



# ADVANCES

in Real-life Respiratory Research

ISSUE SUMMER 2018

The Respiratory Effectiveness Group Newsletter

## REG NEW PUBLICATIONS

page 5



## REG DURING ERS 2018

page 6



## WORKING GROUP SUMMIT UPDATE

page 9



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## THE RESPIRATORY EFFECTIVENESS GROUP NEWSLETTER ISSUE SUMMER 2018

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# CONTENTS



3

## EDITORIAL

**Nikos Papadopoulos**  
REG President



4

## REG TEAM UPDATE

**Michael Walker**  
REG CEO



5

## REG PUBLICATIONS 2018

6

## REG DURING ERS 2018

7

## INTERNATIONAL SEVERE ASTHMA REGISTRY ISAR

8

## REG SUMMIT 2019

9

## WORKING GROUP SUMMIT UPDATE



14

## ORAL ABSTRACT PRIZES

15

## REG SUPPORTERS



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## DEAR FRIENDS

The interest in understanding 'real-life' in biomedicine is increasing quickly and steadily. This is not anymore, a marginal movement of enthusiasts, but a fast-development concept that is penetrating in all aspects of clinical research. Just as I was writing this piece, an article in FDA Voice suggested that

**"BY USING THIS INFORMATION, WE CAN GAIN A DEEPER UNDERSTANDING OF A MEDICAL PRODUCT'S SAFETY AND BENEFITS, ITS ADDITIONAL TREATMENT IMPLICATIONS, AND ITS POTENTIAL LIMITATIONS".**

Well, when a regulator starts embracing a novel approach, we can be sure that 1) it will become standard in the next future and 2) it will soon be... regulated!

This is great news for REG, its collaborators and supporters, who have already taken several steps in defining, delineating and promoting pragmatism (a Greek word ;-). We are in a unique position to improve outcomes for our patients (which is probably the main motivation for all of us), by improving methodologies to become less 'sterile' and more inclusive, representative, leading to more effective treatments!

In this context, I am delighted and honoured to have been elected President of REG and I am certain that I will enjoy working with you to take this research aspect a step forward. To start with, the Board of Directors has reshuffled responsibilities, we have a new CEO, Michael Walker, and specific targets for the next couple of years; more info on this can be found in this newsletter. Most importantly however, as a group, or a 'think-tank' as I prefer to describe us, we are entirely dependent on the creativity, open-mindedness and contribution of all collaborators and supporters, so do come forward with any research ideas, advocacy and educational proposals. We can certainly handle and welcome disruptive innovation!!

**Nikos Papadopoulos**  
REG President

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WELCOME  
DISRUPTIVE  
INNOVATION

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# REG TEAM UPDATE

Since the last edition of the REG Newsletter, there have been a number of changes to the REG team. Back in April 2017, Naomi Lauanders joined REG one of our Scientific Researchers. In Sept/Oct 2017 she was promoted to Senior Scientific Researcher in recognition of her professional management and leadership of her projects. Since April 2018, Sarah Lucas has been away on maternity leave and we are happy to advise that she is now the proud mother of a new baby boy.

In May 2018, Sanne van Kampen took over Sarah's responsibilities for the duration of the maternity leave. I am very pleased to welcome Sanne to the team.

Kathryn Brown continues to support the team on the administration side and is expanding her duties to include the REG website and social media.

At the Summit 2018 REG Board meeting, Catherine Hutton REG CEO advised that she was resigning from her position to focus on her new life in France. In May 2018 I joined the REG

taking over as CEO. My career in business and association management may have allowed our paths to cross in the past and I am very excited to take on this new challenge and working with a great team and the new President and Board members.

Time does not stand still, and neither does the work of the REG. In 2017 REG published 13 manuscripts from the current 14 Working Groups. In 2018 we are on track for a similar number of publications. A project is underway to develop a new corporate branding which you will see across all our materials and website in the coming months.

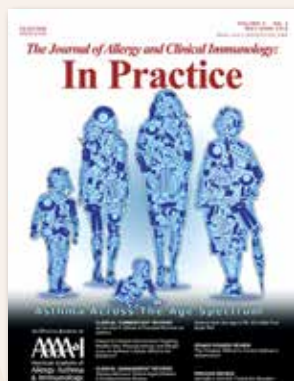
THE REG TEAM AND ITS COLLABORATORS CONTINUE TO DEVELOP NEW PROJECTS AND RESEARCH ACTIVITIES. AN UPDATE CAN BE READ IN THIS EDITION.

