RESPIRATORY EFFECTIVENESS GROUP ANNUAL REPORT 2017

Respiratory Effectiveness Group

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Contents

The Respiratory Effectiveness Group: Aims and Objectives

VISION

A not-for profit, international 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.

MISSION

Promote high-quality, collaborative research, addressing questions unanswered by traditional randomised controlled trials, to integrate real-life evidence into clinical practice guidelines, policy and budgetary decision-making for the benefit of all stakeholders in respiratory medicine.

STRATEGY

REG will achieve its goals 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, EUFOREA, IPCRG, IPSE, ISPOR, patient organisations)
- Developing partnerships with strategic supporters in industry and academia.

Together, REG collaborators, partners, and supporters, will implement a multi-faceted programme of activities aimed at improving the understanding of respiratory medicine

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 observational 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

The year in review

REG has seen another productive year, continuing the momentum achieved by the outputs of our Working Groups. Supported by 2 new research scientists, Naomi Launders and Sarah Lucas, a total of 13 pieces of original research were published in the last year and there are currently 21 active studies.

Still numbering 14, REG has merged the work of the Severe Asthma & Biomarkers Working Groups into one network and introduced a new group on Cough led by Lorcan McGarvey. The Cough Working Group held its inaugural meeting at the ERS in Milan.

In addition to numerous database studies, (now enhanced by an improved collaboration with the Optimum Patient Care Research Database – (OPCRD)) REG is also leading on one large observational study on COPD control and an international assessment of ILD MDTs. 2017 also saw REG confirmed as the academic partner of the International Severe Asthma Registry (ISAR).

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 2017, took place in London at the end of March – a report on this meeting appears later in this update.

Finance continues to be a challenge, with income down in 2017 compared with 2016. However, careful planning and use of resources have enabled REG to deliver an increased year-on-year level of output and a balanced budget. 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.

Our Board have Directors have co-opted 2 additional members to the board, Alan Kaplan and Omar Usmani and their experience, enthusiasm and energy is a valuable addition to REGs ability to deliver on our mission.

Research needs

Our research leads within the Executive Committee, Nicolas Roche and Sinthia Bosnic-Anticevich have examined the many research needs within the field and have compiled a list of statements articulating what we at REG see as our strategic goals in addressing the key issues and requirements for high-quality evidence and standards and provide a clear focus for the future work of REG.
These needs, divided into those relating to clinical practice and to advocacy and quality standards, provide the organisation with clear objectives which will allow REG to achieve the strategic goals. The research needs have been classified as follows:

Clinical Practice

1. Characterise current routine care disease epidemiology and burden for respiratory, allergic and obstructive airways disease outcomes
2. Characterise current routine care prescribing practices (diagnostic and management) and their implications for respiratory and allergic airways disease outcomes
3. Utilise routinely collected data to describe disease characteristics associated with future risk in respiratory and allergic airways disease
4. Assess the real-world safety profile of licensed pharmacological interventions for / as used in patients with respiratory and allergic airway diseases, and associated characteristics of the patients, the disease, the ecology of care
5. Evaluate the comparative effectiveness of treatments (guideline-recommended / not recommended but frequently used) in respiratory and allergic airways disease, and associated characteristics of the patients, the disease, the ecology of care
6. Understand the role of maintenance inhaled therapy particle size on outcomes in respiratory and allergic airways disease
7. Improve understanding of medication adherence behaviours (including inhaler device challenges) in respiratory and allergic airways disease, their implications on clinical and health economic outcomes and optimised management options
8. Understand the clinical and cost implications of comorbidities (and their treatments) in patients with respiratory and allergic airway diseases.

Advocacy and Quality Standards

1. Provide methodological support for high quality real-world research
2. Define, refine and validate clinical tools for the real-world management of respiratory and allergic airways disease
3. Define, refine and validate tools (e.g. databases, indicators) for real-world research on respiratory and allergic airways disease
4. Guide the development of technology-based solutions (TBS) with clinical utility for respiratory and allergic airway diseases.

