



Respiratory
Effectiveness
Group

ADVANCES

in Real-life Respiratory Research

The Respiratory Effectiveness Group Newsletter

ISSUE WINTER 2018/2019

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SUMMIT
2019**

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THE RESPIRATORY EFFECTIVENESS GROUP NEWSLETTER ISSUE WINTER 2018/2019

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DEAR FRIENDS

Science is not the result of logical processes only. Hypothesis and experimental confirmation are indeed the core principles governing the theory of science. In reality however, science is just as prone to passion, fashion and temporary movements, as art or dressing! It is not science's fault of course, but that of scientists, who, not unlike other groups of people, are equally susceptible to simple, flashy concepts that have not necessarily gone through scientific scrutiny.

"WHEN A TREND IS ESTABLISHED, EVERYTHING AROUND IT GETS MORE WEIGHT, MORE IMPACT AND MORE POPULARITY".

There is nothing wrong about that, as long as it is part of a dynamic evolution, where a part of the community subscribes to the trend and another questions it. However, distractions are possible, and a fashion may become dogma. This is not rare, especially during difficult times (such as our own!). Thus, we need to be very cautious, as dogma is probably the worst that can happen to science, slowing down or even stopping progress. It's always good to remember that truth is dynamic, to say the least, and that most of what we strongly believe today will probably be naïve after a generation. Evidence-based medicine – a perfect concept – has become fashion (more among the regulators than the scientists, but still) and has thus been overrated. The 'real-life' approach that REG is doing its best to support, has come as a reminder that we need to keep the balance between form and reality. But of course there is danger that 'real-life research' also becomes trendy. Have you noticed that an increasing number of activities tagged as 'real-life'? To find the balance, it helps remembering that it is the quality of life of our patients that determines what is the best way ahead. And REG has an important role to play here: to guard the limits of 'real life research', not allowing it to become a fashion itself!

Nikos Papadopoulos
REG President

REAL LIFE
RESEARCH

REG TEAM UPDATE

The new year has started with a flurry of activity and changes within the REG team. We welcome back Sarah Lucas, one of our researchers, from maternity leave and wish her a good start back. A big thank you to Sanne van Kampen who has been covering Sarah's projects during her absence and wish her well as she will soon depart on her own maternity leave. We have also had to say goodbye to Kathryn Brown, our Admin Assistant who has decided to move on from REG. Thank you Kathryn for all your hard work and support during your time at REG.

The last few months have been also focused on the preparation of the REG Summit 2019 which will be held in Athens from 28th – 30th March. The programme and speakers have now all be finalised and the schedule for the working group meetings has been prepared. We hope that many of you will be participating in the Summit which is open to all collaborators and sponsors.

2018 was a busy year for many of the working groups with 10 new publications and another 5 manuscripts submitted.

New projects are in development and will be discussed in more detail during the working group meetings at the Summit on Thursday 28th March.

THE ROLLOUT OF THE NEW REG CORPORATE BRANDING IS ONGOING, WITH A NEW LOGO AND LOOK AND STYLE. INCLUDED WITH THIS UPDATE THIS SPRING WILL BE A NEW REG WEBSITE WHICH YOU ARE ALL INVITED TO VISIT. MORE ABOUT THAT IN THE COMING MONTHS.

I would like to acknowledge the support from a number of long-term Sponsors. Without their ongoing support a lot of the work of the REG would not be possible. I hope others are encouraged by the activities of REG and the Summit in March and will collaborate with us later this year or plan for the future.

I look forward meeting our many collaborators and supporters at the REG Summit 2019 in Athens.



Michael Walker
REG CEO

REG NEW PUBLICATIONS 2018



Applying UK real-world primary care data to predict asthma attacks in 3776 well-characterised children: a retrospective cohort study

REFERENCES

Turner S. W., Murray C., Thomas M., Burden A. and Price D. B. (2018) "Applying UK real-world primary care data to predict asthma attacks in 3776 well-characterised children: a retrospective cohort study", *NPJ Prim Care Respir Med*, 28(1), pp. 28.

