



Respiratory
Effectiveness
Group

Respiratory Effectiveness Group Annual Report 2018

Pioneers in real-life respiratory
data and research

effectivenessevaluation.org



Contents

The Respiratory Effectiveness Group looks to a future with RWE.....	1
Our goal	1
What we want to do.....	1
REG strategy	1
REG direction and philosophy	1
Operational objectives	2
REG's Structure.....	2
REG Board.....	2
Board of Directors – Vice Presidents.....	3
The year in review	4
Staff	4
Governance	4
Scientific outputs.....	4
Finance	4
REG summit.....	5
Communications.....	5
International Conference & Congress Activities	5
REG Summit 2018, Amsterdam 22 - 24 March 2018.....	5
ERS Congress, Paris, 15 - 19 September 2018.....	11
WISC Congress, Florence, 6 - 9 December 2018	11
Working group update	11
Adherence Working Group	11
Allergy Working Group.....	11
Asthma-COPD Overlap (ACO) Working Group	11
Child Health Working Group	12
Cost effectiveness Working Group.....	12
COPD Working Group.....	12
Cough Working Group.....	12
Database and Coding Working Group.....	13
ILD/IPF Working Group.....	13
Quality standards Working Group.....	13
Severe Asthma and Biomarkers Working Group.....	13



Sleep Breathing Disorders Working Group	13
Small Airways Working Group.....	14
Technology Working Group	14
Active projects.....	14
Publications in 2018	16
Manuscripts submitted in 2018	17
Future projects seeking funding.....	17
Financial summary.....	19

The Respiratory Effectiveness Group looks to a future with RWE

A global not-for profit, collaboration of clinicians, scientists and epidemiologists, working together to identify and fulfil the real-life research needs in respiratory medicine and advocating for change to drive improved patient management.

Our goal

To transform respiratory patient care by maximising/exploiting/utilising real-life research & evidence

What we want to do

To integrate real-life evidence into clinical practice guidelines, policy and budgetary decision-making for the benefit of all stakeholders in respiratory medicine.

REG strategy

REG will achieve its goal by:

- nurturing an international network of primary and secondary care respiratory experts with an interest and expertise in real-life research
- establishing alliances with partner organizations (e.g., APSR, ATS, EACCI, ENCePP, ERS, ESPACOMP, IPCRG, IPSE, ISPOR, patient organisations)
- Using RWE to address current key questions in respiratory medicine and impact on relevant international guidelines and health policies
- Act as a think-tank to meet challenges in respiratory medicine in a pragmatic way
- Together, REG collaborators, partners and supporters, will implement a multi-faceted programme of activities aimed at improving the understanding of respiratory medicine

REG direction and philosophy

- REG leads the development and promotion of high-quality real-life collaborative research in respiratory medicine'

Setting quality standards

- Real-life research studies, especially database studies, comparative effectiveness research and pragmatic clinical studies
- Databases to be used in real-life observational research
- Use of real-life research by guidelines developers and decision-makers
- Publication of real-life research protocols and results
- Assessment of real-life research protocols and results
- Academic partner to the International Severe Asthma Registry (ISAR)
- Developing and assess methods used in real-life research.
eg. bias reduction, patient selection, outcome measures
- Providing advice and methodological help to researchers developing real-life research projects

Operational objectives

RESEARCH:

- Identify and prioritise the real-life RESEARCH NEEDS in each area of respiratory medicine
- Stimulate and drive and/or facilitate the development of, collaborative real-life research projects to address the identified needs
- Change the perception of real-life research from “the inside”

COLLABORATION:

- Grow and sustain an international collaboration of clinical and scientific expertise in real-life research, meeting and working together either wholly as REG, or in designated Working Groups
- Trigger, facilitate and nurture the development of networks of partners and supporters involved in real-life observational research, (academic researchers, industry, service providers, guideline developers, decision makers, regulatory agencies, editors, funding agencies, scientific societies, institutional bodies, patients’ organisations) to improve levels of expertise and support the research need initiatives.
- Advocate change to the way journals, guideline bodies and regulatory authorities appraise evidence to better integrate high-quality real-life data into recommendations, clinical decisions and policy making

QUALITY METHODOLOGY:

- Define and set quality standards for real-life research in respiratory medicine, through per protocol historic cohort analyses (database studies) and pragmatic clinical studies
- Develop, assess and standardise coding and methodology used in real-life research
- Develop rational prescribing pathways and clinical management & decision support tools
- Drive the publication and appreciation of real-life research validity by
 - Quality publications in high impact journals
 - Incorporation of real-life research into guideline development and health care resource utilisation decision makers
- Be the “Go to” organisation for advice, assistance and training on real-life research in respiratory medicine

REG’s Structure

REG Board

BOARD COMPOSITION 2018-2020

President – Nikos Papadopoulos, Professor of Allergy and Paediatric Allergy, University of Manchester, UK

Vice President for Scientific Outputs – Omar Usmani, Reader in Respiratory Medicine and Consultant Physician at the National Heart and Lung Institute (NHLI), Imperial College London & Royal Brompton Hospital (RBH).

Vice President for Methodology – Nicolas Roche, Pneumologie et soins intensifs respiratoires, groupe hospitalier Cochin, Assistance publique-Hôpitaux de Paris, and Université Paris Descartes, France

Vice President for Internal Organisation – Antonio Anzueto, Pulmonary/Critical Care, University of Texas Health Science Center at San Antonio, USA

Vice President for Global Collaboration – Walter Canonica, Chairman of Dept of Medical Specialties at the University Hospital S. Martino Genoa, Italy

Vice President for Finances and Supporter relationships – Dermot Ryan, Strategic Clinical Director Optimum Patient Care

Vice President for Communications – Sinthia Bosnic-Anticevich, Woolcock Institute of Medical Research, University of Sydney, Australia

Vice President for Events – Alan Kaplan, Department of Family and Community Medicine, University of Toronto, Toronto, Ontario, Canada

Oversight Committee members - Nick May, Trevor Lambert, Keith Allan

The Board members reflect the high calibre of our collaborators and offers wonderful clinical and research expertise with broad geographical reach:

- Asia-Pacific, Europe & North America
- Asthma, Allergy, COPD
- Primary, secondary & pharmacy care
- Adult and paediatric specialisms.

