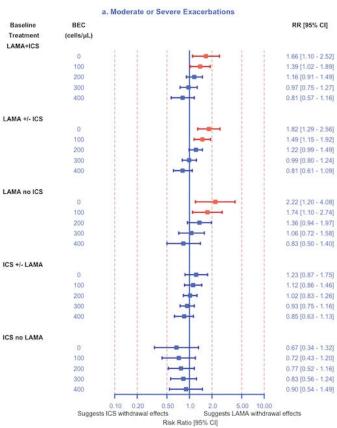
Background: Adherence to inhaled therapies in COPD is often suboptimal, with frequent cycles of treatment initiation and discontinuation observed in real-world settings. Discontinuing inhaled corticosteroids (ICS) may provoke a withdrawal effect, causing a paradoxical increase in exacerbations that exceeds expectations based solely on disease progression. Data on potential withdrawal effects after long-acting muscarinic antagonist (LAMA) discontinuation remain limited. This post-hoc analysis investigated, for the first time, the potential treatment withdrawal effects of LAMA in the FLAME study population, while also further examining previously described ICS withdrawal effects.

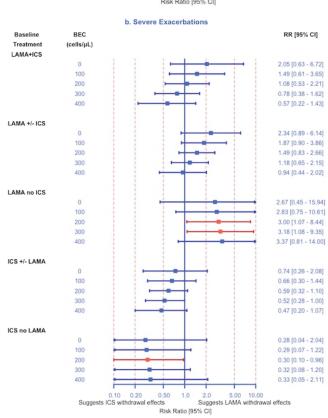
Methods: The FLAME trial was a 52-week, double-blind, non-inferiority randomized controlled trial comparing LABA+LAMA versus LABA+ICS in patients with moderate-to-severe COPD and at least one exacerbation in the previous year. For this analysis, patients were stratified based on their baseline use of ICS or LAMA. Exacerbation outcomes were evaluated using multivariable regression analyses, accounting for the interaction between treatment effects and blood eosinophil counts (BEC). We explored between-group differences in treatment effects in the first versus subsequent follow-up quarters. An increased burden of exacerbations in the LABA+ICS versus LABA+LAMA arm in the first compared to subsequent trial quarters among participants that were receiving LAMA at baseline was considered indicative of LAMA treatment withdrawal effect (and vice versa).

Results: Our analysis revealed significant LAMA withdrawal effects on moderate/severe, presumed non-infective, and presumed infective exacerbations, with a consistent trend observed for severe exacerbations. ICS discontinuation was associated with a short-term increase in severe exacerbations. For example, following LAMA discontinuation, patients with a baseline BEC of 0 cells/µL exhibited a risk ratio of 2.22 (95% CI: 1.20–4.08) for moderate/severe exacerbations, while those with a BEC of 100 cells/µL had a risk ratio of 1.74 (95% CI: 1.10-2.74). In patients with higher BEC, the withdrawal effects were less pronounced due to the enhanced efficacy of ICS.

Conclusions: These findings suggest that discontinuation of both LAMA and ICS can induce withdrawal effects that elevate the risk of exacerbations in COPD patients. Notably, our study likely underestimated ICS withdrawal effects because all patients underwent a run-in period with our ICS, and this period was not captured in our analysis. The study underscores the need to monitor treatment adherence carefully and to account for withdrawal phenomena when evaluating the effectiveness of maintenance therapies. Prospective validation is warranted to better inform clinical practice and improve patient outcomes.







#### L POST-PANDEMIC CHANGES IN RESPIRATORY MORTALITY IN SPAIN

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**PP08** 

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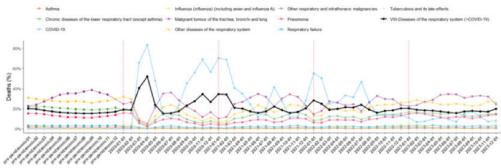
Introduction: Respiratory diseases represent a significant burden to global health, affecting all ages and populations. The COVID-19 pandemic has intensified the focus on respiratory morbidity and mortality, concentarting attention from other equally impactful diseases. Respiratory diseases can be communicable and non-communicable diseases such as COPD, which continue to be a leading cause of death in Spain. This study assesses mortality from all respiratory diseases, including tuberculosis, COVID-19 and lung cancer, in Spain between the pre-pandemic period (2011–2019) and the pandemic period (2020-2023).

Methods: Mortality data from the Spanish National Institute of Statistics (INE) were examined, encompassing 102 causes of death, including tuberculosis, COVID-19, and lung cancer, categorized as respiratory conditions. Analyses included total death counts, proportions by gender, age, and region (Autonomous Community), as well as changes in proportional mortality percentages. Logistic regression was employed to explore factors potentially associated with mortality from COVID-19 and other respiratory conditions.

Results: In 2023, Spain recorded 436,124 deaths from respiratory illnesses, representing 18.0% of the total mortality, and making it the second most common cause of death, just behind cardiovascular diseases. While COVID-19 deaths declined from 2020 (15.2%) to 2021 (8.9%), 2022 (6.8%), and 2023 (1.8%), there was a notable increase in fatalities from other respiratory conditions from 2020 (13.2%), to 2021 (13.0%), 2022 (14.3%), and 2023 (16.2%) (p for trend <0.05), underscoring the pandemic's lingering effects. Key factors associated with higher respiratory mortality included male gender, increasing age, marital status (divorced), and residence in urban settings, with substantial regional disparities observed.

Conclusion: Although total mortality in Spain has returned to levels similar to those before the pandemic, this study emphasizes a considerable variation in deaths from respiratory diseases during the pandemic period compared to the pre-pandemic period, reflecting the enduring impact of the

pandemic on respiratory health.Similar effects should be explored elsewhere in Europe and beyond.



# PREVALENCE OF RESPIRATORY VIRUSES IN STABLE AND ACUTE ASTHMA: A SYSTEMATIC REVIEW AND META-ANALYSIS

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PP09

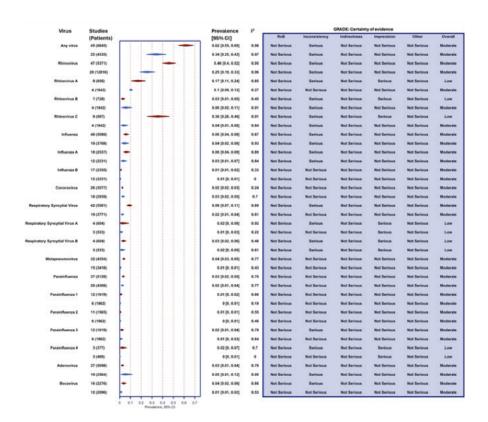
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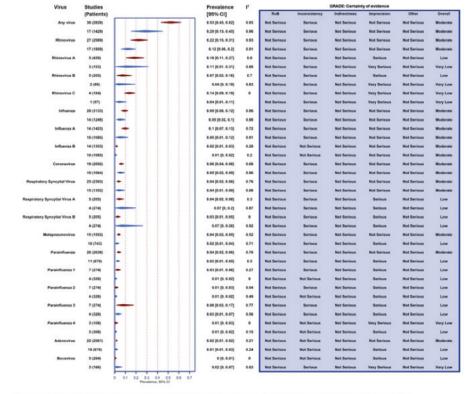
**Introduction:** Assessing the prevalence of respiratory viruses in stable and acute asthma is necessary to clarify the role of these viruses in the aetiology of asthma exacerbations. This is the first meta-analysis to assess differences in the prevalence of specific respiratory viruses between stable and acute asthma (1).

**Methods:** MEDLINE and EMBASE were systematically searched. Studies assessing the prevalence of respiratory viruses using molecular techniques in acute and/or stable asthma were included (1990-2024). Virus prevalence was assessed using meta-analyses of proportions.

Results: 28,702 abstracts were screened and 115 studies were included (68 assessed children and 48 assessed adults, with one study assessing both). The average sample size was 133.8 patients. Paediatric patients were on average 7.4 years old, 61.0% male and had an average FEV1/FVC ratio of 83.9%; adult patients were on average 44.6 years old, 35.1% male and had an average FEV1/ FVC ratio of 75.7%. Virus prevalence was greater in acute asthma in children compared with stable disease (62.0% [55.0 - 69.0%] versus 34.0% [25.0 - 43.0%]; P < 0.001), and in acute asthma in adults compared with stable disease (53.0% [43.0 - 62.0%]) versus 29.0% [15.0- 45.0%]; P = 0.01) (Figure 1). These differences appeared to be driven by an increased prevalence of rhinovirus (P < 0.001), respiratory syncytial virus (P < 0.001) and metapneumovirus (P < 0.001) among children with acute versus stable asthma. Among adults, only rhinovirus C (P = 0.02) and coronavirus NL63 (P = 0.03) were observed significantly more frequently during acute asthma. Overall virus prevalence did not differ between children and adults in both disease states. Adenovirus was significantly more prevalent among children with acute asthma requiring admission (severe) compared with asthma requiring a medical review but not necessarily admission (moderate/severe) (4% [2%-7%] versus 1% [1%-2%]; P =0.01). The prevalence of influenza (8% [4-12%] versus 5% [2%-9%]) and rhinovirus (50% [40%-59%]) versus 42% [34%-51%]) were also numerically higher in severe acute asthma, although not statistically significant.

**Conclusion:** Respiratory viruses are more prevalent in acute asthma compared with stable disease, mainly driven by differences in common respiratory viruses in children between disease states. Adenovirus, influenza and rhinovirus may be associated with more severe exacerbations in children.





#### Figure 1 Prevalence of respiratory viruses in paediatric and adult asthma (red: acute asthma, blue: stable asthma) CI: confidence interval. I2 = heterogeneity

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# THE COMPAIR STUDY: THE CARBON FOOTPRINT OF ASTHMA INHALERS BEFORE AND AFTER INITIATION OF FOSTAIR MART

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**PP10** 

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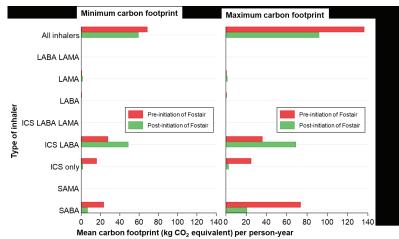
**Introduction:** Since 2021, Global Initiative for Asthma (GINA) guidelines have recommended that people with moderate-to-severe asthma receive inhaled corticosteroids (ICS) and formaterol as both maintenance and reliever therapy (MART) to reduce the risk of severe exacerbations. As ICS-formaterol MART has been shown to reduce exacerbations and improve asthma control, its initiation has the potential to reduce carbon emissions due to inhaler use, but this has not been formally investigated.

Methods: A historical cohort study was conducted using the Optimum Patient Care Research Database, UK, to explore inhaler use pre- and post- initiation of Fostair (beclomethasone/formoterol) MART (FMART) in the UK. Patients with asthma and no other chronic respiratory conditions who had been registered at the GP practice for ≥1 year and initiated FMART for the first time (index date) from July 2012 were followed up for a maximum of 1 year. Prescriptions for all asthma inhalers were collected for 1-year prior and up to 1-year post-index date. The indicative carbon footprint per inhaler was calculated using published data on direct carbon dioxide equivalent emissions, inhaler life cycle and disposal. Mean carbon footprint (kg CO2 equivalent) rate ranges per person-years and Poisson confidence intervals were calculated.