ONLINE LINK

www.nature.com/articles/s41533-018-0095-5.pdf?origin=ppub

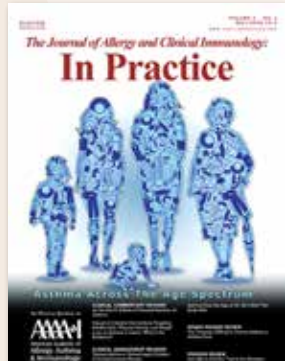
Performance of database-derived severe exacerbations and asthma control measures in asthma: responsiveness and predictive utility in a UK primary care database with linked questionnaire data

REFERENCES

Colice, G., Chisholm, A., Dima, A. L., Reddel, H. K., Burden, A., Martin, R. J., Brusselle, G., Popov, T. A., von Ziegenweidt, J. and Price, D. B. (2018) 'Performance of database-derived severe exacerbations and asthma control measures in asthma: responsiveness and predictive utility in a UK primary care database with linked questionnaire data', *Pragmat Obs Res*, 9, pp. 29-42

ONLINE LINK

www.dovepress.com/performance-of-database-derived-severe-exacerbations-and-asthma-control-peer-reviewed-article-POR



Antibiotic choice and duration associate with repeat prescriptions in infective asthma exacerbations

REFERENCES

Stolbrink, M., Bonnett, L. J. and Blakey, J. D. (2018) 'Antibiotic choice and duration associate with repeat prescriptions in infective asthma exacerbations', *J Allergy Clin Immunol Pract*.

ONLINE LINK

[www.jaci-inpractice.org/article/S2213-2198\(18\)30530-0/abstract](http://www.jaci-inpractice.org/article/S2213-2198(18)30530-0/abstract)



Amoxicillin is associated with a lower risk of further antibiotic prescriptions for lower respiratory tract infections in primary care – A database analysis spanning over 30 years

REFERENCES

Stolbrink, M., Bonnett, L. J. and Blakey, J. D. (2018) 'Amoxicillin is associated with a lower risk of further antibiotic prescriptions for lower respiratory tract infections in primary care – A database analysis spanning over 30 years', *Eur Clin Respir J*, 5(1).

ONLINE LINK

www.ncbi.nlm.nih.gov/pmc/articles/PMC6201792/

Matched cohort study of therapeutic strategies to prevent preschool wheezing/asthma attacks

REFERENCES

Grigg J, Nibber A, Paton JY, Chisholm A, Guilbert TW, Kaplan A, Turner S, Roche N, Hillyer EV, Price DB. (2018) 'Matched cohort study of therapeutic strategies to prevent preschool wheezing/asthma attacks', *J Asthma Allergy*, 11.

ONLINE LINK

www.dovepress.com/matched-cohort-study-of-therapeutic-strategies-to-prevent-preschool-wh-peer-reviewed-fulltext-article-JAA

Abstracts from the 2018 Respiratory Effectiveness Group Summit

REFERENCES

Respiratory Effectiveness Group (2018) 'Abstracts from the 2018 Respiratory Effectiveness Group Summit', *Respiratory Research*, 19 (S1)

ONLINE LINK

respiratory-research.biomedcentral.com/articles/supplements/volume-19-supplement-1

WORKING GROUP UPDATE

In September 2018, the REG team attended the European Respiratory Society congress. On the Saturday and Sunday prior to the main meeting ten of the 14 working groups held meetings, exchanging new ideas, presenting new research from REG projects and identifying priorities in real-life respiratory research. Following the meetings, the REG team have been working with investigators and supporters to drive projects forwards.



ASTHMA-COPD OVERLAP WORKING GROUP

The Asthma-COPD Overlap (ACO) group meeting at ERS 2018 was chaired by Nicolas Roche and Jerry Krishnan. The phase I results from the "ACO proof of concept" study were presented and then the definition of ACO used in this database study was discussed. The group emphasised the importance of a validation phase (phase III), and discussed the planned phase II study, to explore the clinical implications of those patients meeting the given definition of ACO.

Following the meeting, the phase I manuscript was submitted to Annals of the American Thoracic Society, and phase II proposal was drafted and circulated. Nicolas Roche and Chin Kook Rhee agreed to be principle investigators for this next phase. The REG team has also begun to explore the potential of using other databases to validate the ACO definition in phase III.