Board of Directors – Vice Presidents

Vice Presidents have political responsibility for specific domains. They collaborate with the President, the CEO and domain experts to direct the execution of the relevant tasks.

Vice President for Scientific Outputs – Omar Usmani

Works towards maximisation of scientific output impact (papers, abstracts, stand-alone documents), by optimally exploiting the existing and identifying new sources of information (databases, registries, open-source data), optimising the researcher group and identifying the optimal publication platforms

Vice President for Methodology – Nicolas Roche

Ascertains that REG remains at the forefront of developments in real-life research by advocating for the state-of-the-art and developing novel methods for assessing, validating and expanding the scope of the field

Vice President for Internal Organisation – Antonio Anzueto

Responsible for the internal structure, including workgroup organisation, interactions between board, administrators, researchers and collaborators

Vice President for Global Collaboration – Walter Canonica

Liaison and Ambassador with major international organisation

Vice President for Finances and Supporter relationships – Dermot Ryan

Oversees the financial health of the organisation. Builds and conserves relationships with the Supporters

Vice President for Communications – Sinthia Bosnic-Anticevich

Takes the lead in optimising the image of REG towards the academic community as well as towards the public and its media presence, including website, social media and press

Vice President for Events – Alan Kaplan

Takes the lead in proposing, designing and making sure the purpose is met for the REG Summit and other events/meetings

REG will also be changing the name of its website and email address to www.regresearchnetwork.org, which better reflects the activities of the group. To minimise any disruption this may cause, any search or email on the existing site will be automatically redirected to the new address.

The year in review

Staff

During this past year, Catherine Hutton decided to move on from REG and Michael Walker joined the team in May. Supported by Naomi Launders senior research scientist and Sarah Lucas, research scientist a total of 10 pieces of original research were published and 5 manuscripts submitted in 2018 and there are currently 7 active studies. Sarah took some time off during the year to become a proud mother of a baby boy and Sanne van Kampen took over the role temporarily so congratulations to Sarah and thank you to Sanne.

Governance

Our REG Board has meeting regularly during 2018 to address the organisational needs and are well aware of the need to grow collaborations and supporters. Work was completed as a matter of urgency to ensure GDPR compliance and IT security SOPs are in place.

Scientific outputs

REG has seen another productive year, continuing the momentum achieved by the outputs of our Working Groups. Still numbering 14, the working groups continue to develop or execute defined projects in their respective scopes of operation. Working Group meetings were held at the REG Summit in March and in conjunction with the ERS Congress in September. In addition, many Working Groups and projects are in regular communication to progress their projects. For more detailed information on the Working Groups and their projects, please refer to the Working Groups report.

Finance

Finance is never easy and remains a challenge that REG is continuously working on. However, careful planning and use of resources have enabled REG to deliver an equal year-on-year level of output carrying a small operating loss. We continue to question our spending and aim to further reduce our administrative costs over the course of the 5-year financial plan. The valuable work of REG, both in terms of its research networks and its political influence depends on the continued collaboration with our valued supporters and we thank them for their on-going financial and expert contributions.

REG summit

The annual REG Summit remains a key vehicle to showcase the many achievements of the organisation and our valued Collaborators, together with providing an interactive programme of presentations and debates covering the hot topics in respiratory medicine. Summit 2018, took place in Amsterdam at the end of March – a report on this meeting appears later in this update as well as our other congress activities in 2018.

Communications

A corporate rebranding has taken place over the latter part of the year and now the new branding is being applied across all channels. A new website will shortly be online in line with this new branding. The REG Newsletter was re-instituted to provide REG collaborators and supporters with updates of the work of the REG.

International Conference & Congress Activities

REG Summit 2018, Amsterdam 22 - 24 March 2018

This year's REG Summit (2018), titled "Working together to make an impact" lived up to expectations. Taking place in Amsterdam, The Netherlands and being attended by 73 delegates from 22 countries, the event brought together a group engaged researchers, students and industry collaborators who are working together and looking for opportunities to establish new collaborations.

The REG 2018 Summit covering the spectrum of "Working together" from research major global initiatives, research collaborations, engagement with industry and working with professional bodies. The programme included plenary talks, interactive panel sessions and abstract sessions; 30 abstracts were presented over 3 dedicated parallel sessions. Congratulations to the REG 2018 Summit Scientific Programme Committee; Professor George Christoff, Dr Dermot Ryan, Dr Joan B Soriano, Professor Steve Turner and Associate Professor Omar Usmani, for their work in pulling together such a stimulating programme.

Day 1

The opening plenary, "***Global Projects Session: Lessons in Maximising Collaboration and Impact***" kick-started the theme of "working together" with updates and insights from several major global projects, in which REG collaborates. Building on the theme of 'working together' highlighted in the opening plenary, a further two plenary sessions on Using Real-Life Evidence to Change Guidelines and Children Are Not Small Adults...Or Are they?, as well as five sessions covering Global Collaborations, Severe Asthma, Digital Health: Will the Promise be Realised...or does it change anything bar price?, Patient Perspectives and Behaviours, Community Medicine were held on Day 1. A Key Note Presentation on How to Change Perceptions on Real-Life Research to Impact Guidelines concluded the scientific program on Day 1.