All projects currently within the REG portfolio have been classified according to these research needs and the categories will be used to assess proposed projects as one aspect of the Research Review.

The creation of these research needs has also allowed for the organisation to bring a "research match-making" search engine to fruition within the site. The new search functionality allows visitors to the site to search for projects according to specific research needs and also look at projects which have been completed, are in progress or are planned for the future. The aim is to provide a resource for PhD researchers to find ideas and contacts for projects that have been identified by the REG network as a requirement within the field of real-world respiratory research. You can view the new Research Needs page on the website at: www.effectivenessevaluation.org/research-2/ research-needs.

Working Group Activity Overview

REG supports its research collaboration through its various Working Groups, of which there are currently 14. The appointment of 2 new research scientists Naomi Launders and Sarah Lucas has invigorated the activity of these groups, enabling a greater number of projects to be undertaken and drive the completion of existing research. Sarah will be leaving on maternity leave in February 2018, with her position being covered by Sandrine Leroy.

ACO (Asthma-COPD Overlap) working group

There is no clear definition of ACO, and this could provide a barrier to future research, therefore the ACO working group Proof of Concept study was developed to test different smoking and age-related ACO definitions and evaluate the prevalence, using the Optimum Patient Care Research Database (OPCRD). A manuscript resulting from this study, 'Asthma-COPD Overlap in Routine Primary Care Observational Studies: from definition to prevalence and population characteristics', is being prepared for publication.

The group plans to use the OPCRD patients from the Proof of Concept study to begin investigating the implications of a mixed asthma-COPD phenotype vs COPD alone on patient outcomes. Furthermore, there are plans to repeat the analyses from the Proof of Concept study in other national databases to evaluate the ACO definitions. Potential databases have been selected and funding will be sought to cover data costs and analytical support potentially at multiple sites.

Adherence working group

The Adherence working group is undertaking a study to improve understanding of the bi-directional causality relationship between asthma outcomes and adherence. The study will assess whether good control results in poor adherence and/or whether high adherence results in controlled disease. Phase 1 evaluated control patterns and patterns of different adherence measure rates over a continuous 3-year period. A manuscript has been published which found different analysis choices resulted in substantial variation in ICS use estimates, highlighting the need for transparent and clinically relevant methodology. Distinguishing between non-persistence and ICS use is important in clinical practice and may require different interventions in routine consultations. The results from the phase 1 study are being used to inform the phase 2 multilevel interaction analysis of adherence and control, which is currently underway.

Allergy Working Group

The Allergy Working Group have two active studies. The first is a survey of allergic rhinitis sufferers in Australia, which aims to understand the burden of allergic rhinitis in Australia in terms of

healthcare utilisation and medication, symptom control and impact on health-related quality of life. A final report has been produced and production of a manuscript is planned.

The second study focuses on chronic rhinosinusitis and aims to develop algorithms to differentiate between acute and chronic rhinosinusitis using the OPCRD database, to quantify the true burden of disease in the UK. Led by Wytske Fokkens, this project is in manuscript development.

In a collaboration with EUFOREA (European Forum on Research and Education in Allergy), the group are also currently considering three study proposals, investigating presentation and treatment of chronic rhinosinusitis in the UK; the effects of sinus surgery on asthma development, symptoms and control; and the effects of cumulative steroid exposure in allergic disease. The Working Group meeting at the REG Summit 2018 will decide which of these proposals to take forward.

Biomarkers/Severe asthma working group

A study by this working group investigating blood eosinophil count and exacerbation risk in patients with COPD has been published. An article has also been published discussing the use of electronic medical records and biomarkers to manage risk and resource efficiencies. The group are 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. This Working Group also acts as the REG lead for the ISAR (International Severe Asthma Registry) project. Over 2,000 patients from six countries will contribute to this first research project of ISAR. Results will be presented at the REG Summit on March 22nd, 2018!