**Results:** Among 26,534 adult patients, the carbon footprint of all asthma inhalers reduced after initiation of FMART (minimum: 68.7 vs 59.4; maximum: 136.4 vs 92.0). As-needed SABA accounted for 34-54% of this reduction. In addition to SABA, the maximum mean carbon footprint before FMART initiation was higher for patients prescribed ICS monotherapy (25.0 [24.9,25.0] vs 2.8 [2.7,2.8]). Conversely, the maximum mean carbon footprint due to ICS-LABA therapies (including Fostair) was higher post-

initiation of FMART ([pre-] 36.1 vs 69.1).

**Conclusion:** Initiation of FMART was associated with a reduction in the total carbon footprint of all inhaler-related GHG emissions. This study further highlights the need to reduce high SABA use in respiratory care to support low-carbon transitions in healthcare.



**PP11** 

#### REAL-LIFE IMPACT OF ANTI-IL5 THERAPY ON EXACERBATION TYPES IN PATIENTS WITH **OBSTRUCTIVE LUNG DISEASE**

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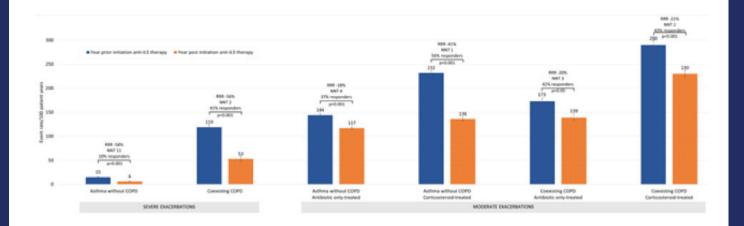
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Introduction: While anti-IL5 therapy has shown to be efficacious to reduce exacerbation rates in patients with severe eosinophilic asthma and might also benefit patients with coexisting COPD, it is unknown whether anti-IL5 therapy reduces all types of exacerbations in heterogeneous real-life patients.

Methods: Adults initiating mepolizumab or benralizumab between 2017-2020 were identified in Belgian nationwide data. The exacerbation rate in the year before anti-IL5 therapy initiation was compared to the year after. Exacerbations were classified as severe (hospitalized) exacerbations or moderate (outpatient) exacerbations treated with antibiotics, oral corticosteroids (OCS) or the combination.

Results: Among 807 patients (58 years, 51% females) initiating anti-IL5 therapy (78% mepolizumab, 22% benralizumab), severe exacerbation rate (ER) was 40±4 exacerbations per 100 patient years pre versus 17±3 post treatment initiation (p<0.001, relative risk reduction(RRR) -56%, number needed to treat(NNT)=4), and significantly reduced both in patients without COPD (n=616, ERpre=15±2, ERpost= $6\pm1$ , p<0.001, NNT=11) as with coexisting COPD (n=191, ERpre=119 $\pm12$ , ERpost= $53\pm9$ , p<0.001, NNT=2). For moderate exacerbations, ER were significantly reduced for all types of exacerbations in both patients with or without COPD, except for OCS only-treated exacerbations in patients with coexisting COPD (p=0.288).

Conclusion: All types of exacerbations were significantly reduced in the year post anti-IL5 therapy initiation compared to the year before, except for exacerbations treated with oral corticosteroids only in real-world patients with coexisting COPD.



# BIOLOGICS AS WELL AS INHALED ANTI-ASTHMATIC THERAPY ACHIEVE CLINICAL REMISSION: EVIDENCE FROM THE SEVERE ASTHMA NETWORK IN ITALY (SANI)

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PP12

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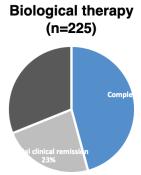
**Background:** This study aimed to evaluate the impact of severe asthma (SA) treatments after 12 months in achieving clinical remission (CR) within the context of the Severe Asthma Network in Italy (SANI) using the recent SANI definition of CR on treatment.

**Methods:** CR has been defined by SANI as complete, partial and no CR. Complete CR is defined by the absence of oral corticosteroids (OCS), no symptoms, no exacerbations, and stable lung function, and partial CR requires the absence of OCS and the fulfillment of 2 out of the other three criteria. Patients who do not meet the previous criteria do not reach CR.

Results: After 12 months of treatment, 283 patients were selected to evaluate the effectiveness of biologics (225 patients) and inhaled therapy (58 patients) in achieving CR. Among patients treated with biologic agents, 45.8% reached complete CR, 23.1% partial CR, and 31.1% no CR. Differences in CR achievement according to type of biologic agent administered were observed. Interesting results were found when assessing the inhaled therapy (ICS/LABA/LAMA and no biologics) effectiveness: 34.5% patients reached complete CR, 34.5% partial CR, and 31.0% did not reach CR (Figure 1). This finding is noteworthy since it further supports the efficacy of inhaled treatment in certain SA patients and highlights the relevance of using CR as a modern outcome of SA treatments. Chronic rhinosinusitis with nasal polyps (CRSwNP) comorbidity was associated, though not significantly, with CR achievement in patients treated with biologics. Asthma Control Test (ACT) and Asthma Control Questionnaire (ACQ) scores significantly impacted CR (p=0.003 and p=0.027, respectively), while biomarkers, namely IgE, blood eosinophils, or fractional exhaled nitric oxide (FeNO), were not associated with CR achievement (Table 1).

**Conclusion:** This study confirmed the effectiveness of biologics in reaching CR and demonstrated also inhaled therapies able to achieve CR. These innovative findings should encourage post hoc analysis of randomized clinical trials or even retrospective analysis of SA patient cohorts to evaluate CR with different inhaled treatments and further define the populations eligible for each treatment.

Abstract from: Canonica GW, et al. World Allergy Organ J. 2025 Jan 18;1 https://doi.org/10.1016/j.waojou.2024.101016 Posters presented at XXXVI CONGRESSO NAZIONALE SIAAIC, Roma 4-6 Ottobre 2024 (Poster Session 2, Saturday 5th October, 8:00AM-9:00AM) and XXV CONGRESSO NAZIONALE DELLA PNEUMOLOGIA, Milano 16-18 Novembre 2024 (E-Poster Exhibition Area).



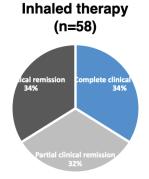


FIGURE 1. Percentage of clinical remission (Complete-Partial-No Remission) reached by treating patients with biologics or just inhaled therapy.

TABLE 1. Baseline patients' demographic, clinical characteristics and comorbidities according to clinical remission status at one-year follow-up visit in biological and inhaled therapy groups.

DEMOGRAPHIC C	HARACTERI	STICS						
	Biological ther	apy group			Inhaled therapy	group		
	Complete CR N = 103	Partial CR N = 52	No CR N = 70	p-val- ue*	Complete CR N = 20	Partial CR N = 20	No CR N = 18	p-val- ue*
Age, median (IQR)	54 (46-62)	57 (52-67)	56 (49-67)	0.179	58 (50-67)	60 (50-67)	63 (50-68)	0.820
Sex, n (%)				0.959				0.770
Female	57 (55.3)	31 (59.6)	40 (57.1)		14 (70.0)	13 (65.0)	13 (72.2)	
Male	46 (44.7)	21 (40.4)	30 (42.9)		6 (30.0)	7 (35.0)	5 (27.8)	
Ethnicity, n (%)				0.902				1
Caucasian	98 (95.1)	50 (96.2)	66 (94.3)		20 (100)	19 (100)	18 (100)	
Other	4 (3.9)	0	2 (2.9)		0	0	0	
Not reported					0	1	0	
BMI, n (%)				0.411				0.708
<30	83 (82.2)	36 (69.2)	57 (82.6)		15 (75.0)	17 (85.0)	16 (88.9)	
≥30	18 (17.8)	16 (30.8)	12 (17.4)		5 (25.0)	3 (15.0)	2 (11.1)	
Not reported	2	0	1		0	0	0	
BMI (kg/m^2), median (IQR)	24.5 (22.5- 28.4)	26.4 (23.4- 32.1)	26.8 (23.3- 28.7)	0.514	24.2 (22.2- 29.7)	24.2 (22.4- 28.9)	23.7 (22.6- 27.0)	0.769
BSA (m^2), median (IQR)	1.8 (1.7-1.9)	1.8 (1.7- 2.0)	1.8 (1.7- 1.9)	0.280	1.8 (1.6-1.9)	1.7 (1.6-1.8)	1.7 (1.6-1.9)	1
Smoking stratus, n (%)				0.699				0.560
Never	69 (67.6)	33 (64.7)	47 (68.1)		13 (65.0)	12 (63.2)	9 (50.0)	
Current smoker	2 (2.0)	2 (3.9)	3 (4.3)		1 (5.0)	2 (10.5)	2 (11.1)	
Ex smoker	31 (30.4)	16 (31.4)	19 (27.5)		6 (30.0)	5 (26.3)	7 (38.9)	
Not reported	1	1	1		0	1	0	
Pack years <sup>a</sup> , median (IQR)	9 (5-18)	9 (4-26)	13 (6-30)	0.365	8 (1-35)	8 (2-12)	6 (3-10)	0.801

#### CLINICAL CHARACTERISTICS

	Biological ther	apy group			Inhaled therapy group				
	Complete CR N = 103	Partial CR N = 52	No CR N = 70	p-val- ue*	Complete CR N = 20	Partial CR N = 20	No CR N = 18	p-val- ue*	
Biomarkers									
Absolute eosinophil count, median (IQR)	0.5 (0.3-0.8)	0.4 (0.2- 0.6)	0.5 (0.2- 0.8)	0.484	0.3 (0.1-0.6)	0.2 (0.1-0.4)	0.5 (0.3-0.6)	0.063	
N missing	18	4	10		6	4	2		
Percentage of eosinophils, median (IQR)	6.5 (3.3 - 10.9)	5.3 (2.5 - 7.2)	5.8 (2.1 - 9.6)	0.919	2.9 (2.4-9.7)	3.0 (2.1-5.4)	5.3 (2.2-10.2)	0.351	
N missing	26	7	11		6	5	4		
Total IgE level (kU/L), median (IQR)	177.5 (67.3- 441.2)	135.0 (59.8- 251.0)	2 0 1 . 0 ( 5 3 . 3 - 626.0)	0.550	83.9 (46.1- 184.0)	211.5 (92.0- 452.0)	238.0 (38.0- 1211.0)	0.777	
N missing	41	19	27		10	6	8		
FeNO (ppb)b, mean (SD)	55.6 (53.6)	45.5 (49.0)	51.4 (42.0)	0.963	31.5 (18.1)	31.5 (25.8)	55.5 (49.2)	0.123	
Pulmonary function FVC pre-BD (L), mean									
(SD)	3.3 (1.0)	3.2 (1.2)	3.1 (0.9)	0.282	2.9 (0.8)	3.0 (0.9)	3.0 (0.9)	0.817	
FVC pre-BD (%), mean (SD)	92.1 (18.7)	94.9 (21.9)	92.1 (20.3)	0.746	91.9 (16.9)	94.1 (16.7)	95.1 (21.1)	0.610	
FVC post-BD (L), mean (SD)	3.3 (1.0)	3.3 (1.2)	3.3 (0.9)	0.996	3.3 (0.9)	2.8 (0.9)	2.3 (0.6)	0.088	
N missing	7	32	51		10	11	13		
FVC post-BD (%), mean (SD)	92.9 (18.3)	98.6 (21.4)	98.6 (10.6)	0.489	89.1 (15.5)	92.3 (9.7)	82.7 (18.0)	0.320	
N missing	70	32	52		10	11	13		
FEV1 pre-BD (L), mean (SD)	2.2 (0.8)	2.1 (0.9)	2.0 (0.7)	0.166	2.0 (0.6)	2.0 (0.7)	2.0 (0.7)	0.987	
FEV1 pre-BD (%), mean (SD)	74.7 (21.4)	77.5 (23.4)	73.1 (19.8)	0.414	76.7 (18.1)	75.1 (18.6)	78.5 (21.9)	0.429	
FEV1 post-BD (L), mean (SD)	2.2 (0.8)	2.1 (0.9)	2.2 (0.8)	0.757	2.2 (0.6)	2.0 (0.6)	2.1 (0.9)	0.429	
N missing	65	30	43		7	10	10		
FEV1 post-BD (%), mean (SD)	83.7 (23.1)	76.5 (24.9)	82.0 (19.1)	0.858	82.3 (16.0)	80.6 (11.9)	78.2 (23.9)	0.573	
N missing	67	30	44		7	10	11		
Tiffeneau index pre-BD, mean (SD)	66.0 (12.6)	66.1 (13.3)	64.6 (11.7)	0.435	69.0 (7.7)	64.4 (7.4)	67.8 (10.0)	0.443	
Tiffeneau index post-BD (%), mean (SD)	69.7 (30.1)	60.9 (25.9)	62.2 (33.0)	0.643	73.3 (8.2)	79.8 (6.9)	92.9 (15.3)	0.097	
N missing	83	43	58		13	15	15		
Tiffeneau index post-BD, mean (SD)	65.9 (12.7)	61.6 (14.7)	66.1 (10.8)	0.604	72.1 (6.4)	69.6 (6.9)	69.1 (12.1)	0.887	
N missing	70	32	51		10	11	13	ĺ	
ACT, mean (SD)	17.0 (5.5)	15.9 (5.3)	14.2 (5.4)	0.003	18.0 (6.3)	18.2 (5.0)	15.9 (4.1)	0.069	