The opening plenary on ***Global Projects Session: Lessons in Maximising Collaboration and Impact*** included presentations relating to the COPD Control Project, The Interstitial Lung Disease Multidisciplinary Team (ILD MDT), the International Severe Asthma Registry (ISAR) and the European Association of Allergy and Clinical Immunology Allergy Immunotherapy Treatment (EAACI AIT) project. Professor Marc Miravittles (University Hospital Vall d'Hebron, Barcelona, Spain) presented on the COPD Control project which is currently being run in 7 countries, with 11 collaborators and

aims to validate the concept of COPD control in clinical practice. Currently the project is in the recruitment phase with 339 participants recruited and data collection expected to be completed by October 2018. This project will have significant impact on clinical decision making regarding an increase or decrease in medication to maintain COPD control. Ms. Naomi Launders (REG Senior Researcher), presented an update of the ILD MDT project on behalf of the project lead, Professor Luca Richeldi. The principal aim of the ILD MDT project is to generate knowledge of the ILD diagnostic process globally. The project is funded by grants received from the Three Lakes Foundation, Boehringer Ingelheim and Roche and has completed the first phase. Collaborators from 457 centres have been recruited from across North and South America, Europe, Africa, Asia-Pacific and the Middle East. A pragmatic approach to questionnaire dissemination was used, relying on the dedicated support from national pulmonary societies and individual investigators disseminating the questionnaire through their professional networks. Over the next few months, the results from phase I will be submitted for publication and the protocol for phase II will be finalised. Phase II is expected to begin in early 2019. An update on ISAR was presented by Ms. Victoria Carter (Research and Director at Observational and Pragmatic Research Institute). This presentation highlighted the challenges and opportunities associated with bringing together collaborators from the UK, USA, Italy, Australia and South Korea to establish the first global severe asthma network. A full update on ISAR is presented in this issue of the REG Newsletter. Professor Antonella Muraro (past president of EAACI, currently University of Padua, Italy) presented an update on the EAACI AIT project. The aim of this project is to develop guidelines and involves a collaboration between many collaborators from across Europe. Good progress has been made which would not have been possible without the significant contribution of collaborators. Professor Muraro highlighted the significant benefit of collaboration and the way in which this can increase the impact of the project.

The **Global Collaborations** session and commenced with a presentation from Dr. Manon Belhassen on therapeutic ratios that predict asthma control. The key finding being that low ICS therapeutic ratios reflected insufficient prescribing of ICS relative to all asthma therapy, which in turn lead to a deterioration of asthma control. A presentation on the latest Astrolab data by Professor Eric Van Ganse followed. Professor Van Ganse reported on the amount of consistency of medical care and self-management support in asthma and the finding that the amount and consistency of asthma primary care can be enhanced through involving practice nurses, making social expectations visible, and providing more training to enhance skills and confidence in asthma care delivery. Ms Naomi Launders presented the latest findings from the global evaluation of Interstitial Lung Disease Diagnostic (ILD) Practice, Agreement and Accuracy project. This project aimed to describe ILD diagnostic practice globally. Responses from 457 centres across 64 countries were included in the analysis and results determined that ILD diagnostic practices of responding centres are broadly similar, with multidisciplinary team meetings widely implemented. However, dedicated ILD centres in academic institutions in well-resourced settings hold more formal diagnostic meetings and have better access to anti-fibrotics. A minimum standard MDT is hard to define and may depend on resources availability and the number of cases seen.

In the **Severe Asthma** session, Professor Rupert Jones presented on the development and validation of the Severe Asthma Questionnaire (SAQ). In the first instance, it was found that in terms of the FDA guidelines for questionnaire construction, the SAQ has better content validity compared with existing questionnaires and meets the criteria for construct and other validity. The SAQ maps onto the health economic measure, EQ-5D, and may have greater sensitivity to differences in oral corticosteroid dose compared to the Mini Asthma Quality of Life Questionnaire. Additionally, the key message for the

development of the SAQ was that patient input and documentation of that input is key to achieving content validity according to FDA guidelines. Assistant Professor Enrico Heffler presented on the first results of the Severe Asthma Network in Italy (SANI): and followed this up with a presentation on Pharmacoeconomic evaluation of oral corticosteroid adverse events in patients with severe asthma. His work concluded that the use of oral corticosteroids in severe asthmatics has a high impact, both in terms of frequency than under a pharmacoeconomic point of view of its adverse effects. Therefore, one of the most relevant unmet need in severe asthma is the reduction (possibly with novel biologic agents) of regular use of oral corticosteroids. In addition, Real life data from the SANI registry show in the severe asthmatics population there is a high prevalence of relevant comorbidities. Ms. Lakmini Bulathsinhala then presented the demographic and clinical characteristics of patients with severe asthma worldwide, from the ISAR. She reported that the demographic and clinical characteristics of patients with severe asthma from five geographically diverse countries support previously reported characteristics of severe asthma patients and that to decipher informative trends in asthma phenotypes and clinical management, country-specific distributions should be compared next.

The third plenary of the day was entitled “***Digital health: Will the promise be realised?***” Talks by Professor Hilary Pinnock, Dr. Mike Baldwin, Professor Thyss van der Molen and Professor Richard Costello explored the themes of the use of technology to improve patient engagement and adherence, and the changing face of the patient-physician interaction. These presentations, and the discussion that followed, detailed the opportunities for improvements in patient-centred care while cautioning that health care systems need to change to incorporate these technologies and that digital health alone is not a panacea.