Attending the EAACI congress in Munich as well as the upcoming ERS congress in Paris are important opportunities for our Working Groups to meet and continue the progress of active projects or discuss the projects in development. It is also a valuable opportunity to meet with our partners and supporters to continue to deliver our real-world research. The support we have received until now is very much appreciated and I hope that our strong and positive collaborations will continue. I look forward meeting our many collaborators and supporters over the coming months.



Michael Walker  
REG CEO

# REG NEW PUBLICATIONS 2018



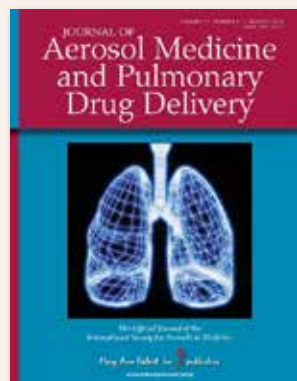
## Extrafine Versus Fine Inhaled Corticosteroids in Relation to Asthma Control: A Systematic Review and Meta-Analysis of Observational Real-Life Studies

### REFERENCES

Sonnappa S., McQueen B., Postma D. S., Martin R. J., Roche N., Grigg J., Guilbert T., Gouder C., Pizzichini E., Niimi A., Phipatanakul W., Chisholm A., Dandurand R. J., Kaplan A., Israel E., Papi A., van Aalderen W. M. C., Usmani O. S. and Price D. B. (2018) "Extrafine Versus Fine Inhaled Corticosteroids in Relation to Asthma Control: A Systematic Review and Meta-Analysis of Observational Real-Life Studies", *J Allergy Clin Immunol Pract*, 6(3), pp. 907-915.e7.

### ONLINE LINK

[www.sciencedirect.com/science/article/pii/S2213219817305573?via%3Dihub](http://www.sciencedirect.com/science/article/pii/S2213219817305573?via%3Dihub)



## Harmonizing the Nomenclature for Therapeutic Aerosol Particle Size: A Proposal

### REFERENCES

Hillyer E. V., Price D. B., Chrystyn H., Martin R. J., Israel E., van Aalderen W. M. C., Papi A., Usmani O. S. and Roche, N. (2018) "Harmonizing the Nomenclature for Therapeutic Aerosol Particle Size: A Proposal", *J Aerosol Med Pulm Drug Deliv*, 31(2), pp. 111-113.

### ONLINE LINK

[www.liebertpub.com/doi/10.1089/jamp.2017.1396](http://www.liebertpub.com/doi/10.1089/jamp.2017.1396)



## Trends of testing for and diagnosis of alpha-1 antitrypsin deficiency in the UK: more testing is needed

### REFERENCES

Soriano J. B., Lucas S. J., Jones R., Miravittles M., Carter V., Small I., Price D., Mahadeva R. and Group, R. E. (2018) "Trends of testing for and diagnosis of alpha-1 antitrypsin deficiency in the UK: more testing is needed", *Eur Respir J*.

### ONLINE LINK

[www.erj.ersjournals.com/content/early/2018/05/10/13993003.00360-2018](http://www.erj.ersjournals.com/content/early/2018/05/10/13993003.00360-2018)



## Evaluation of criteria for clinical control in a prospective, international, multicenter study of patients with COPD

### REFERENCES

Miravittles M., Sliwinski P., Rhee C. K., Costello R. W., Carter V., Tan J., Lapperre T. S., Alcazar B., Gouder C., Esquinas C., García-Rivero J. L., Kempainen A., Tee A., Roman-Rodríguez M., Soler-Cataluña J. J. and Price D. B. (2018) "Evaluation of criteria for clinical control in a prospective, international, multicenter study of patients with COPD", *Respir Med*, 136, pp. 8-14.

### ONLINE LINK

[www.resmedjournal.com/article/S0954-6111\(18\)30028-3/fulltext](http://www.resmedjournal.com/article/S0954-6111(18)30028-3/fulltext)

# REG DURING ERS 2018



The **Respiratory Effectiveness Group** team will be attending the ERS 2018 Congress in Paris, France and we are organising a number of meetings during the congress.

The majority of the meetings will take place on Saturday 15th September. The meetings on this day will be held in the **Mercure Parc des Expositions Hotel, 36 38 rue du moulin, 92170, Vanves.**

Due to the limited availability of meeting rooms at this year's congress, time is limited for Working Group meetings. If you would like to request a meeting in reference to a specific project or Working Group that is not listed on in the provisional timetable, or wish to organise a more informal meeting with other Collaborators or any member of the team, please contact:

[enquiries@effectivenessevaluation.org](mailto:enquiries@effectivenessevaluation.org)

to schedule a time.