N missing	6	3	3		4	1	1	
ACQ, mean (SD)	2.1 (1.6)	2.9 (1.4)	3.0 (1.3)	0.027	2.0 (1.1)	1.7 (1.1)	2.2 (1.2)	0.245
N missing	43	20	13		9	3	4	
Asthma and quality of life								
Age at asthma onset, median (IQR)	35 (25-46)	33 (15-49)	32 (19-49)	0.938	41 (27-50)	32 (10-53)	31 (20-50)	0.948
Age at asthma diagnosis, median (IQR)	35 (26-47)	40 (19-50)	38 (23-50)	0.580	47 (27-50)	50 (23-61)	42 (23-59)	0.964
AQLQ score, mean (SD)	4.6 (1.4)	4.0 (1.3)	3.7 (1.2)	0.001	5.1 (1.3)	5.0 (1.5)	4.2 (1.1)	0.030
Number of workdays lost <sup>c</sup> , median (IQR)	0 (0-10)	0 (0-6)	0 (0-10)	0.568	0 (0 - 5)	0 (0-0)	2 (0-10)	0.093
Low adherence test, n (%)				0.365				0.066
None	90 (94.7)	39 (88.6)	52 (92.9)		18 (100)	13 (92.9)	10 (76.9)	
Yes, clinical evaluation	2 (2.1)	0	3 (5.4)		0	1 (7.1)	1 (7.7)	
Yes, objective clinical examination	0	2 (4.5)	0		0	0	0	
Yes, both	3 (3.2)	3 (6.8)	1 (1.8)		0	0	2 (15.4)	
Not reported	8	8	14		2	6	5	
ICU admissions <sup>c</sup> , n (%)				0.694				0.306
0	91 (100.0)	39 (90.7)	62 (100.0)		19 (100)	15 (100)	14 (93.3)	
1	0	1 (2.3)	0	İ	0	0	1 (6.7)	
≥2	0	3 (7.0)	0		0	0	0	
Not reported	12	9	8		1	5	3	
Emergency room admissions <sup>c</sup> , n (%)				0.016				0.517
0	92 (92.0)	42 (82.4)	51 (72.9)		18 (90.0)	18 (90.0)	15 (83.3)	
1	6 (6.0)	4 (7.8)	10 (14.3)		2 (10.0)	1 (5.0)	2 (11.1)	
2	2 (2.0)	4 (7.8)	6 (8.6)	İ	0	1 (5.0)	0	
≥3	0	1 (2.0)	3 (4.3)	İ	0	0	1 (5.6)	
Not reported	3	1	0	İ	0	0	0	1
Hospitalizations for asth- ma <sup>c</sup> , n (%)				0.302				0.068
0	93 (93.0)	44 (86.3)	59 (84.3)		19 (95.0)	19 (95.0)	14 (77.8)	
1	5 (5.0)	5 (9.8)	7 (10.0)		1 (5.0)	1 (5.0)	3 (16.7)	
≥2	2 (2.0)	2 (3.9)	4 (5.7)		0	0	1 (5.6)	
Not reported	3	1	0		0	0	0	
Number of unscheduled visits <sup>c</sup> , median (IQR)	0 (0-2)	0 (0-1)	0 (0-2)	0.763	0 (0-0)	0 (0-0)	0 (0-2)	0.144
Patients with at least one unscheduled visit, n (%)	30 (33.7)	11 (26.2)	18 (33.3)	0.787	4 (20.0)	3 (15.0)	5 (27.8)	0.295
Number of exacerbations with steroid use <sup>c</sup> , median (IQR)	2 (0-3)	2 (0-3)	2 (1-3)	0.323	1 (0-2)	1 (0-1)	2 (2-5)	0.001
Patients with at least one exacerbation with steroid use, n (%)	63 (63.6)	35 (72.9)	49 (76.6)	0.151	13 (65.0)	9 (45.0)	16 (88.9)	0.031

#### **COMORBIDITIES**

	Biological ther	apy group			Inhaled therapy group				
	Complete CR	Partial CR	No CR N = 70	p-val- ue*	Complete CR	Partial CR N = 20	No CR N = 18	p-val	
Rhinitis, n (%)				0.133			1	0.319	
Never	21 (20.4)	19 (36.5)	21 (30.4)		7 (35.30)	7 (35.0)	9 (50.0)	_	
Yes, former	7 (6.8)	1 (1.9)	8 (11.6)		1 (5.0)	0	1 (5.6)	$\top$	
Yes, ongoing	75 (72.8)	32 (61.5)	40 (58.0)		12 (60.0)	13 (65.0)	8 (44.4)		
Not reported	0	0	1		0	0	0	_	
Chronic rhinosinusitis without polyposis, n (%)				0.392				0.170	
Never	63 (61.8)	34 (65.4)	49 (72.1)		15 (75.0)	10 (50.0)	9 (50.0)		
Yes, former	15 (14.7)	6 (11.5)	8 (11.8)		3 (15.0)	4 (20.0)	1 (5.6)		
Yes, ongoing	24 (23.5)	12 (23.1)	11 (16.2)		2 (10.0)	6 (30.0)	8 (44.4)		
Not reported	1	0	2		0	0	0		
Nasal polyps, n (%)				0.536				0.663	
No	32 (31.1)	30 (57.7)	32 (46.4)	1	14 (70.0)	14 (70.0)	15 (83.3)		
Yes, TC or endoscopic confirmation	65 (63.1)	21 (40.4)	33 (47.8)		6 (30.0)	5 (25.0)	3 (16.7)		
Yes, suspected	6 (5.8)	1 (1.9)	4 (5.8)		0	1 (5.0)	0		
Not reported	0	0	1		0	0	0		
Polyposis grading <sup>d</sup> , n (%)				0.631				0.063	
No polyps	2 (3.7)	0	0		0	0	0		
Small polyps in the middle meatus not reaching below the inferior border of the middle turbinate	23 (42.6)	8 (50.0)	9 (31.0)		0	4 (66.7)	0		
Polyps reaching below the lower border of the middle turbinate	10 (18.5)	3 (18.8)	8 (27.6)		1 (25.0)	1 (16.7)	2 (100)		
Large polyps reaching the lower border of the inferior turbinate or polyps medial to the middle turbinate	15 (27.8)	2 (12.5)	9 (31.0)		3 (75.0)	1 (16.7)	0		
Large polyps causing complete obstruction of the inferior nasal cavity	4 (7.4)	3 (18.8)	3 (10.3)		0	0	0		
Not reported	17	6	8		2	0	1		
Number of polypecto- mies <sup>d</sup> , n (%)				0.194				0.275	
0	9 (16.4)	7 (36.8)	4 (11.8)		2 (40.0)	1 (25.0)	0		
1	18 (32.7)	2 (10.5)	14 (41.2)		0	3 (75.0)	1 (33.3)		
2	16 (29.1)	6 (31.6)	11 (32.4)		2 (40.0)	0	1 (33.3)		
>=3	12 (21.8)	4 (21.1)	5 (14.7)		1 (20.0)	0	1 (33.3)		
Not reported	16	3	3		1	2	0		

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No	54 (65.9)	27 (69.2)	39 (68.4)		10 (76.9)	9 (69.2)	13 (86.7)	
Yes	28 (34.1)	12 (30.8)	18 (31.6)		3 (23.1)	4 (30.8)	2 (13.3)	
Not reported	21	13	13		7	7	3	
Cardiovascular diseases, n (%)				0.090				0.687
No	74 (75.5)	32 (69.6)	37 (61.7)		14 (77.7)	10 (55.6)	11 (61.1)	
Yes	24 (24.5)	14 (30.4)	23 (38.3)		4 (22.2)	8 (44.4)	7 (38.9)	
Not reported	5	6	10		2	2	0	
Kidney failure, n (%)				1				0.321
No	96 (100.0)	48 (98.0)	61 (100.0)		19 (100)	19 (100)	17 (94.4)	
Yes	0	1 (2.0)	0		0	0	1 (5.6)	
Not reported	7	3	9		1	1	0	
Anxiety, n (%)				0.251				0.163
No	92 (95.8)	42 (87.5)	52 (88.1)		16 (88.9)	18 (100)	13 (81.3)	
Yes	4 (4.2)	6 (12.5)	7 (11.9)		2 (11.1)	0	3 (18.7)	
Not reported	7	4	11		2	2	2	
Depression, n (%)				1				0.543
No	94 (95.9)	44 (89.8)	57 (95.0)		16 (94.1)	19 (100)	16 (94.1)	
Yes	4 (4.1)	5 (10.2)	3 (5.0)		1 (5.9)	0	1 (5.9)	
Not reported	5	3	10		3	1	1	
Diabetes, n (%)				1				1
No	90 (91.8)	45 (91.8)	56 (93.3)		18 (94.7)	18 (94.7)	17 (100)	
Yes	8 (8.2)	4 (8.2)	4 (6.7)		1 (5.3)	1 (5.3)	0	
Not reported	5	3	10		1	1	1	

<sup>\*</sup> p-value for Complete or Partial CR vs no CR

- Biological therapy group: n=62 patients in complete CR, n=38 in partial CR, and n=47 in no CR.
- Inhaled therapy group: n=10 patients in complete CR, n=10 in partial CR, and n=14 in no CR.