A topical session, that explored a very relevant topic and close to many attendee’s hearts was the plenary ***Using Real-Life Evidence to Change Guidelines***. The series of presentations highlighted the value of real-life data and its impact through a number of examples. Professor Barbara Yawn presented “Oral and Inhaled Steroids: Friend or Foe?” and showed the risk/benefit of OCS needs to be weighed for each individual patient. The case was presented for revision of guidelines for the management of COPD so that it recommends a preference for LABA + LAMA before adding ICS so to reduce exacerbation risk without introducing the risks of ICS. Professor Rupert Jones presented on the Missed Opportunities for Diagnosis in COPD and the research initiative to explore this. This REG-funded project found that while early diagnosis of COPD is slowly improving, in the 2 years before diagnosis, there are opportunities to diagnose COPD that are missed. Lastly, Professor George Christoff presented on an Alternative View of Current Asthma Guidelines. He gave an overview of the need for guidelines and the role they play in assisting the clinician and then compared the production method, content, evidence source, grading of quality of evidence and strength of recommendations across international asthma guidelines from GINA and NAEPP and country specific guidelines from Australia, Canada and the UK. Finally, he gave an overview of recent literature concerning the use of and adherence to asthma guidelines.

“Patient Perspectives and Behaviours” included a series of presentations identifying patient perspective and behaviours across the spectrum of conditions and patient populations including asthma, allergic rhinitis, adults and children. Professor Sinthia Bosnic-Anticevich from Australia presented research from a project looking at understanding the reasons behind patient self-selection of medications for allergic rhinitis (AR) in the community pharmacy, noting that a vast majority of patients self-select their treatment even when their symptoms are moderate to severe. It is only those patients who report an impact of their AR on their day to day living, who are more likely to

consult a pharmacist i.e. the high incidence of self-selection of OTC treatments for allergic rhinitis symptoms in community pharmacy does not reflect the severity of the condition experienced by patients. A key message is that pharmacists are ideally placed to educate and counsel patients in this regard. Sinthia also presented work on Parent's Perspectives on medication management for their children with asthma: understanding the influences on parents and a social network analysis. The group found that parents have developed their own health networks to aid them in the management of their children's asthma medications, often consisting of multiple individuals and resources apart from the traditional health care professionals. This research highlights the need to consider parent's health contacts and how they may drive and influence children's asthma outcomes and the importance of further exploring why parents' needs are not being met by health care professionals. Dr. Boudewijn Dierick presented on work absence in patients with asthma and/or COPD concluding that patients with asthma and/or COPD have a significantly higher work absence compared to the general population, more frequently in asthma and of longer duration in COPD patients and that age, anxiety and allergy could partially be driving some of these effects. Dr. Alan Kaplan from Canada presented patient perspectives on asthma medication and found that while asthma is an inflammatory disease requiring regular anti-inflammatory treatment, patients have fears about using inhaled corticosteroids.

The ***Community Medicine*** session covered a broad range of important topics from the effects of comorbidities on the asthma to the frequency with which patients claim prescribed therapies. These series of presentations highlight some of the key challenges in the real-life respiratory medicine whether it be related to the translation of guidelines, the lack of evidence for real-life practices or the translation of medication prescribing to medication dispensing. In particular Ms. Naomi Launders reporting on findings from a study exploring the management of Community Acquired Pneumonia (CAP) in Primary Care in the UK. The authors reported that despite CRB65 scores (a composite score based on: confusion, raised respiratory rate, low blood pressure, age 65 or more) being incorporated into NICE guidelines in 2014, they are not well recorded for patients managed in primary care. The components of CRB65 are also poorly recorded, which raises the question of whether the NICE guidelines are being implemented in practice? Dr. Ron Dandurand presented on research associated with the characterisation of COPD by blood eosinophil counts (ECs) in community practice. The authors aimed to determine the prevalence of elevated ECs amongst COPD patients in the community and explore what subject parameters, if any, might be associated with a responsive COPD phenotype. D_{Lco} was the only subject parameter associated with elevated EC. Larger studies in independent populations are required to determine whether this was a chance finding due to the number of parameters surveyed, or whether the findings are indicative of a relative preservation of the D_{Lco} suggesting a more asthma-like phenotype of COPD. Professor Nikos Papadopoulos presented results relating to the effectiveness of the addition of antibiotics to usual care in the management of asthma exacerbations. The message from this work was that the addition of antibiotics to oral steroids in the management of asthma exacerbations does have a small effect on reducing subsequent asthma/wheeze consultations, in adults, but more work is required to draw firm conclusions from this data. Lastly, Dr. Manon Belhassen presented novel findings from France on *How often do asthma patients claim prescribed therapy?* They concluded that in primary care, in their population, 73% of asthma patients claimed the completeness of their prescriptions in community pharmacy and showed the variability of prescribing vs. dispensing of asthma medicines.

The penultimate session for the day was entitled **Children Are Not Small Adults...Or Are They? Lessons From Real-Life Data**. In this session, Dr. Clare Murray presented data on the pre-school aged patient group and found that wheeze/asthma is commoner in pre-schoolers than older children and adults, pre-school wheeze does not predict asthma in adulthood, viruses are common in preschool acute episodes, less preventer medication is used and that exacerbations and hospital admissions are commoner, but mortality is lower. Dr. Mohsen Sadatsafavi presented the research of his team looking at asthma outcomes in children across a number of Canadian provinces. They found that asthma control achieved in the 24 months following diagnosis, that the major determinant of remission was the worst the control, the lowest the likelihood of remission and that this was irrespective of perinatal factors, demographics, and disease characteristics.

The final session of the day was a key note presentation by Associate Professor Álvaro A. Cruz from the Federal University of Bahia, Brazil entitled **How to Change Perceptions on Real-Life Research to Impact Guidelines**. In an insightful presentation, topics explored included what are relevant guidelines' (e.g. GOLD, GINA) literature search strategies, how good is journal acceptance of real-life research papers, where real-life research evidence adds most value, and shared the work done in Brazil using database research. His final observations how to change perceptions on Real-Life Research to impact guidelines included: Real-life research is still underrecognized in guidelines, high-impact journals are opened to real-life research papers, real-life research is of unique value in accessing effectiveness and safety of large-scale interventions in public health and lastly the suggestion for real-life research to be better recognized by guidelines: propose it formally and send suggestions annually to GINA, GOLD, WHO, ATS, ERS.