Child Health working group

The Child Health working group are currently working on a study to evaluate the comparative effectiveness of adding antibiotics to usual care (oral steroids) for the management of asthma exacerbations; phase 1 analysis has been completed and used to guide the analysis for phase 2 which is currently underway. A paper on pre-school-wheeze is currently under development. There are plans for a future study into 'Bronchiolitis and asthma risk (marker or cause of future asthma) in paediatrics'. The working group is also discussing ideas for a future paediatrics adherence study and a severe asthma in paediatrics study.

COPD working group

The group is working on evaluating the clinical validity and utility of the concept of control in COPD. A pilot database study into the concept of control in COPD has been published. An international prospective study in Europe and Asia into COPD control is well underway; 339 patients were enrolled. At the time of writing, 92% had completed their first follow-up visit, 71 their second follow-up and 4% their final follow-up. All third and final follow-up visits are expected to be completed by November 2018. An initial paper investigating the COPD control during the screening and baseline visits of those enrolled in the prospective study has been published.

A pilot study investigating the frequency of testing, incidence and prevalence of alpha1-antitrypsin deficiency in patients with COPD in the UK has been submitted for publication.

The group are seeking funding for two further studies i) A full study into the epidemiology and natural history of alpha1-antitrypsin deficiency and ii) An investigation into the implications of ICS withdrawal in patients with COPD, managed in a primary care, 'real-life' setting.

Cost Effectiveness Working Group

The Cost-Effectiveness Working Group are in the process of reviewing existing active or completed REG projects where cost-effectiveness analysis would add value to the study. A brain-storming session will be held at the REG 2018 Summit to identify key areas of interest and identify funding opportunities for these projects.

Cough working group

This new working group, set up to investigate the cough, is primarily interested in understanding the mechanisms and burden of chronic cough in order to improve its management. The first study by this working group will assess the burden of cough within general practice in the UK. The study aims to assess the prevalence and incidence of cough in UK primary care and to determine the demographic and clinical characteristics associated with different types of cough. It is hoped this study will provide a basis for future research studies into idiopathic and chronic cough.

Databases and Coding Validation working group

A Delphi study in collaboration with the Global Alliance for Chronic Diseases, 'Towards Optimum Reporting of Pulmonary Effectiveness Databases and Outcomes (TORPEDO)', is underway. Phase I, which involved identifying the full scope of variables for an ideal database, was completed. However, it was felt the phase I could be improved by extending participation, therefore phase I will be repeated before undertaking phases II and III, which aim to determine and prioritise the minimally required variables in a database.

The group aims ultimately aim to develop database and coding assessment tools and eventually expand into the area of harmonisation and conversion of terminology, and common data models. The group are collecting and sharing code lists that have been used in previous studies and would encourage everyone to consider sharing their code lists through the REG website.

IPF/ILD Working Group

In January 2017, the IPF/ILD Working Group published a review of the diagnosis of idiopathic pulmonary fibrosis in The Lancet Respiratory Medicine. The group have also been working on a study to identify features of ILD multidisciplinary team meetings associated with more accurate diagnosis. Phase I aimed to characterise diagnostic practice globally and is currently in manuscript development. Phase II is in the final stages of planning and aims to determine diagnostic agreement levels across MDTs globally.

Finally, a project investigating the natural history of IPF was conducted in 2017. The study aimed to explore the clinical presentation and progression of patients with progressive fibrotic lung disease and to characterise healthcare utilisation in the five years prior to diagnosis.

REG/EAACI Quality Standards Taskforce

In 2017, the REG/EAACI Quality Standards Taskforce has worked to finalise two manuscripts from the asthma comparative effectiveness literature and quality assessment tool project and are working on the dissemination of the resulting Real Life Evidence AssessmeNt Tool (RELEVANT). The first manuscript provides an overview of the project, while the second details the methodology used in creating the tool. These manuscripts are currently under review with REG and EAACI committees and it is hoped they will be published in the first half of 2018.

Small Airways Study Group

The Small Airways Working Group published seven papers in 2017, and another, aiming to validate a series of objective asthma control measures, is currently under submission with a journal. The group

are also working on a large database study, the Asthma State of the Union, studying asthma presentation, treatment and control over time. Finally, the group is also planning a commentary on the meaning of "dose", and a database study investigating the link between obesity, weight loss, weight loss surgery and asthma.