## Saturday 15th September

[Mercure Parc des Expositions Hotel](#)

10:00 – 11:00	ILD/IPF Working Group
11:00 – 12:00	ACO Working Group
13:00 – 14:00	Cost Effectiveness Working Group
14:00 – 15:00	Small Airways Working Group
15:00 – 16:00	Database and Coding Working Group
16:00 – 17:00	Technologies Working Group
17:00 – 18:00	Adherence Working Group

## Sunday 16th September

[Paris Expo Porte de Versailles – Room 7.3F](#)

08:00 – 09:00	Child Health Working Group
09:00 – 10:00	COPD Working Group



# INTERNATIONAL SEVERE ASTHMA REGISTRY **ISAR**

The International Severe Asthma Registry (ISAR) is a collaborative initiative set in motion to create the first ever standardised non-drug specific severe asthma registry globally. The close collaboration between Optimum Patient Care (OPC) Global and the Respiratory Effectiveness Group (REG), has set ISAR well on its way to surpass the initial goal of recruiting 10,000 severe asthma patients from 14 countries in 5 years. In ISAR's inaugural year alone, over 5,000 patients data have been shared for ethically approved research, and 29 countries have registered their interest to participate. Further highlights from ISAR's first year include:

◆ **The ISAR Steering Committee (ISC)** - now made up of 34 members across 29 countries. Our collaborators and steering committee members have met five times during key respiratory conferences in 2017 and 2018, including the REG summit.

◆ **Real-life electronic capture systems (REDCap, CISIV, OpenClinica)** - multiple data capture systems supported to accommodate the preferences and requirements unique to each country.

◆ **Enhanced data capture** - now supporting enhanced data capture to facilitate future safety and effectiveness research in severe asthma globally.

◆ **Academic research outputs** - 8 academic datasets have now been prioritised for delivery by ISAR collaborators in the coming year:

1. Safety and Efficacy of Switching Biologics
2. Hidden Severe Asthma Patients in Primary Care
3. Assess the Overlap (reliability) of Collected Biomarkers
4. Identify Predictors (e.g. biomarkers) of Response to Biologics
5. The Role of Exacerbations on Lung Function Trajectory
6. Hidden Chronic Asthma within the COPD/ACO Population
7. Onset of Asthma in Severe Asthma patients
8. Association between Low Socioeconomic Status and Asthma Severity

◆ **Publications planned for 2018** - ISAR publication lead, Ruth Murray will be focusing on the following core publications from ISAR in 2018:

1. "Development of the international severe asthma registry (ISAR): a modified Delphi study" - describes the Delphi process used to determine the minimum set of core variables that all countries participating in ISAR will collect. This will soon be published in JACI In Practice.
2. "International Severe Asthma Registry (ISAR): Mission Statement"
3. "Demographic and Clinical Characteristics of Severe Asthma Patients Worldwide"
4. "Global Inventory of Severe Asthma Registries" - showcasing data fields of all severe asthma registries

For further information regarding this exciting initiative please visit the ISAR website: [www.isaregistries.org](http://www.isaregistries.org)

**SAVE  
THE  
DATE**

RESPIRATORY  
**REG**

**THE RESPIRATORY  
EFFECTIVENESS GROUP**

**REG**

**SUMMIT 2019**

**Capitalizing on real-life research  
for best clinical guidance**

*“Truth is simple and its  
proclamation even simpler”  
Euripides*

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# WORKING GROUP SUMMIT UPDATE

Twelve of the Working Groups met at the **REG summit in Amsterdam**. The meetings were held in parallel sessions on 22nd March, allowing time for reporting of results, critique of methodologies, discussion of new ideas and prioritisation of future projects.



## ASTHMA-COPD OVERLAP WORKING GROUP



The Asthma-COPD Overlap (ACO) group meeting was chaired by Nicolas Roche and David Price. The group briefly discussed the ongoing proof of concept study to assess the prevalence and population characteristics of people with ACO using the OPCR. Phase 1 of the study has been completed. It was agreed to finalise the manuscript within a few months. Phase 2 of the study will look at the clinical implications on ACO using the same dataset and a full protocol will be developed following completion of the Phase 1 manuscript. Further, plans for future projects were discussed, especially a study to repeat the proof of concept study in other national databases to evaluate ACO definitions. Five European databases seems most suitable and non-European databases would also be explored. Suggestions were made around variable inclusion and potential funders.