Day 1 concluded with drinks and the summit dinner, spent in the company of friends and collaborators.

Day 2

Day 2 of the REG 2018 Summit further built on the theme of 'working together', commencing with an engaging plenary exploring the Means and Mechanisms for International Collaboration with professional bodies, following by sessions on Quality and Impact, Technologies and a final plenary on 7 Ages of Cough.

In Day 2 opening plenary, **Means and Mechanisms for International Collaboration**, Professor Jerry Krishnan presented with regards to engagement with the ATS, Professor Nikos Papadopoulos with regards to EAACI and Professor Nicolas Roche with regards the ERS. Professor Chin Kook Rhee presented on improving engagement with Asia. Work across geographical regions as well as working with important regional medical associations was recognised as the only way forward to help raise the understanding and value of real-life research in contributing to the improvement of patient care and outcomes. In doing so, engagement at multiple levels is discussed from research initiatives to Task Force engagement, through SIGs and leadership roles.

The **"Quality and Impact"** session covered a range of topics, including the observational of global study NOVELTY, presented by Dr. Maria Gerhardsson de Verdier from Astra Zeneca. The NOVELTY study, a 3-year long observational longitudinal study aims to describe the patient characteristics, treatment patterns and the burden of illness over time of people with a diagnosis of asthma and/or COPD in order to identify phenotypes and endotypes associated with differential outcomes. It is anticipated that the findings of this study may support future development of personalised

treatment strategies. With data collection from over 12,000 patients, 19 countries (except China) completed, baseline data is anticipated Q3 2018. Professor Rupert Jones presented on Database Studies in Uganda which brought into focus the plight of chronic respiratory diseases in Africa. To begin to address chronic lung disease in Africa (which have risen by 35% in the last 10 years) a review was made of existing datasets generated from cross-sectional surveys, longitudinal cohorts and other trials. It was found that many existing datasets with high quality data in Uganda have the potential to address the current respiratory disease burden and can be utilised for a relatively small investment to generate and optimise longitudinal datasets. Dr. Manon Belhassen presented the results of a claims data study looking at changes in asthma drug use in France between 2006 and 2016. The key observations were that the prevalence of asthma controller therapy use remained stable between 2006 and 2016 but fixed dose combination products tended to replace other asthma medications and that the use of oral corticosteroids increased during the period. Professor Nicolas Roche's presentation focused on the RELEVANT tool, the first quality checklist to assist in the appraisal of published observational comparative effectiveness research (CER) and the opportunities to implement the tool into research practice including collaborations with scientific societies, guidelines developers and other stakeholders. Dr. Alex Mathioudakis presented an assessment of the real-life challenges of conducting clinical research in populations of paediatric patients with asthma. The key message was that there is a need for an international paediatric asthma network aiming to promote high-quality clinical research, the development of an international paediatric asthma registry and evidence-based recommendations. Finally, Ms. Lakmini Bulathsinhala presented a comparison of severe asthma databases globally and showed that severe asthma databases across the globe converge on collecting similar data field categories, while they differ significantly on the specific data fields included. A standard list of variables captured across countries will increase the statistical power of future studies by allowing for data interoperability.

The penultimate session "**Technology**" also included late breaking abstracts. Ms. Naomi Launders presented on the "Assessing the availability, functionality, utility and acceptance of smart inhalers" project in which a review of the current availability, functionality, utility and acceptability of smart inhalers is being used to inform further research into the use of technologies to predict and detect exacerbations and to optimise patient adherence. This research, run internally by REG, is currently in progress. Dr. Alan Kaplan, presented on "A desktop helper for asthma management". This research highlights that a 'desktop helper' can guide clinicians to support a decrease in inhaler corticosteroid overuse in COPD in clinical daily practice. Dr. Ron Dandurand presented research on the topic question relating to the relative importance of spirometry and oscillometry in the management of respiratory disease. The findings indicate that while both spirometry and oscillometry demonstrate significant differences between subjects with and without a history of respiratory disease, oscillometry correlated more strongly with patient reported outcomes than spirometry. A disease defining threshold of 10-20 cmH₂O/L I oscillometry was confirmed. Dr. Mihaela Stefan presented on smoking cessation therapies in hospitalised surgical patients with COPD and found that despite strong evidence that smoking is associated with surgical complications and the potential benefit to initiating therapy during hospitalization, smoking cessation pharmacotherapy is rarely used in the postoperative period in patients with active smoking and with a COPD diagnosis. Dr. Alex Dima's research explored the bi-directional relationship between ICS adherence and asthma control, indicating that adherence evaluated by the interval between the issuing of prescriptions had a small positive association with asthma control, while overusing SABA, being prescribed antibiotics and asthma-related outpatient visits were negatively associated with adherence in the same interval.

These results suggest that patients adapt their use of medication, despite the practices of health care providers which may be consistent with guidelines.

The final session of the scientific programme reviewed the 7 Ages of Cough, from birth and neonates all the way through to the elderly and the end of life. The session was an extensive review cough through the patient lifespan. It highlighted some of the challenges of identifying the causes of cough throughout early life, spanning all the way through to the end of life. This series of presentations delivered by Professor Nikolas Papadopoulos, Dr Lorcan McGarvey, Professor Leif Bjermer, Dr Omar Usmani, Professor Jacky Smith and Professor Chin Kook Rhee highlighted the complexity of this common yet highly variable symptom associated with a range of respiratory and non-respiratory causes.