Abbreviations: ACT, asthma control test; ACQ: asthma control questionnaire; AQLQ, asthma quality of life questionnaire; BMI, body mass index; BD: bronchodilator; BSA, body surface area; CR, clinical remission; FeNO, fractional exhaled nitric oxide; FEV1, forced expiratory volume in the first second; FVC, forced vital capacity; ICU, intensive care unit; IQR, interquantile range; SD, standard deviation.

<sup>&</sup>lt;sup>a</sup> Pack years was calculated among current and ex smokers.

<sup>&</sup>lt;sup>b</sup> FeNO result was calculated among patients for which it was applicable:

<sup>&</sup>lt;sup>c</sup> The variable was evaluated in the last 12 months.

<sup>&</sup>lt;sup>d</sup> Polyposis grading and number of polypectomies were reported among patients with nasal polyps (confirmed or suspected).

PP13

# EXPOSURE TO WOOD SMOKE AND RISK OF PULMONARY HYPERTENSION IN COPD PATIENTS RESIDING AT HIGH ALTITUDE

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**Introduction:** In patients with COPD residing at high altitudes, a higher prevalence of pulmonary hypertension (PH) has been demonstrated compared to those living at sea level. Additionally, it has been suggested that COPD due to biomass exposure carries a greater risk of developing PH. There are no studies evaluating this association at high altitudes, which is why this study was designed to assess the risk factors associated with PH and the role of exposure to firewood smoke in its development.

**Methods:** Eligible patients from the OLPGA study (Evaluation of Long-Term Oxygen Therapy Criteria in COPD at High Altitude) were included. The inclusion criteria were: a diagnosis of COPD (defined as FEV1/FVC < 0.7 and exposure to a risk factor), resting hypoxemia (PaO2  $\geq$  50 and  $\leq$  55 mmHg), or exercise-induced hypoxemia (SpO2  $\leq$  85% with a  $\geq$  5% drop during the six-minute walk test [6MWT]), and permanent residence at high altitude (Bogotá, 2,640 m). Pulmonary hypertension (PH) was defined as a PSAP > 40 mmHg on echocardiogram. A cross-sectional analytical study was conducted, comparing patients with and without PH. Multivariate analysis was performed to identify associated risk factors.

**Results:** A total of 265 COPD patients were included, 209 without PH and 56 with PH. No significant differences were observed in age, sex, body mass index, or COPD severity. Compared to those without PH, patients with PH had higher exposure to wood smoke, more frequent and severe dyspnea, and lower PaO2, diffusion capacity, and exercise capacity (6MWT). Wood smoke exposure and tobacco use were significantly associated with PH (OR: 4.13, 95% CI: 1.84-9.31).

**Conclusion:** Patients with COPD and hypoxemia, residing at high altitude, who have PH, show more severe oxygen disparities, along with more frequent reductions in exercise capacity and diffusion capacity, compared to those without PH. E Wood smoke exposure is associated with the presence of PH, warranting further investigation of the underlying mechanisms and clinical implications.

# REAL-WORLD EFFECTIVENESS OF BENRALIZUMAB TREATMENT FOR SEVERE EOSINOPHILIC ASTHMA IN COLOMBIA: INSIGHTS FROM THE BENRACOL STUDY

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**PP14** 

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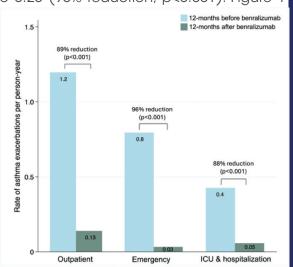
**Introduction:** The eosinophilic phenotype is commonly observed in patients with severe asthma in Colombia, affecting approximately 66% of cases. Benralizumab, an anti-IL-5Ra biologic therapy, has proven effective for managing these patients. However, there is limited data on its effectiveness in middle-income countries like Colombia, where benralizumab is accessible through the National Health System.

**Methods:** This real-world, retrospective, multicenter, observational study used a before-and-after design to evaluate benralizumab's effectiveness. Adults aged 18 and older with severe eosinophilic asthma (SEA), defined as ≥ 300 eosinophils/mm³ or ≥ 150-300 eosinophils/mm³ on oral corticosteroids, were included. Patients received benralizumab as either a first biologic treatment or a switch from another biologic due to inadequate response. A one-year treatment period with benralizumab was compared to the year before initiation. Key outcomes measured at baseline, 3, 6, and 12 months included: clinically significant exacerbations (requiring systemic corticosteroids for more than three days, emergency room visits, or hospitalization), asthma control (measured by ACQ or ACT), spirometry (FEV1, FVC, FEV1/FVC), and asthma medication usage. To be included, patients must have received benralizumab for at least three months. Patients who discontinued due to failure or adverse events before one year were also included in the analysis.

**Results:** A total of 122 patients with severe eosinophilic asthma (SEA) were included (mean age  $54.9 \pm 13.3$  years, 73% female, median BMI: 27.2 kg/m²). The most common T2 comorbidities were allergic rhinitis (55.7%) and nasal polyposis (34.4%). Before benralizumab, 80.3% had exacerbations in the last year. After one year of treatment, 16.6% had exacerbations, a reduction of 80% (p<0.001). The annualized exacerbation rate decreased from 2.40 to 0.23 (90% reduction; p<0.001). Figure 1

shows exacerbation rates by setting. After 12 months, 72% of patients achieved well control, 15.7% partial control, and 11.8% remained uncontrolled. OCS use decreased from 26.2% to 13.1% (50% reduction; p<0.001). Of patients, 91.1% were responders and 8.9% non-responders. Clinical remission was seen in 11.5%. Mild adverse events, including local pain and headaches, occurred in 17.9%.

**Conclusion:** In Colombia, a middle-income country with notable healthcare disparities, benralizumab proves to be both effective and safe for the management of uncontrolled severe eosinophilic asthma (SEA) in real-world settings. The outcomes observed in this study are consistent with those reported in high-income countries with more favorable healthcare conditions.



PP15

THE IMPACT OF SOCIOECONOMIC DEPRIVATION ON INTERSTITIAL LUNG DISEASE PROGRESSION: INSIGHTS FROM AN EAST LONDON COHORT

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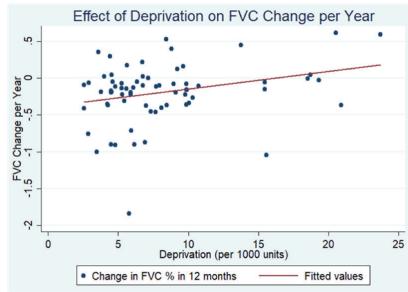
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**Introduction:** Increasing socioeconomic deprivation has been linked to higher mortality in patients with interstitial lung disease (ILD). This retrospective cohort study aims to characterise the impact of deprivation on FVC decline in patients with all types of interstitial lung disease. Quantifying the role of socioeconomic deprivation in ILD could lead to targeted interventions to support patients with ILD in low socioeconomic areas.

**Methods:** This retrospective observational study evaluated the impact of deprivation on lung function decline in patients with ILD at an East London hospital. Socioeconomic deprivation was measured using the neighbourhood-based Indices of Deprivation which ranks areas within the country from 1 being most deprived to 32,844 being least deprived. Deprivation was assessed using deprivation quartiles and a continuous deprivation rank. Descriptive statistics were used to summarize baseline demographic and clinical characteristics across deprivation quartiles. Linear regression was used to assess the relationship between deprivation (primary exposure) and annualized forced vital capacity (FVC) change (primary outcome). To evaluate whether the effect of deprivation varied by ethnicity, an interaction term between deprivation and ethnicity was included in a multiple regression model, with an F-test comparing models with and without the interaction. A stepwise regression approach was used to identify additional predictors of FVC change. Statistical significance was set at p < 0.05. Analyses were conducted in Stata.

**Results:** Our sample of 70 patients show a statistically significant correlation between worsening deprivation and more rapid FVC decline over time on univariate analysis (p=0.02). We found that for every 1000 ranks that deprivation worsened, annual rate of FVC decline was 23ml greater. This relationship was not preserved in the multivariate analysis upon introduction of the interaction term between deprivation and ethnicity though this may have been due to underpowering. The introduction of the interaction term was not statistically significant on the F-Test. Asian ethnicity had a protective effect on rate of FVC decline compared to Caucasians (p=0.01). None of the other variables were correlated with FVC decline.

**Conclusion:** Increasing socioeconomic deprivation is associated with increased rate of progression in a cohort of all forms ILD. While there was no clear interaction between ethnicity and deprivation in this data, more data collection is required to better define the relationship between deprivation and FVC decline in a multivariate model to understand how confounders affect this relationship.



#### COMORBIDITIES AND ALLERGIC SENSITIZATION PROFILES OF SEVERE ASTHMATIC PATIENTS IN MEXICO WITH AND WITHOUT BIOLOGIC THERAPY

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**PP16** 

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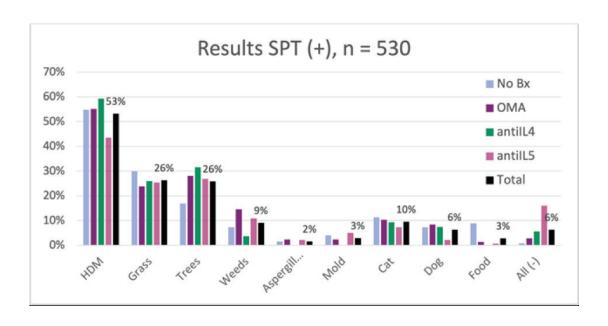
Background: Mexico has participated in the International Severe Asthma (SA) Registry (ISAR), a global registry of SA patients since 2019. We search to describe the allergic profile -allergic comorbidities and allergic sensitizations- of the Mexican SA patients in the ISAR database: those on biologic therapy (omalizumab, dupilumab, mepolizumab and benralizumab) as well as those who are not on any biologic (NoBx), and to compare with some global data of SA patients.

Method: data from SA patients 4-85yo were uploaded into the ISAR online platform in 13 establishments throughout the country, both from social security and private clinics. Allergic comorbidities included allergic rhinitis (AR), chronic rhinosinusitis (CRS), nasal polyps (NP) and atopic dermatitis (AD) and non-allergic comorbidities anxiety, depression, sleep apnea and GERD; sensitization profiles contained the full set of national aeroallergens. All patients were divided into two groups according to their actual therapy: Bx or NoBx and in the biologic therapy subgroups and compared with X-square test.

Results: There were a total of 530 patients. Of those, there were 124 noBx, 214 (40%) OMA, 54 (10%) DUPI and 138 (26%) were on an antilL5. Table 1 shows the frequency of comorbidities in the four different groups and in total. Table 2 shows the sensitization profiles in the four different groups and in total. CRS and NP were more frequent in the anti-IL5 group. AD in the noBx and anti-IL4/13 group. Mental disorders were more frequent in noBx (p<0.01) and in second place in anti-IL5, while GERD was here most frequent (p<0.05). There were no major differences between groups in sensitization profile, reflecting Mexican national sensitization data, while the sensitization frequency (94%) was higher than the global ISAR data (79%, p<0.005).

Conclusion: In this large registry-based Latin-American SA patient group allergies are more frequent as in the global ISAR cohort, and there are some differences in comorbidity frequency between the different biologic groups, partly due to lack of availability of some biologics (dupilumab) in several centers. Patients not started on Bx have more (especially non-allergic) comorbidities.