## COPD WORKING GROUP



Chaired by Marc Miravittles, the COPD group provided an update on current projects and discussed plans for future projects. Firstly, a prospective trial to validate the concept of COPD control in clinical practice is well underway and data collection on patients from 11 sites is expected to be completed in November 2018. Preliminary results were discussed and could be used in future studies to develop a primary care tool to define COPD control. Secondly, a pilot study to assess the modern epidemiology of alpha-1-antitrypsin deficiency (AATD) in the UK has been completed and results have been published in ERJ 2018. These suggest that more testing of AATD among COPD patients is needed. An idea was presented to plan a full database study investigating the prevalence, incidence and clinical outcomes in people with AATD. Finally, the group discussed a planned study to assess the implications of ICS withdrawal in the real-life management of COPD. Good suggestions were made for the protocol and additional study outcomes.





## OBSTRUCTIVE SLEEP APNOEA WORKING GROUP



The session was chaired by Mihaela Stefan and current projects discussed. A study protocol has been finalised to look at the impact of sleep-related breathing disorder (SBD) diagnosis on healthcare resource utilisation in patients with obstructive lung disease. Phase 1 of the study will evaluate the coding of SBD and related patient characteristics, including COPD and asthma diagnosis, using a small pilot dataset from OPCRD. A dataset will be generated shortly. Next, a full-scale supported study is planned to evaluate the prevalence of SBD and the impact of SBD diagnosis (with and without CPAP treatment) on clinical outcomes and healthcare resource utilization in a representative population of patients in the UK with comorbid obstructive lung disease. It was suggested that future relevant REG studies should consider the overlap between SBD and obstructive lung disease.

## ALLERGY WORKING GROUP



The group, chaired by Sven Seys, discussed a range of ongoing and proposed projects. It was agreed that the ongoing project to assess the incidence of acute and chronic rhinosinusitis using the OPCRD was a useful basis for a proposed study to look at diagnostic pathways, healthcare utilisation and natural history of rhinosinusitis. The eventual aim of this characterisation work would be to build clinical decision algorithms to expedite referral. Another ongoing project, a survey of allergic rhinitis sufferers, got good feedback from the group and a publication strategy was discussed. Finally, the group considered three further proposed studies, all of which plan to use the OPCRD. One study aims to examine the effects of cumulative steroid exposure in patients with chronic rhinosinusitis and other comorbidities treated with steroids, another to analyse the effect of sinus surgery on asthma symptoms and control, and a third to look at urticaria management. The studies were discussed in detail and many good suggestions made.

## CHILD HEALTH WORKING GROUP



Nikos Papadopoulos chaired the session, where the current project examining the comparative effectiveness of adding antibiotics to usual care for the management of asthma exacerbations was presented. A number of future projects were also discussed, including bronchiolitis and future risk of asthma; severe asthma in paediatrics; rhinitis in children; and the production of an evidence-based paediatric consensus statement.



## CHILD HEALTH WORKING GROUP

Nikos Papadopoulos chaired the session, where the current project examining the comparative effectiveness of adding antibiotics to usual care for the management of asthma exacerbations was presented. A number of future projects were also discussed, including bronchiolitis and future risk of asthma; severe asthma in paediatrics; rhinitis in children; and the production of an evidence-based paediatric consensus statement.



## SMALL AIRWAYS WORKING GROUP

Chaired by Omar Usmani, the discussion centred on the future of the group, the direction of the group and whether it should be a standalone group or combined with another. The group has been very active in the past, but fine dose research is reducing. A decision was made to discuss further at ERS 2018. Two proposed studies were also discussed. One proposed to use the OPCRD to investigate the effects of obesity, weight loss and weight loss surgery on asthma; the other looks at what "dose" means to different specialities and stakeholders in asthma research. Both of these proposals were well received and are currently being developed into project protocols.



## ADHERENCE WORKING GROUP

The session was chaired by Alexandra Dima. The main project was discussed to improve understanding of the bi-directional causality relationship between asthma outcomes and adherence. Phase 1 of the study looked at how ICS adherence can best be measured in medical databases and was published in 2016. Phase 2 was a retrospective cohort study following asthma patients for three years and the results of this study are now being written up. Challenges were discussed including limitations of measuring adherence using drug prescription data and potential bias of using patients with at least two years of follow-up data. Suggestions for future studies included assessing the clinician's role and the effects of behavioural change after exacerbations on adherence.



## COST EFFECTIVENESS WORKING GROUP



The cost effectiveness group met to brain storm new ideas. After a fruitful brainstorming session in which many ideas were suggested, it was decided that the group would focus on the cost burden of COPD in the non-smoking population. Job van Boven is leading on producing a proposal for this project and it will be presented in the working group meetings at ERS 2018.