COPD WORKING GROUP

In October 2018, the last patient visit was recorded for the "concept of control in COPD" prospective pragmatic trial, and in November the data was signed off by investigators. This ambitious project is now moving into the data analysis phase. At ERS the working group, chaired by Marc Miravittles, discussed the project and the enthusiasm shown by the participating sites. It was suggested that the working group consider another pragmatic trial. Following the ERS meeting, a proposal was developed to look at the predictive value of FeNO in COPD exacerbations and the steering committee is in active discussion to finalise the project design.

Also discussed at the ERS meeting was a planned database study to assess the implications of ICS reduction or withdrawal in the management of COPD. A proposal has now been drawn up and Helgo Magnussen, author of the original WISDOM trial, has agreed to be principle investigator. Further planning is underway.

Finally, in June 2018 the results of the alpha-1-antitrypsin deficiency (AATD) pilot study were published. Potential follow up studies were discussed during the working group meeting, though given the lack of licensed treatments in the UK it was felt this may be better performed in other databases. This study is now on hold, pending further discussions around data access and funding.

SLEEP BREATHING DISORDERS WORKING GROUP

While this working group did not meet at ERS 2018, REG have been working with Mihaela Stefan to test the feasibility of using the OPCR database to investigate sleep apnoea and how this interacts with asthma and COPD. It looks unlikely that OPCR can be used for the proposed study, and so REG are looking at other data sources and asking the group what other research opportunities there may be.

ALLERGY WORKING GROUP

The allergy working group did not meet at ERS 2018, as historically there has been higher attendance at other meetings (such as EAACI). Peter Hellings has stepped down as Working Group lead and his work is very gratefully acknowledged. Moises Calderon has agreed to take up the leadership of the working Group. He has several new ideas which will be discussed in more detail at the REG summit 2019, with the hope of taking some of them forward in the near future.

CHILD HEALTH WORKING GROUP

In July 2018, a paper part-funded by REG, regarding the use of primary care data to predict asthma attacks in children was published in Primary Care Respiratory Medicine, reporting that the strongest predictor of future asthma attacks in a cohort of well characterised children was past asthma attacks.

Following on from this work, a number of potential project ideas were discussed at ERS 2018, in a meeting chaired by Steve Turner. The group also discussed the ongoing comparative effectiveness project regarding antibiotics vs. normal care in asthma exacerbations. This project had been on hold, awaiting the return of Sarah Lucas, the REG researchers leading the data analysis. As Sarah returned in January, the analysis phase of this project is now progressing.

The Paediatric Asthma in Real Life (PeARL) project, led by Nikos Papadopoulos, was discussed at ERS 2018. This project aims to produce evidence-based recommendations regarding controversial aspects of paediatric asthma, through the use of knowledge gaps surveys, systematic reviews, meta-analyses and Delphi exercises. Since the meeting, a proposal has been written, funding is being sought and parts of the project are underway.



WORKING GROUP UPDATE



SMALL AIRWAYS WORKING GROUP

The small airways group have had four publications in 2018, and a number of new ideas were discussed at the working group meeting at ERS 2018, chaired by Sinthia Bosnic-Anticevich. A commentary of what "dose" means to various professionals was discussed. This project stemmed from a reviewer's comment to a recently published paper and the realisation that "dose" can mean different things to different people. This project is now underway, led by Omar Usmani.

The group also discussed a proposal for a study to investigate the effects of obesity and weight loss on asthma. It was decided that while this is an interesting idea, the methodology requires some work and there is a lack of obvious funding opportunities. This idea is therefore on hold, pending further discussion.

Finally, Ron Dandurand discussed his ongoing work in oscillometry and potential collaborative projects with REG. REG have continued to investigate this collaboration and work to seek funding for this continues.



BIOMARKERS AND SEVERE ASTHMA WORKING GROUP

While this group did not hold a meeting at ERS 2018, there was a small meeting held to discuss the knowledge gaps regarding the use of FeNO in respiratory disease. This round table discussion lead to several study ideas relating to FeNO in asthma which are still under discussion. It also reinforced the need for further research regarding FeNO in COPD, which the COPD group have now created a proposal for. Work is also continuing, led by Kjell Alving, to update a letter regarding the use of biomarkers in asthma management.