Sleep Breathing Disorders working group

The Obstructive Sleep Apnoea (OSA) working group has been renamed the Sleep Breathing Disorders (SBD) to better reflect the groups interests. The first study by this working group 'Impact of obstructive sleep apnoea diagnosis on healthcare resource utilisation in patients with obstructive lung disease' is underway. Since this is the first time the Optimum Patient Care Research Database has been used to investigate sleep-related breathing disorders (SBD) the study will initially focus on determining the frequency of testing, the prevalence of SBDs (including obstructive sleep apnoea, OSA) and the prevalence of continuous positive airway pressure (CPAP) therapy prescribing, in a UK primary care population. The clinical and demographic characteristics of SBD patients will be assessed according to the type of obstructive lung disease (asthma, COPD or asthma-COPD overlap) and in those for whom CPAP treatment is recorded versus not recorded. This study ultimately aims to evaluate the impact of SBD diagnosis (with and without CPAP treatment) on clinical outcomes and healthcare resource utilisation in SBD patients in the UK who have comorbid obstructive lung disease (OLD).

Technologies Working Group

In 2017 the technologies group wrote a letter to the editor in Pragmatic Observational Research calling for stakeholder engagement in the deployment of technology-supported management of chronic respiratory conditions. The working group also published a paper on identifying risk of future asthma attacks and created a "Future Asthma Risk Calculator" which is available on the REG website. Funding is currently being sought for a project to validate the asthma risk prediction model using claims-based data.

Work has also begun on a protocol for a systematic review of Smart Inhaler availability, acceptability and function and an accompanying Delphi exercise to investigate healthcare professionals' opinions of Smart Inhalers.

Ad-hoc projects

During 2017, REG worked on several projects that did not fall under a working group. A manuscript from a project to evaluate the cardiovascular risk profile of nicotine replacement therapy was published in April 2017, while analysis is underway on a project to evaluate the management of community acquired pneumonia in the primary care in the UK. A collaboration with the University of Liverpool has enabled a project on the optimum duration of antibiotics for respiratory infections.

Our Current Activities

REG's activities are driven forward by our specialist Working Groups. Each working group brings together experts from around the world with shared expertise and interest in a particular area that real-life research methodologies are particularly well-suited to address.

The membership of any Working Group is open to anyone with a passion for research and furthering their understanding of a particular area. New members and new ideas are always welcome.

Below is a list of the 21 currently active REG studies:

STUDY TITLE	Lead investigators	Study Stage
ACOS Proof of Concept Study: Develop tools to support real-life research involving patients with a mixed asthma-COPD phenotype & the clinical implications of a mixed asthma-COPD phenotype	Nicolas Roche and Jerry Krishnan	Manuscript being finalised
Adherence: bi-directional relationship between asthma outcomes and adherence	Alex Dima	Final report submitted
Assess the incidence of acute and chronic rhinosinusitis	Wystke Fokkens	Analysis complete
NICE/GINA FENO letter to the Editor: Biomarkers in asthma management: should we move forward?	Kjell Alving, Leif Bjermer	Manuscript underway
Usual Care ± antibiotics for the management of asthma exacerbations	Nikos Papadopoulos	Analysis underway
Validation of the Concept of Control of COPD in Clinical Practice	Marc Miravitlles	Phase 1 complete - manuscript published Phase 2: FU 2 visits 70% complete. Final visits commenced
UNLOCK Study: the prevalence of comorbidities in COPD patients and their impact on the quality of life and COPD symptoms in primary care patients	Pedro Teixeira & Bjorn Stallberg	Analysis ongoing
Alpha 1 [AATD] Burden: Characterise the natural history of patients with alpha-1 antitrypsin deficiency in routine care patients with/without COPD	Joan Soriano	Manuscript submitted