Allergic*	Allergic rhinitis		RS		Atopic dermatitis		Nasal polyps	
No Bx (N=123)	98%	121	61%	75	41%	50	22%	27
OMA (N=212)	87%	184	38%	81	9%	19	16%	34
antilL4 (N=54)	55%	30	19%	10	32%	17	13%	7
antilL5 (N=138)	73%	101	68%	94	9%	12	59%	81
527	N total	435		260		99		149
		83%		49%		19%		28%
404	N, only Bx	315		185		49		122
		78%		46%		12%		30%
Non-allergic**	Anxiety		Depression		Sleep apnea		GERD	
No Bx (n=123)	21%	26	14%	17	25%	31	4%	5
OMA (209)	4%	8	2%	4	3%	6	9%	19
anti-IL4 (n=54)	0	0	2%	1	0	0	5%	3
anti-IL5 (n= 138)	11%	15	9%	12	1%	1	21%	29
524	N total	49		35		38		55
		9%		7%		7%		11%
401	N, only Bx	24		18		8		50
		6%		4%		2%		13%



#### TIME FROM INITIAL REFERRAL FOR SPECIALIST CARE UNTIL BIOLOGIC THERAPY PRESCRIPTION FOR PATIENTS WITH SEVERE UNCONTROLLED ASTHMA

David Price1, John Blakey2, John Busby3, Li Ping Chung4, Mark Hew5, Nelson Hu6, David J. Jackson<sup>7</sup>, Gregory Katsoulotos<sup>8</sup>, Hilary Pinnock<sup>9</sup>, Dermot Ryan<sup>10</sup>, Philip J Thompson<sup>11</sup>, Paola Accalai<sup>12</sup>, Heath Heatley<sup>12</sup>, Porsche Le Cheng<sup>1</sup>, Chantal Le Lievre<sup>1</sup>, Tracy Armstrong<sup>13</sup>, Fabio Botini<sup>1</sup>, Nicholas Bushell<sup>1</sup>, Victoria Carter<sup>1</sup>, Eve Denton<sup>5</sup>, Kerry L. Hancock<sup>15</sup>, Florian Heraud<sup>16</sup>, Thao Le<sup>1</sup>, Lucy Morgan<sup>17</sup>, Kanchanamala Ranasinghe<sup>18</sup>, Alexander Roussos<sup>1</sup>, Deb Stewart<sup>19</sup>, Francis Thien<sup>20</sup>, Emma Vincent<sup>1</sup>, Amanda Xu Wen<sup>21</sup>, Russell Wiseman<sup>22</sup>, Celia Zubrinich<sup>23</sup>

**PP17** 

<sup>1</sup>Optimum Patient Care, ,Australia , <sup>2</sup>Sir Charles Gairdner Hospital, ,Australia, <sup>3</sup>Queen's University Belfast, ,UK, <sup>4</sup>Fiona Stanley Hospital, , Australia, <sup>5</sup>Alleray, Asthma & Clinical Immunology Service/Alfred Health, , Australia, <sup>6</sup>Alfred Health, , Australia, <sup>7</sup>King's College London, , UK, <sup>8</sup>The University of Notre Dame, , Australia, <sup>9</sup>Asthma UK Centre for Applied Research/Usher Institute/The University of Edinburgh, , UK, 10 University of Edinburgh, , UK, <sup>11</sup>The Lung Health Clinic/Hollywood Medical Centre, , Australia, <sup>12</sup>Observational and Pragmatic Research Institute, , Singapore, <sup>13</sup>AstraZeneca Pty Ltd., , Australia, <sup>14</sup>Allergy, Asthma & Clinical Immunology/Alfred Health, , Australia, <sup>15</sup>The University of Melbourne, , Australia, <sup>16</sup>Queensland Health, , Australia, <sup>17</sup>University of Sydney, , Australia, 18Griffith University, , Australia, 19Health Consultant, , Australia, 20Monash University, , Australia, <sup>21</sup>University of Queensland, , Australia, <sup>22</sup>Suncoast Medical Centre, , Australia, <sup>23</sup>Melbourne Allergy Asthma & Immunology Consultants, , Australia

Introduction: Biological therapies for asthma are innovative medicines used for targeted treatment of severe asthma in specialist care. This study analyzed databases of asthma patients treated in primary and secondary care settings to evaluate the time from first being referred for specialist treatment until the first documented biologic prescription in the United Kingdom (UK) and in Australia (AU).

Methods: Study populations were identified from electronic medical records (EMR) from November 2007 to December 2023 held by the UK Optimum Patient Care Research Database (OPCRD) and the Optimum Patient Care Research Database Australia (OPCRDA), which include approximately 29 million primary care patients and approximately 1 million primary and secondary care patients, respectively.

The selection criteria were: age ≥12 years, active asthma (asthma diagnostic code and ≥1 asthma medication prescribed within 2 years prior), and prescribed high-dose ICS/LABA with ≥1 exacerbation or hospitalization/emergency visit for an exacerbation in the previous 12 months. Times between the first referral from primary to specialist care, an initial specialist consultation, and the first recorded biologic prescription, were determined for patients with EMR of these events.

Results: The study included 1,273 UK patients and 245 AU patients who were prescribed biologic asthma therapies (Figure 1). 1,012 (79%) UK patients and 111 (45%) AU patients had a secondary care event in their primary care EMRs. The median times from referral to having a specialist consultation were 124 days in the UK and 45 days in AU. A biologic asthma treatment was initiated 1,830 and 755 days (median) after the first specialist assessment in the UK and AU, respectively. The median interval between initial referral from primary care and the first recorded biologic prescription was 1,600 days in the UK and 1,192 days in AU.

Conclusions: In this large population of patients with severe asthma (1,273 UK and 245 AU) who received specialist treatment using biologics, there was a median interval of 4.4 years in the UK and 3.3 years in AU between initial referral from primary care and initial biologic therapy prescription. For patients with severe and uncontrolled asthma a long wait to receive effective and necessary medication is undesirable and may contribute to suboptimal outcomes. 1 Further clinical studies are needed to assess whether involving GP clinics and community respiratory clinics under respiratory specialists may provide better and quicker access to this patient group, with outreach clinics worldwide.

#### Reference:

1.Bush A, Pavord ID. Stop the Asthma Treatment Elevator, We Need to Get Off!. Am J Respir Criti Care Med. 2025 Jan 21.doi: 10.1164/rccm.202412-2431VP.

**Funding Statement:** Data from OPCRDA was collected through the DTT Asthma QI program, which is partially funded by AstraZeneca and Optimum Patient Care Australia (OPCA). The analysis of the Australian data was fully funded by OPCA, while Optimum Patient Care Global provided funding for the analysis and inclusion of data from the UK OPCRD.

Acknowledgements: David Neil, of the Observational and Pragmatic Research Institute, Singapore, provided writing and editorial support. We wish to also acknowledge and thank Nadeeka De Silva, Christie Mellerick, Syed Zain Abbas, Victoria Lim, Christie Mellerick, Liam G. Heaney, Pujan Patel, Paul E. Pfeffer, Pete Smith, Kwok Yan, John Upham, Scott Claxton, Elizabeth Da Silva, Russell Goudge, Jhanavi Iyer, Wayne Kelly, Birgit Marchand, Tracy Smith, Joseph Doan, John Upham, Peter Del Fante, Sinthia Z. Bosnic-Anticevich, Anita Sharma, Ata Kichkin, Bruce Willett, Chi Ming Lau, Dominique Novic, Ian Miles, John Pakos, Josephine Samuel-King, Lisa Sugg, Majella Soumakiyan, Marion Magee, Nicole O'Sullivan, Ondrej Rejda, Rob Campbell, Sheryl Bradley, Ying Liu of the OPCA High-Risk asthma for their valuable contributions.

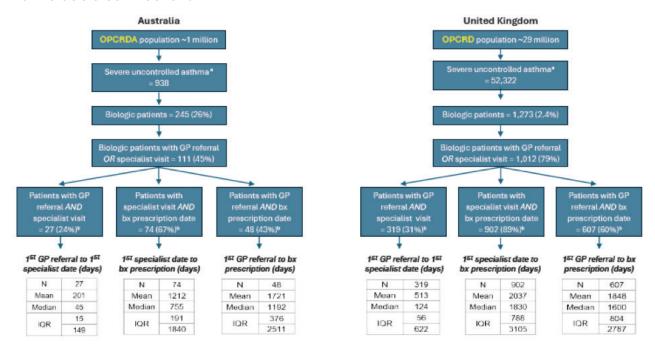


Figure 1. Time from first GP referral for specialist asthma treatment until biologic asthma therapy prescription in the UK and Australia

Abbreviations. OPCRD, Optimum Patient Care Research Database; OPCRDA, OPCRD Australia; GINA, Global Initiative for Asthma; OCS, oral corticosteroids; GP, General Practitioner; bx, biologic.

\* Categories are not mutually exclusive.

**PP18** 

HOW HAS IPD MORTALITY EVOLVED IN ANDALUSIA OVER THE LAST 20 YEARS? Ayoub Hammadi Ahmed, Bernardino Alcázar Navarrete, Lucía Álvarez Muro, Adela Murillo Rodriquez

Hospital Universitario Virgen De Las Nieves, Granada, España

Introduction: Idiopathic Pulmonary Fibrosis (IPF) is a progressive and fatal interstitial lung disease of unknown cause. Although considered rare, recent studies suggest an increasing incidence, likely due to improved diagnostic accuracy and population aging. Mortality trends provide crucial insights into disease burden, healthcare impact, and potential advancements in management. This study aims to evaluate IPF mortality trends in Andalusia over the past two decades and compare them to national trends.

Methods: We retrieved age-adjusted IPF mortality rates per 100,000 inhabitants from the Statistical Portal of the Spanish Ministry of Health for men and women in Spain and Andalusia from 1999 to 2021. Mortality data were classified using ICD-10 code J84 (other interstitial lung diseases). A joinpoint regression analysis was performed to identify trend changes and estimate the annual percentage change (APC). Statistical significance was set at p<0.05.

Results: Between 1999 and 2021, IPF mortality rates in Spain increased from 3.73 to 4.92 deaths per 100,000 inhabitants. In Andalusia, rates rose from 3.61 to 5.10 per 100,000. Stratified by sex, both men and women exhibited two distinct trend phases: an initial increase followed by a later decline. These trends were parallel in Andalusia and Spain, suggesting shared influencing factors (Figures 1 and 2).

**Discussion:** The initial increase in mortality aligns with growing disease awareness, improved diagnostic tools (such as HRCT), and better case identification. The later decline may reflect earlier diagnosis, multidisciplinary management, and the introduction of antifibratic therapies (e.g., pirfenidone, nintedanib), which have been shown to slow disease progression. However, regional variations and differences in healthcare access must be considered when interpreting these trends.

Conclusions: Over the last 20 years, IPF mortality rates in Andalusia have undergone two distinct phases—an initial rise followed by a decline—mirroring national trends. These findings highlight the dynamic nature of IPF epidemiology and underscore the need for continued research, early diagnosis strategies, and access to effective treatments to further reduce mortality.