ERS Congress, Paris, 15 - 19 September 2018

REG held a full time-table of Working Group meetings on Saturday and Sunday 15 & 16 September in conjunction with the ERS Congress in Paris. Sessions were held to progress work by most Working Groups as well very invigorating discussions on some of the broad issues that still require a clear methodology to investigate further.

WISC Congress, Florence, 6 - 9 December 2018

REG participated in the WAO International Scientific Conference with a symposium on Saturday 8 December. The symposium was chaired by Claudio Cricelli & Nikos Papadopoulos with Nichola Roche presenting on the REG Manifesto on real-life studies and Dermot Ryan presenting on the relevance of real-life studies in primary care.

Working group update

Adherence Working Group

The group has been working on a project looking at the bi-directional relationship of adherence and control in asthma. The results of this study were presented by Alex Dima at the ERS 2018 working group meeting, and these interesting results subsequently discussed. A manuscript has now been submitted. Several new project ideas have been raised, and these now need prioritising.

Alex Dima has stepped down as working group lead, and Sinthia Bosnic-Anticevich has agreed to act as interim working group lead.

Allergy Working Group

In 2018, Peter Hellings stepped down as lead of the allergy working group; REG thanks him for his work. Moises Calderon has agreed to take up the leadership of the working group, and will be discussing a way forwards for this group at the 2019 REG summit.

Asthma-COPD Overlap (ACO) Working Group

The ACO group is working on an ACO proof of concept study, which aims to test different ACO definitions using the Optimum Patient Care Research Database (OPCRD). At the REG summit and ERS 2018 the results of this study were presented and the definition of ACO used was discussed. The phase I manuscript has now been submitted to Annals of the American Thoracic Society.

The group has discussed the planned phase II study which will explore the clinical implications for those patients meeting the given definition of ACO. Nicolas Roche and Chin Kook Rhee have agreed to be principle investigators for this next phase, a proposal has been drafted and circulated, and the study is currently seeking funding. The group believe it is importance to conduct a phase III project to validate the definition in other databases; the REG team has also begun to explore potential databases for phase III.

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, several potential project ideas were discussed at ERS 2018.

The PaEdiatric Asthma in Real Life (PeARL) project, led by Nikos Papadopoulos, aims to produce evidence-based recommendations regarding controversial aspects of paediatric asthma, by using knowledge gaps surveys, systematic reviews, meta-analyses and Delphi exercises. A proposal has been written and funding is being sought, parts of the project are already underway.

The study into the comparative effectiveness of the addition of antibiotics versus normal care in asthma exacerbations has been on hold. Data analysis will now resume following the return of Sarah Lucas, the REG researcher leading the analysis.

Cost effectiveness Working Group

The Cost Effectiveness group met at the REG summit in March 2018, where it was proposed that the group investigate the cost of COPD in non-smokers. The cost effectiveness group are now working with the COPD group to finalise a proposal. The group are also working towards producing a description of their work so as to better engage with other REG working groups.

COPD Working Group

The COPD group has been conducting an international prospective study in Europe and Asia into the clinical validity and utility of the concept of control in COPD led by Marc Miravittles. In November, with the final follow-up visits completed, the data was signed off by the investigators; 290 of the 339 enrolled patients completed all visits. Data analysis is currently underway. Due to the enthusiasm shown by the participating sites the working group is considering another pragmatic trial. Following a working group meeting at ERS, a proposal was developed to look at the predictive value of FeNO in COPD exacerbations.

A proposal has written to conduct a database study to assess the implications of ICS reduction or withdrawal in the management of COPD. Helgo Magnussen, author of the original WISDOM trial, has agreed to be principle investigator. Funding is now being sought.

The “Trends of testing for and diagnosis of alpha-1 antitrypsin deficiency in the UK: more testing is needed” pilot study led by Joan Soriano has been published in the European Respiratory Journal.

Cough Working Group

During 2018, the cough working group, led by Lorcan McGarvey, have been working to progress a project on the characterisation of cough consultations in UK primary care, utilising the OPCR database. This is the first phase, with the ultimate aim of better defining chronic cough and its

associated burden in primary care. The protocol for this project is now finalised and it is hoped that data analysis will begin in early 2019.

Database and Coding Working Group

The group are aiming to develop a checklist with the optimum and minimum required variables for respiratory research using a Delphi exercise: Towards Optimum Reporting of Pulmonary Effectiveness Databases and Outcomes (TORPEDO). The phase I, to determine the full scope of variables for an ideal database, was completed having been expanded to cover low- and middle-income countries. The phase II was conducted to determine the minimally required variables, and the results of this were presented by Katia Verhamme and Job van Boven at the working group meeting at ERS 2018 and at the Global Alliance for Chronic Disease (GACD) 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. The group has discussed some potential future projects including a common data model.

ILD/IPF Working Group

In 2018, the ILD/IPF working group produced manuscripts for two projects. The first was a database study looking at how IPF presents in primary care prior to diagnosis. The second was a large questionnaire-based study to better characterise how ILDs are diagnosed globally, focusing on the use of multidisciplinary team meetings. The manuscript describes the ILD diagnostic practice from 457 centres globally and has been accepted for publication in *European Respiratory Journal: Open Research*. In parallel, work continued to finalise the proposal for phase II of the project; which aims to determine the diagnostic agreement across centres globally by providing them with anonymised cases to diagnose in their usual practice. The proposal has been circulated to funders and discussions regarding funding are ongoing.

Quality standards Working Group

In 2018, the quality standards working group 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.

Severe Asthma and Biomarkers Working Group

The group have been reworking an Editorial piece highlighting the differences (reasons for and implications of) in the National Institute for Health and Care Excellence's (NICE) and the Global Initiative for Asthma (GINA) recommendations on the use of FeNO. The letter is currently being updated ready for re-submission.