ADHERENCE WORKING GROUP

The on-going project looking at the bi-directional relationship of adherence and control in asthma is now complete, and a manuscript has been submitted. The interesting results from this study were discussed at length at the ERS 2018 working group meeting, presented and chaired by Alex Dima. Following this, a number of new project ideas were raised, and these ideas now need prioritising. Alex Dima announced that she was stepping down as lead of the group, and REG continues to seek a suitable replacement.



DATABASE AND CODING WORKING GROUP

The database and coding group have been working on the project, Towards Optimum Reporting of Pulmonary Effectiveness Databases and Outcomes (TORPEDO). Katia Verhamme and Job van Boven presented the results of phase II to the working group at ERS 2018 and also at the Global Alliance for Chronic Disease (GADC) meeting in November 2018. The final list of variables is due to be presented to the working group, followed by a decision-making process regarding the format and measures for each variable.



COST EFFECTIVENESS WORKING GROUP



The cost effectiveness group met at ERS 2018, chaired by Job van Boven. They presented the proposed project to determine the cost of COPD in non-smokers. A productive discussion was held and the investigators continue to work on the idea. Several new ideas were raised, including the use of artificial intelligence and machine learning, which REG will be investigating further.

COUGH WORKING GROUP



The cough working group did not meet at ERS 2018, however the REG team did meet with Lorcan McGarvey the cough working group lead. A database project looking to first characterise cough, and then define and investigate chronic cough is underway. The protocol for this project is now finalised and it is hoped that data analysis will begin in early 2019.

TECHNOLOGY WORKING GROUP



The technology working group meeting at ERS 2018 was chaired by Richard Costello. The group discussed a project to review the feasibility and utility of smart inhalers from the point of view of primary care physicians. A proposal for a systematic review on this subject has been produced and is with potential funders, seeking their opinions.

The long-standing idea to validate the REG asthma risk prediction tool was also discussed. The current plan is to use claims-based data from Canada to perform this. REG continues to work with the principle investigator, Mohsen Sadatsafavi, to explore the feasibility and potential funding option for the project.

Following the working group meeting, discussion with funders resulted in a brainstorming e-mail regarding the feasibility of a study regarding the use of technology to predict asthma exacerbations. Potential PIs for this project have now been identified and the scope of the project is being discussed.

REG are also working to appoint a lead for this group.

ILD/IPF WORKING GROUP



The ILD/IPF working group have recently submitted a manuscript on the first phase, of a project to characterise ILD diagnostic practice globally. The discussion of the second phase of this project was the main topic at the working group meeting at ERS 2018. The first phase of this project collected questionnaire data on diagnostic practice from 457 centres globally, defining for the first time what diagnostic practice looks like around the world. The protocol for the second phase is nearly complete and funders have been approached. The second phase, aims to determine the diagnostic agreement across these centres by providing them with anonymised cases to diagnose in their usual practice.

The group are also in the process of submitting a manuscript on a database study to identify the missed opportunities to diagnose IPF in primary care.

QUALITY STANDARDS WORKING GROUP



The quality standards working group have recently submitted the results of the REG-EAACI taskforce project to produce a tool to judge the quality of comparative effectiveness literature to the Clinical and Translational Allergy (CTA) journal. The tool (REal Life EVIDence Assessment Tool; RELEVANT) is available for use on the REG website. The group did not meet at ERS 2018, and will look to discuss possible new project ideas at the REG Summit in 2019.





REG SUMMIT 2019



This year Athens will host the REG Summit 2019. The Summit will bring together real-life research experts from around the world to discuss the latest findings and new areas for collaboration in their respective fields of respiratory research.

The REG Summit is a well-known meeting of global respiratory key opinion leaders who actively conduct real-life research using and creating Real World Evidence. REG collaborators (researchers, clinicians, general practitioners and allied health professionals) have conducted numerous database projects as well as prospective pragmatic trials and continue to seek answers to the many complex issues faced by respiratory patients.