#### **FPIMortality Women**

Joinpoint - V4.9.0.0 Joinpoint Session - 7 - output results-2 11-16-2023

#### Session Parameters

Input File Tab:

Input File Name: c:\users\balca\dropbox\trabajos pendientes\mortalidad por fpi españa 1999- 2021\mortalidad 1999-2021 fpi para

jointpoint mujeres.xlsx

Delimiters: Tab Missing Character: Space File Contains Column Headers: Y

By Variables: CCAA

Independent Variable: AÑO
Shift Data Points: 0

Dependent Variable:

Run Type: Provided in Data File Count/Numerator: Type of Variable: Age-Adjusted Rate Pop/Denominator:

Rate/Proportion/Pct: TASA

Standard Error:

Heteroscedastic Error Option: Adjustment Variable:

Constant Variance Standard Population:

(Homoscedasticity)

Delay Variable:

 $\label{eq:logTransformation: Yes {ln(y) = xb}} \end{math} \begin{tabular}{ll} Delay Standard Error. \end{math}$ 

Method and Parameters Tab:

Method: Grid Search

Minimum number of observations from a joinpoint to either end of the data: 2

Minimum number of observations between two joinpoints: 2

Number of points to place between adjacent observed x values in the grid search: 0

Min. percentage points difference between consecutive APC segments (MADWD): Not Used

Number of Joinpoints:

Number Joinpoints: Minimum: 0 Maximum: 4

Autocorrelated Errors Options: Fit an uncorrelated errors model

Model Selection Method: BIC3

APC/AAPC/Tau Confidence Intervals: Parametric # of Resamples: Not Applicable

AAPC Segment Ranges:

Ranges: Entire Range ,

Additional Ranges:

Advanced Analysis Tools Tab:

Advanced Analyses: None

Pairwise Comparison:

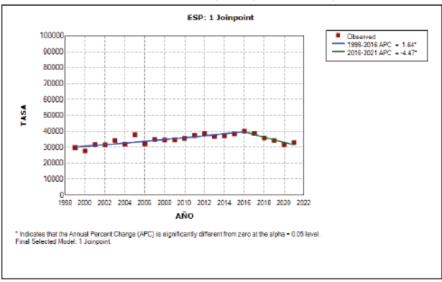
Pairwise Comparison: Not Applicable
Significance level: Not Applicable
Max number of randomly permuted data sets: Not Applicable

Jump Model / Comparability Ratio: None

Jump Location: -1 Comparability Ratio: -1 Variance of CR: -1

Joinpoint - V4.9.0.0 Joinpoint Session - 7 - output results-2 11-16-2023





Confidence Intervals: Parametric method

3 of 6

Joinpoint - V4.9.0.0 Joinpoint Session - 7 - output results-2

Job Submitted: 11/16/2023 13:42:21

11-16-2023

ESP, Number of Joinpoints: 1 (Final Selected Model) continued...

Observed and Modeled Data Points								
X Value	Observed TASA	Modeled TASA	JP Location					
1999	29805.00	30149.86						
2000	27795.00	30645.54						
2001	31729.00	31149.36						
2002	31556.00	31661.47						
2003	34294.00	32181.99						
2004	32069.00	32711.08						
2005	37911.00	33248.86						
2006	32176.00	33795.48						
2007	35034.00	34351.09						
2008	34685.00	34915.83						
2009	34725.00	35489.86						
2010	35623.00	36073.33						
2011	37424.00	36666.39						
2012	38782.00	37269.19						
2013	36802.00	37881.91						
2014	37249.00	38504.70						
2015	38457.00	39137.74						
2016	40168.00	39781.17	Joinpoin t1					
2017	38877.00	38003.93						
2018	35943.00	36306.09						
2019	34343.00	34684.10						
2020	31676.00	33134.58						
2021	32993.00	31654.27						

Joinpoint - V4.9.0.0 Joinpoint Session - 7 - output results-2 11-16-2023

ESP, Number of Joinpoints: 1 (Final Selected Model) continued...

Model Statistics								
Cohort	Number of Joinpoints	Number of Observations	Number of Parameters	Degrees of Freedom	Sum of Squared Errors	Mean Squared Error	Autocorrelation Parameter	
ESP	1	23	4	19	0.04394	0.00231	Uncorrelated	

	Estimated J	Joinpoints			
Cohort	Joinpoint	Estimate	Lower CI	Upper CI	
ESP	1	2016	2014	2018	
	Estimated R	Regression Coeffici	ents (Beta)		
	Stan	dard Parameterizat	ion		
Cohort	Parameter	Param Estimate	Standard Error	Test Statistic (t)	Prob >  t
ESP	Intercept 1	-22.283101	4.902733	-4.545037	0.000251
ESP	Slope 1	0.016307	0.002443	6.675376	0.000003
ESP	Slope 2 - Slope 1	-0.062011	0.015793	-3.926354	0.000990

<sup>-</sup> The statistic could not be calculated.

	General Parameterization									
Cohort	Parameter	Param Estimate	Standard Error	Test Statistic (t)	Prob >  t					
ESP	Intercept 1	-22.283101	4.902733	-4.545037	0.000251					
ESP	Intercept 2	102.730643	31.503303	3.260948	0.004339					
ESP	Slope 1	0.016307	0.002443	6.675376	0.000003					
ESP	Slope 2	-0.045704	0.015603	-2.929110	0.008963					

<sup>-</sup> The statistic could not be calculated.

	Estimated Joinpoints							
Cohort	Cohort Joinpoint Estimate Lower CI Upper CI							
ESP	1	2016	2014	2018				

Joinpoint - V4.9.0.0 Joinpoint Session - 7 - output results-2 11-16-2023

ESP, Number of Joinpoints: 1 (Final Selected Model) continued...

	Annual Percent Change (APC)										
Cohort	Segment	Lower EndPoint	Upper Endpoint	APC	Lower CI	Upper CI	Test Statistic (t)	Prob >  t			
ESP	1	1999	2016	1.6*	1.1	2.2	6.7	< 0.001			
ESP	2	2016	2021	-4.5"	-7.5	-1.3	-2.9	0.009			

<sup>\*</sup> Indicates that the Annual Percent Change (APC) is significantly different from zero at the alpha = 0.05 level.

- The Staustic	ne statistic could not be calculated.										
	Average Annual Percent Change (AAPC)										
								DW 1 4			
Cohort	Range	Lower EndPoint	Upper Endpoint	AAPC	Lower CI	Upper CI	Test Statistic *	P-Value *			
ESP	Full Range	1999	2021	0.2	-0.6	1.0	0.6	0.582			

<sup>-</sup> The statistic could not be calculated.

Mod	el Selection Method
Cohort	Model Selection Method
ESP	BIC3

			Test for Numbe	r of Joinpoints			
Cohort	Model	Number of Joinpoints	Number of Observations	Number of Parameters	Degrees of Freedom	Sum of Squared Errors	Bayesian Information Criterion
ESP	#1	0 Joinpoint(s)	23	2	21	0.1379251	-4.8438867
ESP	#2	1 Joinpoint(s) ^	23	4	19	0.0439386	-5.5788280
ESP	#3	2 Joinpoint(s)	23	6	17	0.0369153	-5.3440170
ESP	#4	3 Joinpoint(s)	23	8	15	0.0339381	-5.0191256
ESP	#5	4 Joinpoint(s)	23	10	13	0.0328762	-4.6419396

<sup>^</sup> Selected Model

 $<sup>^*</sup>$  Indicates that the AAPC is significantly different from zero at the alpha = 0.05 level.  $\sim$  If the AAPC is within one segment, the t-distribution is used. Otherwise, the normal (z) distribution is used.

### **FPIMortality men**

Joinpoint - V4.9.0.0 11-16-2023 Joinpoint Session - 5 - output results-4

Autocorrelated Errors Options: Fit an uncorrelated errors model

Model Selection Method: Weighted BIC

# of Resamples: APC/AAPC/Tau Confidence Intervals: Parametric Not Applicable

AAPC Segment Ranges:

Entire Range Ranges:

Additional Ranges:

Advanced Analysis Tools Tab:

Advanced Analyses: None

Pairwise Comparison:

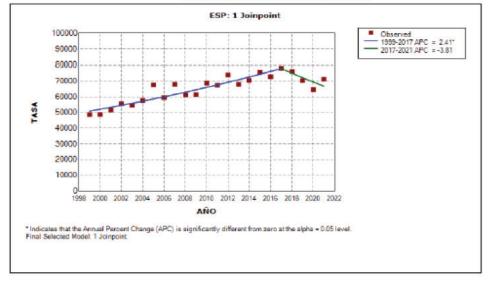
Not Applicable Pairwise Comparison: Significance level: Not Applicable Max number of randomly permuted data sets: Not Applicable

Jump Model / Comparability Ratio: None

Jump Location: -1 Comparability Ratio: -1 Variance of CR: -1

Joinpoint - V4.9.0.0 Joinpoint Session - 5 - output results-4 11-16-2023





Confidence Intervals: Parametric method

3 of 6 Job Submitted: 11/16/2023 13:13:04

Joinpoint - V4.9.0.0 Joinpoint Session - 5 - output results-4 11-16-2023

ESP, Number of Joinpoints: 1 (Final Selected Model) continued...

ODOBIV	ed and Mod	Jeleu Data	PUIILO
X Value	Observed TASA	Modeled TASA	JP Location
1999	48796.00	50864.18	
2000	48840.00	52088.86	
2001	51666.00	53343.04	
2002	55738.00	54627.41	
2003	54751.00	55942.70	
2004	57710.00	57289.67	
2005	67653.00	58669.07	
2006	59502.00	60081.67	
2007	67999.00	61528.30	
2008	61227.00	63009.75	
2009	61576.00	64526.87	
2010	68743.00	66080.52	
2011	67342.00	67671.58	
2012	73892.00	69300.95	
2013	67954.00	70969.54	
2014	70479.00	72678.32	
2015	75631.00	74428.24	
2016	72737.00	76220.29	
2017	78030.00	78055.49	Joinpoin t 1
2018	76237.00	75078.10	
2019	70450.00	72214.29	
2020	64639.00	69459.71	
2021	71118.00	66810.21	

4 of 6 Job Submitted: 11/16/2023 13:13:04

11-16-2023 Joinpoint - V4.9.0.0 Joinpoint Session - 5 - output results-4

ESP, Number of Joinpoints: 1 (Final Selected Model) continued...

Model Statistics							
Cohort		Number of Observations	Number of Parameters		Sum of Squared Errors	Mean Squared Error	Autocorrelation Parameter
ESP	1	23	4	19	0.06212	0.00327	Uncorrelated

	Estimated Joinpoints										
Cohort	Cohort Joinpoint Estimate Lower CI Upper CI										
ESP	ESP 1 2017 2004 2019										
	Estimated Regression Coefficients (Beta)										
	Stan	dard Parameteriza	tion								
Cohort	Parameter	Param Estimate	Standard Error	Test Statistic (t)	Prob >  t						
ESP	ESP Intercept 1 -36.723853 5.330902 -6.888862 0.000002										
ESP	Slope 1	0.023792	0.002655	8.959676	0.000000						
ESP	Slope 2 - Slope 1	-0.062683	0.026275	-2.385705	0.028243						

<sup>-</sup> The statistic could not be calculated.

General Parameterization								
Cohort	Parameter	Param Estimate	Standard Error	Test Statistic (t)	Prob >  t			
ESP	Intercept 1	-36.723853	5.330902	-6.888862	0.000002			
ESP	Intercept 2	89.708354	52.789743	1.699352	0.106469			
ESP	Slope 1	0.023792	0.002655	8.959676	0.000000			
ESP	Slope 2	-0.038891	0.026140	-1.487797	0.154114			

<sup>-</sup> The statistic could not be calculated.

	Estimated Joinpoints						
Cohort	Joinpoint	Estimate	Lower CI	Upper CI			
ESP	1	2017	2004	2019			

Joinpoint - V4.9.0.0 Joinpoint Session - 5 - output results-4 11-16-2023

ESP, Number of Joinpoints: 1 (Final Selected Model) continued...