Towards Optimum Reporting of Pulmonary Effectiveness Databases and Outcomes (TORPEDO): a REG/UNLOCK initiative	Job van Boven Jon Campbell Katia Verhamme	Delphi study underway
UNLOCK study: are pharmacological RCTs relevant to real life asthma populations?	Pedro Teixeira & Karin Lisspers	Analysis on-going
Missed diagnostic opportunities in IPF	Luca Richeldi	Analysis complete
Characterisation of interstitial lung disease (ILD) diagnostic practice around the world and implications on diagnostic agreement and access to licensed therapies	Luca Richeldi, Kevin Flaherty, Fernando Martinez, Simon Walsh, Jeffery Myers	Phase 1 complete - manuscript under review Phase 2: Protocol being finalised
Clinical and Cost implications of OLDOSA (comorbid obstructive sleep apnea in patients with obstructive lung disease)	Mihaela Stefan	Protocol developed
REG/EAACI Taskforce Asthma Comparative Effectiveness Literature Quality Review	Nicolas Roche & Jon Campbell	Manuscripts under final review
State of the Union: current asthma morbidity in the UK	David Price	Re-analysis underway
Systematic review of smart inhalers	tbc	Protocol development
Pre-school asthma / wheeze ("asthma under 5s")	Jonathan Grigg	Responding to reviewers comments
Evaluation of fulfilment of NICE CAP recommendations in UK clinical practice	Chris Winchester	Analysis Underway
Optimum Antibiotic Course Duration: Utilise routine care data to identify the optimum duration of antibiotics for respiratory infections	John Blakey	Manuscript drafted
The effects of obesity, weight loss and gastro-oesophageal reflux disease on asthma	Therese Lapperre	Protocol drafted
Device Optimisation for improved adherence and outcomes	tbc	Protocol under development

Publications

In addition to the REG abstracts publication, a total of 13 pieces of original research by REG were published in 2017, up from 9 in 2016.

A full list of all REG publications can be found on the REG website.

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

2017 - European Respiratory Journal - Blood eosinophil count and exacerbation risk in patients with COPD

Marjan Kerkhof, Samatha Sonnappa, Dirkje. Postma, Guy Brusselle, Alvar Agustí, Antonio Anzueto, R upert Jones, Alberto Papi, Ian Pavord, Emilio Pizzichini, Todor Popov, Nicolas Roche, Dermot Ryan, M ike Thomas, Claus Vogelmeier, Alison Chisholm, Daryl Freeman, Mona Bafadhel, Elizabeth V. Hillyer, David B. Price

European Respiratory Journal 2017 50: 1700761; DOI: 10.1183/13993003.00761-2017

2017 – Pragmatic and Observational Research - Effective deployment of technology-supported management of chronic respiratory conditions: a call for stakeholder engagement.

Costello, R. W., A. L. Dima, D. Ryan, R. A. McIvor, K. Boycott, A. Chisholm, D. Price and J. D. Blakey. https://doi.org/10.2147/POR.S132316

2017 – Pulmonary Therapy - Cohort Analysis of Exacerbation Rates in Adolescent and Adult Patients Initiating Inhaled Corticosteroids for Asthma: Different Dose–Response Profile

Postma DS; Kaplan A; Soriano JB; Grigg J; Guilbert T; van Aalderen W; Roche N; Burden A; Hillyer EV; Israel E; Price DB. doi:10.1007/s41030-017-0037-3

2017 – J Allergy Clin Immunol Pract - Real-Life Outcomes for Patients with Asthma Prescribed Spacers for Use with Either Extrafine- or Fine-Particle Inhaled Corticosteroids

Guilbert, T. W., G. Colice, J. Grigg, W. van Aalderen, R. J. Martin, E. Israel, D. S. Postma, N. Roche, W. Phipatanakul, E. V. Hillyer, J. M. Evans, M. B. Dolovich, D. B. Price and Respiratory Effectiveness Group DOI: 10.1016/j.jaip.2016.11.026

2017 – Lancet Respiratory Medicine - The diagnosis of idiopathic pulmonary fibrosis: current and future approaches

Martinez, F. J., A. Chisholm, H. R. Collard, K. R. Flaherty, J. Myers, G. Raghu, S. L. Walsh, E. S. White and L. Richeldi. 10.1016/S2213-2600(16)30325-3