A small meeting was held at ERS to discuss the knowledge gaps regarding the use of FeNO in respiratory disease. This round table discussion led to several study ideas relating to FeNO in asthma, which are still under discussion.

Sleep Breathing Disorders Working Group

REG, working with Mihaela Stefan, have carried out a feasibility study into using the OPCR database to investigate the impact of obstructive sleep apnoea diagnosis on healthcare resource utilisation in patients with obstructive lung disease. There is insufficient reporting of sleep apnoea in OPCR to

conduct this study, so REG are looking into other data sources and determining whether there is interest in other sleep breathing disorder research activities.

Small Airways Working Group

In 2018, the small airways group, led by Omar Usmani, published a call to harmonise particle size nomenclature. Following a reviewers comment the group then embarked on a project to determine what lung dose means to different professionals. This project is currently ongoing. In 2018 the group also published a systematic review of extra-fine vs. fine inhaled corticosteroids and were involved in a study to determine how well database measures of severe asthma exacerbations correlate to questionnaire data.

Technology Working Group

In 2017 John Blakey stepped down as lead of the technologies group; though he continues to be involved with REG projects. REG thank him for his leadership of the group and his continued support. The technology working group is currently seeking funding for a project to review the feasibility and utility of smart inhalers from the point of view of primary care physicians. They are also working on a proposal on the definition and early detection of exacerbations.

Active projects

Project name	Description	Current phase
ACO		
ACOS Proof of Concept Study: Phase I	A database study to develop tools to support real-life research involving patients with a mixed asthma-COPD phenotype	Submitted to ATS Annals
Adherence		
Adherence: bi-directional relationship between asthma outcomes and adherence: P2	A database study to improve understanding of the bi-directional causality relationship between asthma outcomes and adherence	Submitted to JACI in Practice
Child health		
Usual Care ± antibiotics for the management of asthma exacerbations	A database study to assess the clinical implications of combining antibiotics with usual care (oral steroids) for the management of asthma exacerbations	Data analysis underway
COPD		
Validation of the Concept of Control of COPD in Clinical Practice: Phase II	An 18-month international prospective study to assess the levels of COPD control and the clinical implications of control status	Data analysis underway
Database and coding		



Towards Optimum Reporting of Pulmonary Effectiveness Databases and Outcomes (TORPEDO): a REG/UNLOCK initiative	A Delphi study to provide recommendations and tools to help inform the design of databases for observational research in respiratory and allergic airways disease	Phase two of the Delphi exercise is complete, phase three is underway.
ILD/IPF		
Missed diagnostic opportunities in IPF	A database study to characterise primary care interactions in the years prior to idiopathic pulmonary fibrosis (IPF) diagnosis and potential missed diagnostic opportunities	Manuscript finalised
ILD MDT: Global Evaluation of ILD Diagnostic Practice: Phase I	A survey to characterise interstitial lung disease (ILD) diagnostic practice around the world	Accepted for publication in ERJ Open Research
Quality Standards		
REG/EAACI Taskforce Asthma Comparative Effectiveness Literature Quality Review	A project to develop tools to facilitate quality appraisal of published respiratory comparative effectiveness research	Two manuscripts accepted for publication in Clinical and Translational Allergy
Severe asthma and biomarkers		
NICE/GINA FENO letter to the Editor: Biomarkers in asthma management: should we move forward?	A letter reviewing the latest developments in biomarkers in asthma	Writing in progress
Small airways		
State of the Union: current asthma morbidity in the UK	A database study to characterise trends over time of asthma management practice and asthma-related morbidity	Low priority as unfunded. Protocol approved.
Making sense of dose	An opinion seeking study to investigate the views of different disciplines regarding what “dose” means to them, in order to explore and potentially harmonise the terminology around ICS dosing	Recruitment of multidisciplinary team underway
Other		
Evaluation of fulfilment of NICE CAP recommendations in UK clinical practice	A database study to investigate the implementation of national recommendations for	Manuscript in draft



community acquired
pneumonia in routine care

Publications in 2018

In 2018, REG produced 10 peer reviewed publications – nine REG research projects, and the abstracts from the 2018 REG Summit. A further five manuscripts were submitted in 2018 and accepted for publication in early 2019. A full list of REG research publications is available on the REG website:

<http://effectivenessevaluation.org/reg-research-publications/>

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

Grigg J, Nibber A, Paton JY, Chisholm A, Guilbert TW, Kaplan A, Turner S, Roche N, Hillyer EV, Price DB. (2018), *J Asthma Allergy*, 11

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

Stolbrink, M., Bonnett, L. J. and Blakey, J. D. (2018), *Eur Clin Respir J*, 5(1).

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

Stolbrink, M., Bonnett, L. J. and Blakey, J. D. (2018), *J Allergy Clin Immunol Pract*.

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

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), *Pragmat Obs Res*, 9, pp. 29-42

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

Turner, S. W., Murray, C., Thomas, M., Burden, A. and Price, D. B. (2018), *NPJ Prim Care Respir Med*, 28(1), pp. 28.

Harmonizing the Nomenclature for Therapeutic Aerosol Particle Size: A Proposal

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), *J Aerosol Med Pulm Drug Deliv*, 31(2), pp. 111-113.

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

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), *J Allergy Clin Immunol Pract*, 6(3), pp. 907-915.e7.

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

Soriano, J. B., Lucas, S. J., Jones, R., Miravittles, M., Carter, V., Small, I., Price, D., Mahadeva, R. and Group, R. E. (2018), *Eur Respir J*.