The REG Summit starts on Thursday 28th March with the REG Working Groups meeting to review progress on projects as well as developing new ideas and areas for further investigation. The scientific programme follows all day on Friday 29th and concludes at 13:00 on Saturday 30th March.

The scientific programme will include robust and informative discussions and debate on the latest thinking on treatment strategies and what are the needs to move the field forward to have a better understanding of how to improve patient outcomes. Participants will debate the hottest topics in the field, in a variety of interactive and informative sessions.

This year the programme welcomes an impressive list of experts who will be speaking on challenges and treatment options in severe, mild and paediatric asthma, reviewing controversies in management of COPD, looking at mechanisms to improve adherence to therapy, the role of immunotherapy in asthma and whether early treatment is the right strategy in IPF patients.

The meeting also provides an excellent opportunity for networking with some of the world's leading experts in the respiratory field. The REG summit 2019 will be the years' most important meeting in the field of real-life research and everyone is encouraged to participate and get involved with the REG and its projects.

We look forward to seeing you in Athens!





28-30 ATHENS
 March 2019 **GREECE**
 DIVANI PALACE ACROPOLIS

REG SUMMIT 2019 | Programme

THURSDAY 28TH MARCH

13:00 – 19:00 **REG Working Group Meetings**

FRIDAY 29TH MARCH

08:00 – 08:45 **REG Supporters Meeting**

08:50 – 09:00 **Welcome**
 Prof. Nikos Papadopoulos

09:00 – 10:30 **COPD: Should Patients with Severe COPD be Treated with ICS?**
 Chair: Dr Alan Kaplan
Pro | Prof Alberto Papi
Con | Pro Marc Miravittles

10:30 – 11:00 **Coffee Break**

11:00 – 12:00 **Role of Immunotherapy in Asthma**
 Chair: Prof. Moises Calderon
AIT & Asthma in daily practice around the world | Prof. Frederic de Blay
Responders and non-responders to AIT for asthma | Prof. Carmen Vidal
Immunotherapy versus Biologicals | Prof. Nikos Papadopoulos

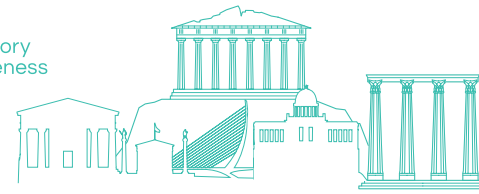
12:00 – 12:30 **Maximizing the First International Severe Asthma registry for Research**
Introduction | Prof. Giorgio Walter Canonica, Prof. David Price
Research agenda | Prof. Chin Kook Rhee, Prof. Andrew Menzies-Gow
New tools | Dr. Rupert Jones, Dr. Luis Pérez-de-Llano

12:30 – 13:30 **Lunch Break**

13:30 – 14:00 **IPF: Does Early Treatment Make a Difference?**
 Chair: Prof. Mark Jones
 Speaker: Prof. Kevin Flaherty

14:00 – 15:00 **New Paradigms in Mild Asthma: Regular ICS therapy is better than prn ICS/LABA in mild asthma**
 Chair: Dr. Alan Kaplan
Pro | Prof. Ken Chapman
Con | Prof. Mark Fitzgerald

15:00 – 15:30 **Coffee Break**



REG SUMMIT 2019 | Programme

FRIDAY 29TH MARCH

- 15:30 – 17:00 **Controversies in Pediatric Asthma**
Chair: Prof. Nikos Papadopoulos
- The term “preschool wheeze” should be abandoned**
Pro | Prof. Adnan Custovic
Con | Prof. Steve Turner
- The limits and distribution of asthma severity in kids: where should we draw the line**
Prof. Francine Ducharme
- Next-generation Guidelines: are phenotype/endotype-based recommendations feasible/preferable?**
Pro | Prof. Antonio Nieto
Con | Prof. Clare Murray

- 17:00 – 17:40 **Treatable Traits**
Chair: Joan Soriano & Dermot Ryan
Speakers: Prof. Nicolas Roche - Specialist, Prof. Rupert Jones - GP

- 17:40 – 18:10 **Inhaler Techniques and Adherence**
Chair: Prof Sinthia Bosnic-Anticevich
Speaker: Prof. Janwillem Kocks