2107 – Journal of Aerosol Medicine and Pulmonary Drug Delivery – Harmonizing the nomenclature for therapeutic aerosol particle size – a proposal

E. V. Hillyer, D. B. Price, H. Chrystyn, R. J. Martin, E. Israel, W. M.C. van Aalderen, A. Papi, O. S. Usmani, N. Roche, on behalf of the Respiratory Effectiveness Group, Small Airways Study Group

2017 – Allergy Asthma Immunology Res - Asthma-Related Outcomes in Patients Initiating Extrafine Ciclesonide or Fine-Particle Inhaled Corticosteroids

Postma, D. S., R. Dekhuijzen, T. van der Molen, R. J. Martin, W. van Aalderen, N. Roche, T. W. Guilbert, E. Israel, D. van Eickels, J. M. Khalid, R. M. Herings, J. A. Overbeek, C. Miglio, V. Thomas, C. Hutton, E. V. Hillyer and D. B. Price doi: 10.4168/aair.2017.9.2.116

2017 – European Clinical Respiratory Journal - Use of electronic medical records and biomarkers to manage risk and resource efficiencies

Ryan, D., J. Blakey, A. Chisholm, D. Price, M. Thomas, B. Ställberg, K. Lisspers, J. W. H. Kocks and Respiratory Effectiveness Group. doi: 10.1080/20018525.2017.1293386

2017 - NPJ - Primary Care Respiratory Medicine - Abstracts from the 2017 Respiratory Effectiveness Group Summit: what lies ahead?

2017 - PLOS One - Risk of Pneumonia in Obstructive Lung Disease: A real-life study comparing extra-fine and fine-particle inhaled corticosteroids
Samantha Sonnappa, Richard Martin, Elliot Israel, Dirkje S. Postma, Wim van Aalderen, Annie Burden, Omar S. Usmani, David B. Price, on behalf of Respiratory Effectiveness Group Small Airways Study Group.

2017 - COPD: Journal of Chronic Obstructive Pulmonary Disease - Validating the Concept of COPD Control: A Real-world Cohort Study from the United Kingdom:
Anjan Nibber, Alison Chisholm, Juan José Soler-Cataluña, Bernardino Alcazar, David Price, Marc Miravitlles

2017 - The Journal of Allergy and Clinical Immunology in Practice - Inhaled Corticosteroid Adherence Patterns In a Longitudinal Asthma Cohort:

Souverein PC, Koster ES, Colice G, van Ganse E, Chisholm A, Price D, Dima AL

2017 - The Journal of Allergy and Clinical Immunology in Practice - Identifying Risk of Future Asthma Attacks Using UK Medical Record Data: A Respiratory Effectiveness Group Initiative
John D. Blakey, PhD, David B. Price, MD, Emilio Pizzichini, MD, Todor A. Popov, MD, Borislav D. Dimitrov, DM/PhD, Dirkje S. Postma, MD, Lynn K. Josephs, DM, Alan Kaplan, MD, Alberto Papi, MD,

Marjan Kerkhof, PhD, Elizabeth V. Hillyer, DVM, Alison Chisholm, MS, and Mike Thomas, PhD. doi: http://dx.doi.org/10.1016/j.jaip.2016.11.007

2017 - npj Primary Care Respiratory Medicine - Personalising care of adults with asthma from Asia: a modified e-Delphi consensus study to inform management tailored to attitude and control profiles
Alison Chisholm, David B Price, Hilary Pinnock, Tan Tze Lee, Camilo Roa, Sang-Heon Cho, Aileen David-Wang, Gary Wong, Thys van der Molen, Dermot Ryan, Nina Castillo-Carandang, Yee Vern Yong, on behalf of the Respiratory Effectiveness Group. doi:10.1038/npjpcrm.2016.89

International Conference & Congress Activities

ATS Congress 2017

REG held a Working Group meeting during the ATS Congress in Washington DC. The IPF/ILD Working group received the initial report of Phase 1 of the MDT study. Additional analyses and clarifications were suggested – this phase is now at manuscript review stage. Discussions also surrounded the plans for Phase 2, which will be finalised at the REG Summit in 2018. The ILD group also had an abstract accepted for poster presentation at the conference on this study. REG also attended the ISAR Steering committee meeting, of which it is the academic partner.