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

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., Kemppinen, A., Tee, A., Roman-Rodríguez, M., Soler-Cataluña, J. J. and Price, D. B. (2018), *Respir Med*, 136, pp. 8-14

Abstracts from the 2018 Respiratory Effectiveness Group Summit

Respiratory Effectiveness Group (2018), *Respiratory Research*, 19 (S1)

Manuscripts submitted in 2018

Prevalence and characteristics of asthma-COPD overlap in routine primary care practices

Krishnan, J. A., Nibber, A., Chisholm, A., Price, D., Bateman, E. D., Bjermer, L., van Boven, J. F. M., Brusselle, G., Costello, R.W., Dandurand, R. J., Diamant, Z., Van Ganse, E., Gouder, C., van Kampen, S. C., Kaplan, A., Kocks, J., Miravittles, M., Niimi, A., Pizzichini, E., Kook Rhee, C., Soriano, J. B., Vogelmeier, C. and Roche, N.

The relationship between real-world inhaled corticosteroids adherence and asthma outcomes: a multilevel approach in a longitudinal asthma cohort

Vervloet, M., van Dijk, L., Spreeuwenberg, P., Price, D., Chisholm, A., Van Ganse, E., Pinnock, H., Rand, C., Eaking, M., Schermer T., Souverein, P. and Dima, A.

The characterisation of interstitial lung disease multidisciplinary team meetings: A global study

Richeldi, L., Lauanders, N., Martinez, F., Walsh, S. L. F., Myers, J., Wang, B., Jones, M., Chisholm, A. and Flaherty, K.R.

Quality standards in respiratory real-life effectiveness research: report from the Respiratory Effectiveness Group – European Academy of Allergy and Clinical Immunology Task Force

Roche, N. Campbell, J. D., Krishnan, J. A., Brusselle, G., Chisholm, A., Bjermer, L., Thomas, M., Van Ganse, E., van den Berge, M., Christoff, G., Quint, J., Papadopoulos, N. G. and Price, D.

The REal Life EVIDence Assessment Tool (RELEVANT): development of a novel quality assurance asset

Campbell, J. D., Perry, R., Papadopoulos, N. G., Krishnan, J. A., Brusselle, G., Chisholm, A., Bjermer, L., Thomas, M., Van Ganse, E., van den Berge, M., Quint, J., Price, D. and Roche, N.

Future projects seeking funding

Project name	Description
ACO	
ACOS Proof of Concept Study: Phase II	A database study to determine the functional consequences of an ACO diagnosis, in terms of treatments, outcomes and healthcare utilisation, compared to either asthma or COPD diagnosis alone
Child health	
PeARL: Paediatric Asthma in Real Life	A standard setting exercise in paediatric asthma based on systematic review, expert consensus and ontological analysis of the unanswered questions in paediatric asthma
Cough	
Burden of cough in UK primary care: Phase I	A database study to characterise cough in primary care



COPD	
Real life WISDOM	A database study to determine the effect of withdrawing or reducing inhaled corticosteroids
FeNO in COPD	A prospective trial to assess the role of FeNO in predicting COPD exacerbations
ILD/IPF	
ILD MDT: Global Evaluation of ILD Diagnostic Practice: Phase II	A study utilising ILD case information to determine how varying diagnostic practice and settings affects diagnostic agreement
Technologies	
Systematic review of smart inhalers	A scoping review of user needs, acceptance, feasibility and utility of smart inhalers from a medical professional's point of view



Financial summary

Profit & Loss		
Respiratory Effectiveness Limited Trading as REG [Respiratory Effectiveness Group]		
1 January 2018 to 31 December 18		
	31 Dec 18	31 Dec 17
Income		
Restricted Income	£161,010.00	£287,988.00
Unrestricted income	£219,062.00	£126,895.00
Total Income	£380,072.00	£414,883.00
Less Cost of Sales		
Research Costs	£134,649.00	£180,763.00
Summit Costs	£98,633.00	£80,462.00
Total restricted costs	£233,282.00	£261,225.00
Administrative costs	£170,030.00	£149,038.00
Total Costs	£403,311.00	£410,263.00
Net Profit/(Loss)	(£23,239.00)	£4,620.00

Balance Sheet		
Respiratory Effectiveness Limited Trading as REG		
As at 31 December 2018		
	31 Dec 2018	31 Dec 2017
Assets		
Bank		
BARC EUR	£6,949.00	£2,247.09
BARC GBP	£30,167.00	£62,691.00
BARC USD	£100,551.00	£41,269.33
PYPL	£0.00	£0.00
Total Bank	£137,667.00	£106,207.42
Current Assets		
Accounts Receivable	£1,096.00	£225,610.29
Loans	£0.00	£0.00
Prepayments	£1,895.00	£51,197.66
Total Current Assets	£2,991.00	£276,807.95
Fixed Assets		
Office Equipment – accumulated depreciation	-(£63.00)	-(£62.69)
Office Equipment - at cost	£586.00	£586.33
Total Fixed Assets	£523.00	£523.64
Total Assets	£141,181.00	£383,539.01

Liabilities		
Current Liabilities		
Accounts Payable	£68,062.00	£56,537.38
Accruals	£14,705.00	£4,250.00
Deferred Revenue	£66,642.00	£307,586.85
Others	£(40.00)	£0.00
PAYE & NIC Control	£4,810.00	£2,822.19
Pension Fund	£210.00	£124.15
REG Barclaycard	£77.00	£112.29
VAT Control	£485.00	£2,638.00
Total Current Liabilities	£154,951.00	£374,070.86
Total Liabilities	£154,951.00	£374,070.86
Net Assets	£(13,770.00)	£9,468.15
Equity		
Accumulated Surplus	£9,468.00	£4,847.45
Current Year Earnings	£(23,238.00)	£4,620.70
Total Equity	£(13,770.00)	£9,468.15