SATURDAY 30TH MARCH

- 09:00 – 09:30 **Vaccinating Your Respiratory Patient**
Chair: Prof. Antonio Anzueto
Speaker: Dr. Alan Kaplan

- 09:30 – 11:30 **Severe Asthma: The Evolving Algorithm of Biological Selection in Severe Asthma Creating and Algorithm for Care**
Chair: Prof. Mark Fitzgerald and Prof. Nikos Papadopoulos
- Severe asthma overview** | Prof. Mina Gaga
Non biologic treatment | Prof. Peter Barnes
Treatment with anti-IL5 | Prof. Liam Heaney
Treatment with anti-IgE | Prof. Andrew Menzies-Gow
Treatment with anti IL4/13 | Prof. Walter Canonica

- 11:30 – 12:00 **Coffee Break**

- 12:00 – 13:00 **Key Note: Real-Life Research and its Role in the Future**
Chair: Prof. Mina Gaga
Speaker: Prof. Jean Bousquet

- 13:00 **MEETING CLOSE**

The Working Group meetings

	THURSDAY 28 TH MARCH			FRIDAY 29 TH MARCH
	ROOM 1	ROOM 2	ROOM 3	PLENARY ROOM
12:00 - 13:00	NETWORKING / LUNCH	NETWORKING / LUNCH		19:00 - 19:30 Child health
13:00 - 14:00	Allergy	Adherence		
14:00 - 15:00		Technologies		
15:00 - 16:00	Chronic Cough	Biomarkers & Severe asthma		
16:00 - 16:30	COFFEE	COFFEE		
16:30 - 17:30	Database & Coding	Small Airways / Non Severe Asthma		
17:30 - 18:30	Cost Effectiveness	COPD	ILD/IPF	
18:30 - 19:30		ACO	ILD/IPF	

Additional meetings and Activities

THURSDAY 28 TH MARCH	FRIDAY 29 TH MARCH	SATURDAY 30 TH MARCH
MEETING ROOM 1	PLENARY ROOM	PLENARY ROOM
19:30 - 21:30 REG Board meeting	08:00 - 08:45 REG Supporters Meeting 18:15 - 19:00 REG AGM 19:00 - 19:30 Drinks reception 19:30 - 22:00 Networking dinner	08:00 - 09:00 REG Council Meeting

General Information

About Athens

One of the most ancient cities of the world, Athens Greece is famous as the birthplace of democracy. With a history of over 3,000 years, Athens is the best town for sightseeing. A visit to Athens is certainly not complete without a visit to the Acropolis and the New Acropolis Museum, the Ancient Agora and the Roman Agora. Today's capital integrates the ancient and medieval history into the contemporary era. Monuments can be found all around the city center, side by side with contemporary constructions.

Summit Venue

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Accreditation - CME credits



The REG Summit 2019, in Athens, Greece, 28-30 March has been accredited by the European Accreditation Council for Continuing Medical Education (EACCME®) with **11 European CME credits (ECMEC®s)**. Each medical specialist should claim only those hours of credit that he/she actually spent in the educational activity.

WHAT REG MEANS TO ME

A decade ago, times were different. The benchmark for research was the randomised clinical trial and those of us who took a more pragmatic interest and approach to generating new knowledge were often struggling to get funding and impact in the broader context. REG provided a much needed platform which brought together like-minded researchers who understood the importance and impact of real-world evidence. For me, being a researcher in Australia, it opened up a community of researchers who worked in complementary and aligned fields of research. REG has provided invaluable inspiration, enabled opportunities to collaborate and has broadened the impact of my research. REG continues to provide intellectual inspiration and opportunities through impactful collaborations and connections from which not only benefit all members of my research group, but most importantly, the field of research as we continue to generate new real-world knowledge which impacts on the day-to-day care of patients living with respiratory disease.

Prof Synthia Bosnic-Anticevich

is founder and team leader of the Quality Use of Respiratory Medicines Group at the Woolcock Institute of Medical Research, University of Sydney.