## QUALITY STANDARDS WORKING GROUP



The quality standards group have one ongoing project, RELEVANT, which aims to create a tool for the assessment of quality of published real-life asthma studies. The group discussed potential journals for the two manuscripts under review with EAACI, and how best to disseminate the RELEVANT tool.

## DATABASE & CODING WORKING GROUP



Katie Verhamme chaired the session and reported the progress of the TORPEDO project. The project aims to characterise existing routine care databases and develop a set of core and additional variables for respiratory and lung health databases. The first round of the consensus reaching exercise is complete, with excellent agreement on the majority of questions. During the meeting, good progress was made in agreeing the variables for the second round.

## TECHNOLOGY WORKING GROUP



Naomi Lauanders presented a proposed study to investigate the feasibility, utility and user acceptance of smart inhalers. The first phase of the study would be a systematic review, and there was useful discussion around the methodology for the second phase – Delphi or focus group, and which groups of users to include – primary care physicians, nurses, specialist physicians, patients, physiotherapists. Following that, the group discussed areas of future research. It was felt the group could benefit from a definition or mission statement, and should frame issues as “what are the problems and can technology solve them?” Future ideas for projects included the development of a standard for data from smart inhalers, apps, dashboards and other interfaces; exploring health app use over time; smart inhalers in children; and the changing patient-physician interface.

## COUGH WORKING GROUP



Chaired by Lorcan McGarvey, this session set out to discuss an approach to utilizing OPCR to determine the burden of cough in UK primary care. A protocol has been drafted to undertake a pilot study to estimate the size of the population with cough in primary care in UK (descriptive), including prevalence, incidence and characteristics of patients with cough. The variability in codes for cough used in primary care databases was discussed and how to capture these in a database study. It was suggested to start with analysing all codes in order to be as comprehensive as possible in the pilot study. Another discussion point was how to define chronic versus active cough and especially the cut-off point. It was suggested to look at a subpopulation of people with persistent cough for one year because this is routinely used in clinical trials. The protocol will be finalised using these suggestions.

# ORAL ABSTRACT PRIZES



**ERIC VAN GANSE**

 **REGABS18001**

THERAPEUTIC RATIOS PREDICT ASTHMA CONTROL IN THE ASTROLAB COHORT

Manon Belhassen, Alexandra L. Dima, Maëva Nolin, Nathalie Texier, Montse Ferrer, Marijn de Bruin and the ASTROLAB group

1



**LAKMINI BULATHSINHALA**

 **REGABS18010**

DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF PATIENTS WITH SEVERE ASTHMA WORLDWIDE

British Thoracic Society, Severe Asthma Network Italy, Severe Asthma Web-based Database, Korean Academy of Asthma, Allergy and Clinical Immunology, National Jewish Health, David Price

2

**RUPERT JONES**

 **REGABS1021**

DATABASE STUDIES IN UGANDA- AN OPPORTUNITY FOR GLOBAL RESEARCH WHERE CHRONIC LUNG DISEASE MATTERS

Bruce Kirenga, Wincelas Katagira, Andrew Barton, Trishul Siddharthan, William Checkley

5

**BOUDEWIJN DIERICK**

 **REGABS18011**

WORK ABSENCE IN PATIENTS WITH ASTHMA AND/OR COPD

Bertine M.J. Flokstra-de Blok, Thys van der Molen, Núria Toledo-Pons<sup>2</sup>, Miguel Román-Rodríguez, Borja G. Cosío, Joan B. Soriano, Job F.M. van Boven, Janwillem W. H. Kocks

3

**RONALD DANDURAND**

 **REGABS18017**

CHARACTERIZATION OF COMMUNITY PRACTICE COPD BY BLOOD EOSINOPHILS

Ronald J. Dandurand

6

**RONALD DANDURAND**

 **REGABS18026**

OSCILLOMETRY UPPER LIMIT OF NORMAL AT WORLD COPD DAY 2017

Ryan Nantal-Smith, Matthew Shorofsky, Stephanie Alexandre, Sarah Cadet, Jessica Ghaleb, Tara Glover, Chantal Forget, Belhadj Mohamed and Zoltan Hantos

4

# ACKNOWLEDGEMENTS

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

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

We welcome any suggestions from Supporters and would be happy to meet to discuss your ideas in more detail. A good opportunity to meet could be at the upcoming ERS Congress in Paris.

You can always get in contact with the REG team by email at [enquiries@effectivenessevaluation.org](mailto:enquiries@effectivenessevaluation.org)

or write to Michael Walker, REG CEO at [michael@effectivenessevaluation.org](mailto:michael@effectivenessevaluation.org)

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