Annual Percent Change (APC)									
Cohort Segment Lower EndPoint Upper Endpoint APC Lower CI Upper CI Test Statistic (t) Pro								Prob >  t	
ESP	1	1999	2017	2.4*	1.8	3.0	9.0	< 0.001	
ESP	2	2017	2021	-3.8	-9.0	1.6	-1.5	0.154	

<sup>\*</sup> Indicates that the Annual Percent Change (APC) is significantly different from zero at the alpha = 0.05 level.

<sup>-</sup> The statistic could not be calculated.

	Average Annual Percent Change (AAPC)									
Cohort	Range	Lower EndPoint	Upper Endpoint	AAPC	Lower CI	Upper CI	Test Statistic *	P-Value *		
ESP	Full Range	1999	2021	1.2*	0.2	2.3	2.4	0.018		

The statistic could not be calculated

- The statistic could not be calcu	lateu.
Mode	el Selection Method
Cohort	Model Selection Method
ESP	Weighted BIC

			Test for Numbe	r of Joinpoints			
Cohort	Model	Number of Joinpoints	Number of Observations	Number of Parameters	Degrees of Freedom	Sum of Squared Errors	Bayesian Information Criterion
ESP	#1	0 Joinpoint(s)	23	2	21	0.1240861	-4.9496222
ESP	#2	1 Joinpoint(s) ^	23	4	19	0.0621197	-5.3008039
ESP	#3	2 Joinpoint(s)	23	6	17	0.0454200	-5.2749004
ESP	#4	3 Joinpoint(s)	23	8	15	0.0423775	-4.9874536
ESP	#5	4 Joinpoint(s)	23	10	13	0.0406709	-4.6683333

<sup>^</sup> Selected Model

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<sup>\*</sup> Indicates that the AAPC is significantly different from zero at the alpha = 0.05 level.

~ If the AAPC is within one segment, the t-distribution is used. Otherwise, the normal (z) distribution is used.

# **CLINICAL MANAGEMENT PERSPECTIVE**



Job F.M. van Boven PharmD, PhD, Associate Professor of Respiratory Drug Utilization, Groningen Research Institute for Asthma and COPD (GRIAC), University Medical Center Groningen, The Netherlands

### DIGITAL INHALERS IN AIRWAYS DISEASE MANAGEMENT

Inhalers containing corticosteroids and bronchodilators are the basis of asthma and COPD treatment. In clinical trials, these inhaled medicines have been found to be highly effective with minimal side effects. However, their clinical benefits in daily real-world practice are typically much lower. One of the main reasons for this reduced efficacy is suboptimal use of the inhaler, being it less use than prescribed and/or using it with an incorrect technique. Indeed, this "non-adherence" is a widespread phenomenon, present in up to 50-70% of all patients. Of note, not only is this associated with poorer clinical outcomes (e.g. more uncontrolled disease, exacerbations), it can also lead to higher costs (due to more healthcare utilization, or additional therapies prescribed).[1]

Newly developed "digital" inhalers and spacers may be a solution to tackle this longstanding problem. Over the last decade, we have seen a cumulation of their features, not merely monitoring adherence, but now also providing personalized intake reminders and motivational messages, supporting inhaler technique education, guidance follow-up treatment (e.g., decision to start a biologic) and even allowing prediction of future exacerbations.[2] Alongside their enhanced capabilities, the clinical and cost-effectiveness evidence base has been steadily improved [3], and they have become part of GINA and GOLD strategy documents as tools to monitor and improve adherence and technique. Finally, in the clinical trial setting they may facilitate decentralized clinical trials, help explain variability in drug response and allow for more personalized dosing.[4]

### How digital inhalers could help facilitate clinical management...

- 1. Monitor adherence and inhaler technique
- 2. Proactively support patients' adherence and inhaler technique
- 3. Help understand drug response and need for step-up or step-down treatment
- 4. Predict, early detection and management of exacerbations

### References

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**NORKING** 





### **ADHERENCE** WORKING GROUP

At the REG Summit in March 2025, Amy, WG Chair, discussed in with members the research ideas first introduced at the virtual meeting in Dec 2024. Among the proposals, the exploration of biologics use in asthma and the role of electronic medical devices (EMDs) in asthma and COPD were considered the most attractive, reflecting current clinical and scientific interest. The WG is now planning next steps to take these projects forward.

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### **ALLERGY** WORKING GROUP

The group has developed a proposal on allergen immunotherapy missed opportunities and resource expenditure in the UK which has been shared with several AIT companies for feedback and sponsorship and we are awaiting responses from companies. Following discussions at the REG Summit in March, the group are currently developing new project ideas in allergic asthma and rhinitis with/without nasal polyps.

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### CHILD HEALTH WORKING GROUP

The WG has completed the database study "Prevalence and Incidence of Severe Asthma in Children in UK Primary Care between 2010 and 2020", using OPCRD data. The study was finalised and submitted to JACI in July 2025 and is now under review. In parallel, the WG is finalising the manuscript on biomarkers as part of the PEARL project, which is expected to be submitted to a peer-reviewed journal in 2025.





### **COPD** WORKING GROUP

As part of the PIF in COPD study, the WG has worked on two manuscripts. The first, based on baseline data — "Assessment of Peak Inspiratory Flow in Patients with Chronic Obstructive Pulmonary Disease: A Multicentre, Observational, Prospective, Real-life Study" — has completed its second revision with BMJ Open Respiratory Research and is now awaiting the final steps toward publication. The second, based on follow-up visits — "Suboptimal Peak Inspiratory Flow, COPD Exacerbations, Hospitalisations, and Disease Burden: A Longitudinal Follow-Up in a Multicentre Real-World Study" — is under revision by the authors and will soon be submitted to ERJ Open Research.

The WG has also finalised the manuscript "Development and Validation of the PRECISE-X Model: Predicting First Severe Exacerbation in COPD," which has been submitted to Thorax and is currently under review. Building on this, the group is developing a follow-up study to validate PRECISE-X using additional international databases beyond CPRD (UK), with the proposal now under discussion with pharmaceutical partners.

The group is now progressing with its new project on triple therapy in COPD, with investigators currently applying for ethical approvals before starting patient data collection.

REG is actively seeking more sites to join this project and for more information please contact the research leader, Valeria Perugini valeria@regresearchnetwork.org.

Finally, the WG has developed a registry project to define key clinical variables for severe COPD patients, covering both pharmacological and advanced therapies (e.g. biologics, bronchoscopic, surgical). The aim is to standardise data collection across registries to enable comparability and pooling. A proposal and budget have been prepared and will now be shared with companies to seek funding.

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### COST EFFECTIVENESS WORKING GROUP

The AstraZeneca-funded project, "A Global Evaluation of the Economic Impact of Time to Initiation of Biologic Treatment of Severe Asthma Patients," is underway, with preliminary results from the economic modelling being produced and discussed among the steering committee for feedback and guidance prior to the final analysis and results. The project seeks to assess the national-level cost-effectiveness of biologic treatment, examining and comparing the economic impact and lifelong disease burden associated with time to initiation of treatment between countries.



### DATABASES AND CODING WORKING GROUP

The WG has finalised the study proposal "Exploring the Combined Effects of COPD and Type 2 Diabetes Mellitus on Health Outcomes and Mortality, with Insights into GLP-1 Receptor Agonists." The proposal has been shared with pharmaceutical companies, and the group is now awaiting feedback.



### ENVIRONMENT, EPIDEMIOLOGY AND AIRWAYS WORKING GROUP

The manuscript "Respiratory Effectiveness Group Position Statement: Inhaler Choice: Balancing Personalised Healthcare and Environmental Responsibility" has been published in the Journal of Aerosol Medicine and Pulmonary Drug Delivery. As a result, the group was asked to write a comment piece for the Hospital Healthcare Europe. This was written and is titled "Aligning patient-centred care and sustainability in inhaler choice: a Respiratory Effectiveness Group approach" It is awaiting publication.

### **ILD** WORKING GROUP

The group has developed the flagship ILD project proposal "Towards Standardisation in IPF / PPF Registry Data: A Global Initiative", which has been separated into three subprojects:

Project 1: "Identifying Key Variables through a Global Prioritisation Task".

Project 2: "Identifying Data Elements for Disease Management".

Project 3: "Development of a Global Composite Staging System for IPF/PPF Disease Progression".

Project 1 proposal has been shared with funders, and we have secured funding for 50% of the budget for Project 1. We are awaiting responses from other funders and are actively seeking additional potential funders.

The group is also developing a proposal to study acute exacerbations in ILD patients with the aims of predicting mortality, lung transplant needs, and recurrent exacerbations in these patients. The project will also assess the economic impact of delayed treatment or missed exacerbations, quantifying potential savings through reduced hospitalisations, transplant avoidance, and access to palliative care.

The Group is providing support as a collaborator to a ILD-Delphi study aiming to identify centres around the world where genomic testing is offered for ILD cases and characterize the existing practice and reach consensus on the utility of genomic testing and screening of relatives for early ILD diagnosis.

### SEVERE ASTHMA AND BIOMARKERS WORKING GROUP

At the REG Summit in March 2025, the WG developed research ideas around the use of oscillometry, FeNO, and blood tests to assess exacerbations in patients with asthma. Building on this discussion, the group is now working on ways to take the project a step further by developing a study proposal.

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### TECHNOLOGY WORKING GROUP

The group is developing new project ideas, looking at the use of oscillometry for the early detection and/or diagnosis of COPD, asthma and small airways disease (SAD), as well as using it to monitor treatable traits of SAD and the reversal of asthma.

Following discussions at the REG Summit in March, the group is developing proposals for the use of nebulisers in COPD patients.

### **VACCINES** WORKING GROUP

A proposal for the project "Vaccine Uptake and Clinical Outcomes in High-Risk Chronic Respiratory Patients: A Retrospective Database Study" has been developed and shared with several companies for feedback and sponsorship. We are awaiting responses from companies. The project aims to examine vaccine coverage and uptake trends in high-risk chronic respiratory patients, as well as identify the clinical and economic impacts of vaccination.





# T **REG** MEANS TO

To me, REG represents a vibrant, dynamic, and productive community. It brings together health professionals, statisticians, methodologists, and industry partners, all united by a shared commitment to advancing respiratory research and patient care by maximising the value of real-world evidence. What makes REG stand out is its "doer's approach": discussions methodically evolve into concrete projects, informed by international clinical insights, academic expertise, and rigorous methodology, and translated into impactful outputs. The diversity of expertise ensures that multiple perspectives are represented, while the collaborative spirit creates a unique environment where meaningful progress is made.

I first joined REG in 2015, and since then it has been a valuable platform for collaboration and exchange. REG meetings have offered excellent opportunities to learn, present my work, receive feedback, and connect with world-leading experts as well as dynamic emerging leaders. Working alongside them has allowed me to contribute to international, clinically relevant projects. The working group meetings have been particularly rewarding, offering space for open discussion, multidisciplinary input, and joint problem-solving.

As a Steering Committee member of the Paediatric Asthma in Real Life (PeARL) think tank (a REG initiative), I have contributed to the development of the much needed paediatric asthma guidelines, supporting methodology and co-ordinating systematic reviews. During the COVID-19 pandemic, we rapidly generated evidence on its impact on paediatric asthma, which directly informed clinical practice and public health.