To me, the Respiratory Effectiveness Groups means inspiration, collaboration and dissemination in the field of real-world respiratory interventions and outcomes. Its unique features, that make REG stand out from other respiratory platforms, are the small-scale meetings and (multidisciplinary) working groups with plenty of room for interaction and discussions. Within REG, people work together with a genuine and open mindset and a true common vision to advance the real-world respiratory care and research field. As such, REG has already made a huge impact on the quality and global recognition of real-world respiratory research. Personally, especially as an early/mid career researcher, I have hugely benefitted from REG as a networking platform that brings together young as well as very experienced clinicians and researchers. I have got the opportunity to be actively involved and also being the lead, in multiple projects related to medication adherence and cost-effectiveness while working together with some of the world's leading, passionate and outstanding people in these areas. REG has brought likeminded people from all over the world in touch and has been one of the main reasons I wanted to pursue my career in health economics and real-world outcomes in respiratory medicine. I sincerely hope REG will remain the inspirational and disruptive "thinktank" it has proven to be so far and am looking forward to another great meeting in Athens!

Job van Boven

Assistant Professor, University
Medical Center Groningen,
The Netherlands



The Respiratory Effectiveness Group (REG) is an investigator-led, not-for-profit research initiative that brings together over 300 leading experts from 40 countries focused on implementing real-life research to inform meaningful practice guidelines, drug licensing and prescribing decisions.

I have enjoyed my interactions with the child focused and small airways working groups and learning initiatives throughout the group and have been amazed at the high quality, evidence-based publications that have arisen from this organization. We get together when we can at different meeting venues and have regular, efficient communications. The productivity and camaraderie from the group is fantastic. REG provides answers to important knowledge gaps that the classic randomised, double-blind, placebo controlled trial can not necessarily achieve well. I find bridging the experience from the group in evidence-based real world investigations is extremely important.

Thanks to REG and their team and leadership in facilitating success in this very important work and including me in these efforts.

Wanda Phipatanakul
Professor of Pediatrics, Harvard
Medical School, Boston, USA



The first clues of REG's birth were indirect. A chat with a colleague satisfied that a European group of experts was (at last) convening to define "quality criteria for respiratory epidemiology research", and a chance meeting in London with Alison Chisholm, the then REG chief scientific officer, at an EMA meeting (happy times!...:-)...) devoted to an inventory of existing European resources for PharmacoEpidemiological Research.

Then, at an ERS meeting, the "shock": while attempting to run behind a speedy gentleman in Hawaiian dress (my God!), pulling a small/noisy cabin bag, the understanding that he might well be David (Dr Price, I presume?)...

The first reactions to REG were relief and happiness: "no longer alone" to tell the actors (the usual trio: academia, regulators, and industry), that observational studies deserve interest, support, and nice publications. No longer alone to explain that medications lead a long life, and that information must be collected all along the population use, particularly after marketing approval (appropriate use, adherence, safety, comparative effectiveness, outcomes research, ..., relying on "enriched datasets", exploited with innovative methods).

And now, finally, we understand that the truth is coming from patients ("listen to your patients, idiot!"), and with the development of data linkages and the outbreak of digital medicine, we can identify and understand individual behaviors, a prerequisite for

effective interventions, and for precision medicine (which intervention for which patient?), moving to the new paradigms: "what are the patients actually doing to available therapy, and how can we optimize these interactions?"

It has been a chance and a pleasure for the PELyon team to be involved in the core of the REG efforts, to interact regularly with REG's colleagues, and to contribute to the dissemination of our common beliefs: the assumption that we can explain, and ultimately, predict the effectiveness of interventions in respiratory medicine, to improve the health status of our patients.

Thank you, David, thanks to the nice and effective REG team, and thanks to the many excellent colleagues met along these years!

Long life to REG!

Manon Belhassen
Pharmacoepidemiologie-
Directeur études HEOR
Pharmaco
Epidemiology Lyon
Lyon, France



Eric van Ganse
Associate Professor, Claude-Bernard Lyon
University, Lyon, France

INTERNATIONAL SEVERE ASTHMA REGISTRY



year in review:
updates from 2018

ISAR, the first international registry of severe asthma patients (<http://isaregistries.org/>) is celebrating its second year of successful operation. Spreading its wings to new horizons of severe asthma, ISAR is dedicated to improving and standardizing the assessment and management of patients with severe asthma.

New Countries updates: Owing to rapidly growing interest and funding support from AstraZeneca, ISAR has surpassed initially planned 14 countries over a 5-year period (2017-2022) and extended to overall 25 countries spreading to Middle-East, Asia-Pacific and Latin American countries.

Data updates: So far, 5601 severe asthma patients' data are shared for ISAR research from 13 countries. By 2021, patients will be recruited from over 160 within participating countries.

Country	Sites	Patient-level	Aggregate level
USA	1	3,378	-
Italy	61	564	-
Korea	20	22	439
Greece	1	28	-
Spain	15	54	-
Bulgaria	6	35	-
Ireland	1	55	-
Japan	4	Ethics approved	-
Canada	6	41	-
Kuwait	1	30	-
UK	6	-	696
Denmark	8	-	-
Australia/SG/NZ	26	-	259
Total	156	4,207	1,394



Research Updates: Currently, ISAR has 11 active research projects, prioritised by ISAR Steering Committee:

Global Core Project 2017: Demographic and Clinical Characteristics of Severe Asthma Patients Worldwide

Status

- Manuscript drafted
- Publication – March 2019

Global Core Project 2018: The Characterisation and Comparison of Eosinophilic and Non-Eosinophilic Phenotypes in Severe Asthma

Status

- Protocol finalised
- Pilot results to be presented at the REG summit 2019

Hidden Severe Asthma in Primary Care vs ISAR

Status

- Protocol drafted
- Planned abstract for ERS 2019 showing pilot framework to identify hidden severe asthma patients

Outcomes of Switching Biologics

Status

- Protocol drafted
- Discussion with project steering committee at the REG summit 2019

Impact of exacerbation burden on lung function trajectory in a broad and severe asthma population

Status

- Supplementary data sources identified
- Sources for primary and secondary care data linkage identified
- Draft protocol by March 2019

Comparative effectiveness of biologics versus OCS in severe asthma

Status Draft protocol by April 2019

Other academic research projects currently active in ISAR

- Assessment of the overlap (reliability) of collected biomarkers
- Identification of predictors (i.e. biomarkers) of response to biologics
- Hidden chronic asthma within the COPD/ACO population
- Onset of asthma in severe asthma patients
- Relationship between low socio-economic status and asthma outcomes

Status

- Research working groups finalised
- Epidemiologists/ researchers assigned
- Timelines agreed, and study initiated with leads

Publication Updates

Manuscripts

Development of the International Severe Asthma Registry (ISAR): A Modified Delphi Study

Status

- Published in *JACI in Practice*
- Bulathsinhala, Lakmini, et al. «Development of the International Severe Asthma Registry (ISAR): A Modified Delphi Study.» *The Journal of Allergy and Clinical Immunology: In Practice* (2018).

ISAR mission statement

Status Submitted to *Chest*

ISAR protocol

Status Currently being drafted

Severe asthma registries: a global comparison

Status Currently being drafted

Demographic and clinical characteristics of severe asthma patients worldwide: data from the International Severe Asthma Registry (ISAR)

Status Currently being drafted

Abstracts

ISAR: Clinical characteristics of severe asthma patients worldwide

Status Accepted at ATS 2019

Mission and vision of ISAR

Status Accepted at ATS 2019

Overlap of biomarkers and T2 comorbidities in global severe asthma population

Status Submitted to REG 2019

Comparison of data fields captured by regional severe asthma registries participating in ISAR

Status Submitted to EACCI 2019

International Severe Asthma Registry (ISAR): Mission statement

Status Submitted to EACCI 2019

ISAR protocol

Status Submitted to ERS 2019

Epidemiology of lung function in a global severe asthma population

Status Submitted to ERS 2019

Identifying hidden severe asthma in primary care

Status Submitted to ERS 2019

Call for 2019 research proposals is now open!

If you have a research question and would like to seek access to ISAR data, do not hesitate to contact us through ISAR home page (<http://isaregistries.org/>). Simply click the 'submit a proposal or research request' tab and let us know of your interest. The call for proposals for the year 2019 will close by Feb 28th, 2019, so hurry up and don't miss the chance!

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

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