Overall, for me, REG has been both a professional network and an inspiring community. It has enabled me to collaborate, contribute, and learn, while demonstrating how collective effort across disciplines can generate evidence that informs both practice and policy. Beyond individual projects, REG has also provided a model of how inclusive, international research networks can accelerate progress, nurture collaboration, and ensure that research remains clinically meaningful and patient-centred.

### ALEXANDER G. MATHIOUDAKIS MD,

MRCP(UK), PhD, FHEA, FERS. Senior Lecturer in Respiratory Medicine, The University of Manchester Consultant Respiratory Physician, Manchester University NHS Foundation Trust



Imagine a treasure chest - not of gold and jewels, but of knowledge, collaboration, and game-changing insights. That's what REG is to me: a box of endless opportunity, overflowing with chances to learn, grow, and transform respiratory research.

As a newcomer to REG, stepping into the 2025 London event for the first time was like unlocking that chest and being instantly immersed in its energy. I found myself surrounded by brilliant minds, bold ideas, and a shared commitment to making respiratory care more relevant, more responsive, and more real. It was inspiring, energizing and most of all - refreshingly human. The conversations went beyond data, touching on the everyday realities of patients and the challenges clinicians face in translating evidence into practice. But REG goes beyond science - it's a career catalyst, a hub for mentors and innovators, and, let's be honest, a pretty fantastic excuse to travel to conferences that make you feel smarter just by walking in. It's where research

becomes real-world change, shaping guidelines and ensuring therapies work in the unpredictable coughridden chaos of everyday life.

So, if REG is a box, it's not one you want to leave gathering dust. It's an invitation to think bigger, collaborate better, and maybe, just maybe, make respiratory health a little less serious and a lot more exciting.

### STEFANIA GALLO, MD PHD

Staff Otolaryngologist, ASST Sette Laghi, Varese (Italy), Steering committee RINET registry (Rhinosinusitis Italian Network)



# WHAT **REG** MEANS TO ME



As a pulmonologist and Medical Group Lead in Respiratory at Roche, The Respiratory Effectiveness Group (REG) represents, for me, much more than a scientific network—it is a true community where collaboration, innovation, and patient-centered science meet.

REG is an important partner for all of us committed to advancing the standard of care in respiratory medicine. Its mission to generate robust real-world evidence directly complements the work we do at Roche, where our goal is to translate scientific innovation into meaningful outcomes for patients living with chronic respiratory diseases.

While randomized controlled trials remain the foundation of medical evidence, we know they cannot fully capture the complexity of daily clinical practice. Patients present with comorbidities, diverse treatment pathways, and challenges in adherence that go far beyond controlled study settings. REG plays a critical role in addressing this gap—conducting high-quality, methodologically sound, effective research that ensures evidence is both scientifically rigorous and directly applicable to realworld patient care.

Equally important is the collaborative structure that REG fosters. Through its working groups, scientific meetings, and global summits, REG brings together clinicians, academic researchers, professional societies, and

industry partners to exchange insights and align on priorities. This multidisciplinary dialogue is essential for accelerating the development and implementation of new treatment approaches, and ultimately for shaping evidence-based guidelines that improve patient outcomes.

What REG represents for me is not only methodological excellence and scientific credibility, but also a shared vision: to ensure that every patient receives care that reflects the realities of their lives. By building bridges between clinical research, healthcare systems, and industry, REG exemplifies how collaboration can drive sustainable impact.

At Roche, we are proud to contribute to this collective effort. Together with REG and the wider respiratory community, we have the opportunity to generate the evidence needed to raise the profile of respiratory disease and deliver the improvements in care our patients deserve.

DR. KATERINA SAMARA Global Medical Affairs Group Lead Respiratory F. Hoffmann-La Roche



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# INTERNATIONAL SEVERE ISAR ASTHMA REGISTRY

### ISAR Country Updates

We celebrate the International Severe Asthma Registry (ISAR)'s recruitment of 34,721 severe asthma patients from 29 countries, with the achievement of 35 publications and 63 abstracts and posters. We thank all our ISAR collaborators for their contributions!

### ISAR in 2025: Publications

ISAR has published 7 articles in the first half of 2025. To view ISAR's publications, please visit the ISAR website.

Chen W., et al.

"Impact of biologic initiation on oral corticosteroid use in the **International Severe Asthma** Registry and the Optimum Patient Care Research Database: a pooled analysis of real-world evidence (SOLAR I)"

J Allergy Clin Immunol Pract, 2025

Full Article Press Release

Slide Deck

Key Findings: Biologic initiation in patients with severe asthma led to substantial reduction in total oral corticosteroid (OCS) exposure, particularly in the first year.

Sadatsafavi M., et al.

"Prevention of cardiovascular and other systemic adverse outcomes in asthma patients treated with biologics (SOLAR II)"

Am J Respir Crit Care Med, 2025

Full Article

Press Release

Slide Deck

Key Findings: Biologics prevent new-onset OCSrelated adverse outcomes (including diabetes, major cardiovascular events and anxiety/depression) in patients with severe asthma

Tran T.N., et al.

"Real-World Biologic Use Patterns in Severe Asthma, 2015-2021: the **CLEAR Study**"

Pragmat Obs Res, 2025

Full Article

Press Release

Slide Deck

Key Findings: Biologic continuers had fewer exacerbations, lower long-term OCS use and better asthma control than switchers or stoppers at follow-up.



### Schleich F. et al.

"Biomarker profile and disease burden associated with intermittent and long-term oral corticosteroid use in patients with severe asthma prior to biologic initiation in real-life (STAR)"

World Allergy Organization J, 2025

Full Article Press Release Slide Deck

Key Findings: OCS (intermittent or long-term) use affects BEC distribution and disease burden was high among long-term OCS users irrespective of BEC.

Larenas-Linnemann D., et al.

"International Severe Asthma Registry (ISAR) - 2017-2024 Status and Progress Update"

Tuberc Respir Dis (Seoul), 2025

Full Article

Key Findings: ISAR's origins, Delphi studies, research, ongoing quality improvement initiatives, and vision for the future are summarized.

### Côté A., et al.

"Poor agreement among asthma specialists on the choice and timing of initiation of a biologic treatment for severe asthma patients. (CHOIX BIO)"

J Allergy Clin Immunol Pract, 2025

**Key Findings:** There was weak interobserver agreement among asthma specialists in initiating biologics and selecting treatment.

### Yadav C.P., et al.

"Prediction pathway for severe asthma exacerbations: a Bayesian Network analysis"

CHEST, 2025

Full Article Press Release

Slide Deck

Key Findings: T2 and non-T2 inflammatory pathways predict severe asthma exacerbations.

### ISAR in 2025: Abstracts

ISAR presented a late-breaking poster (SOLAR II) at ATS 2025. To view ISAR's abstracts, please visit the ISAR website

Price D.B., et al.

"Impact of Biologic Initiation on **New-Onset of Corticosteroid-Related** Adverse Effects in Patients with Severe Asthma (SOLAR II)" Am J Respir Crit Care Med, 2025

**Key Findings:** Initiation of biologics in patients with severe asthma was associated with reduction in their risk of new-onset OCS-related adverse events, including diabetes, anxiety/depression, and major cardiovascular events.

#### **Abstract**

We are pleased to share that 2 abstracts have been accepted as poster presentations at ERS 2025.

Alotaibi N, Bergeron C, et al.

"Novel Insights into the Comorbidity Burden of Severe Asthma in Canada: Analysis of the Canadian Severe Asthma Registry"

To be presented at ERS 202

Session details:

Presenter: Dr. Nawaf Alotaibi

Session Name: Clinical Management of Severe Asthma

Session Date: Monday, 29 September 2025

Session Time: 12:30 PM - 2:00 PM Session Location: Poster Area

Poster Row: PS-17.

Larenas-Linnemann D, et al.

"Clinical profile of severe asthma (SA) patients Mexican vs Global data and evolution once in the international severe asthma registry (ISAR)"

To be presented at ERS 2025

Session details:

Presenter: Désirée Larenas-Linnemann

Session Name: Remission/stability in airway diseases:

how to achieve and what is next?

Session Date: Tuesday, 30 September 2025

Session Time: 12:30 PM - 2:00 PM Session Location: Poster Area

Poster Row: PS-16

### ISAR in 2025: Events



Respiratory Effectiveness Group (REG) Summit London, United Kingdom 20-22 March 2025

### **Highlights:**

- 58 collaborators from 28 countries attended ISAR events (in person and online).
- ISAR research projects 2025 (SHINE and MOONLIGHT) were introduced; updates for the ISAR research projects 2024 (GLEAM and SPOTLIGHT) were presented.
- Ideas for practice change and the long-term sustainability of ISAR were discussed.
- 20 country meetings were held to promote engagement in quality improvement.
- ISAR Session (co-chaired by David Price and Veronica Mendez):
  - Luis Perez-de-Llano presented findings from FULL BEAM II.
  - Walter Canonica and Victoria Carter introduced GLEAM and SPOTLIGHT.
  - Désirée Larenas-Linnemann and CelineGoh discussed practice change.
  - Piotr Kuna presented the ground-breaking **SOLAR II** study.
  - Pujan Patel and Freya Tyrer presented trends in OCS use in ISAR patients.



### ISAR in 2025: Events



**American Thoracic Society (ATS) Congress** San Francisco, United States 16-21 May 2025

### **Highlights:**

- 23 collaborators attended ISAR events (in person and online).
- SOLAR II was presented as a late-breaking poster (by Ghislaine Scelo) and at a prestigious NEJM/ AJRCCM/ JAMA journal session (by David Price).
- Updates for SPOTLIGHT, SHINE and MOONLIGHT were presented.
- ISAR's quality improvement goal 2025, the elimination of long-term OCS use and frequent intermittent OCS use, was discussed.
- Upcoming quality improvement tools were showcased:
  - REDCap Lite streamlines the clinical consultation form to a single page and encourages broader use of REDCap as a clinical tool.
  - ISAR OCS risk calculator predicts health risks linked to OCS use in patients with asthma.

### Upcoming ISAR Event 2025



**European Respiratory Society** (ERS) Congress Amsterdam, Netherlands

27 Sep - 1 Oct 2025

### Saturday 27th September

Hotel Okura, Amsterdam

14:30 - 15:00 | ISAR Steering Committee | MOONLIGHT working group meeting: Impact of biologics on inhaled corticosteroid reduction

15:00 - 15:30 | SPOTLIGHT working group meeting: Impact of remission on long-term clinical outcomes

15:45 - 16:30 | ISAR Quality Improvement | ENLIGHTEN working group meeting: Assessment of quality improvement in ISAR

16:45 - 17:30 | Research Updates | SHINE working group meeting: Maintenance of long-term remission and the causes of secondary failure to biologics

17:30 - 19:00 | Reception



### Join ISAR today!

To register interest as a collaborating country, or to submit a research request or proposal, please contact us here.

# THANKS TO OUR SUPP

The work of REG would not be possible without the contributions of our invaluable supporters to fund innovative research projects developed by our expert collaborators.

REG is looking to launch a number of ambitious research initiatives that offer the opportunity to impact clinical management guidelines and patient care.

We welcome any suggestions from supporters and would be happy to discuss your ideas in more detail.

> You can always get in contact with the REG team by email at enquiries@regresearchnetwork.org,

> > or write to Michael Walker, REG, CEO, at michael@regresearchnetwork.org



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# THE RESPIRATORY EFFECTIVENESS GROUP



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