ERS Conference 2017

In addition to the presentation of two posters: “Global characterisation of routine care interstitial lung disease diagnostic practice” and “Comparative effectiveness of therapies for preschool children with recurrent wheezing”, REG held a full time-table of Working Group meetings at the ERS in Milan. Sessions were held to progress work by nearly all Working Groups, with the exception of Sleep Breathing disorders and Cost effectiveness. The conference also saw the launch of a new REG working Group – Cough, which will continue its work at the REG Summit.

During the Congress, REG held its AGM, postponed from the March meeting. Minutes of this meeting will be available at the next AGM in March 2018 and on the REG website.

REG Summit 2017

The REG 2018 Summit in London, combined the usual working group meetings, plenary talks with interactive panel sessions, pro-con debates and abstract sessions. The theme of the Summit was “What Lies Ahead? Translating the Value and Potential of Real-Life Evidence”

The Summit proved to be an excellent forum for sharing the many successes and results of various research projects undertaken by the REG Working Groups. These groups work collaboratively to develop protocols and to deliver research that not only addresses those evidence gaps, but also provides worked examples of REG quality standards in practice.

Prof. Walter G. Canonica opened the Summit, chairing a session on Solutions to Services Under Pressure, covering areas such as technological solutions to adherence, targeted resources and streamlined referral pathways, the session ended with an open discussion on what barriers exist and what are the REG-supported solutions.

Dr Marc Miravitlles and Prof. Shu Hashimoto held a lively pro-con debate on ACO – Is it real or imagined? No real consensus emerged, but everyone agreed individual patient management was the key.

A double session then followed on "Will emerging therapies realise their potential?", firstly looking at IPF and then at Immunotherapy and Biologics. With both areas currently the focus of much research and development, much discussion centred around the value proposition and important evidence gaps.

The keynote session was a lively debate on "e-cigarettes - a silver bullet or ticking time bomb?" The question centred on how far can we agree? Despite a spirited case put for e-cigarettes by Martin Dockrell from Public Health England, the REG answer was that more evidence is needed…. for now.

Joergen Vestbo and Guy Brusselle took the respective pro and con sides in a debate on Triple Therapy: To TT or Not to TT? As with ACO, the consensus at the end was for individual patient plans rather than a proscriptive solution.

The final session "What lies ahead... Will the flowers of innovation bloom or die?" was chaired by Omar Usmani, with contributions from Andrew McIvor, Walter Canonica and John Blakey, the session finished by discussing REG's role in guiding and shaping respiratory technologies.

Throughout the Summit, there were breakout presentations of the 20 abstracts submitted to the Summit. Copies of the original abstracts can be downloaded from http://images.nature.com/full/nature-assets/npjpcrm/abstracts/npjpcrm20179.pdf

The REG Summit is a vital part of the busy REG event calendar which demonstrates the strength of collaboration within the organisation. This was shown both in the results presented on active research projects and the number of research needs highlighted in the field of real-life respiratory research.

An example of this quality focus can be seen in the work of the joint REG / European Academy of Asthma and Clinical Immunology (EAACI) taskforce, formed in response to calls for a more integrated approach to evidence evaluation when developing guidelines.

Changes to REG's Structure

Over the past year, REG has continued to evolve its management structure. The members of the Executive Committee are all now Directors of REG, expanding our governance capabilities and two new directors, Alan Kaplan and Omar Usmani have been appointed. REG continues to work towards being registered for charitable status, and its 2017 accounts will be audited by Price Bailey as part of this process. Following this audit, an application to change status will be made to the Charity Commission. This registration will provide additional compliance oversight, in addition to the valuable work of our Oversight Committee. From a collaborator point of view, we will have to maintain up-to-date membership lists, which will be administered annually through our website.

Following the 2018 Summit, 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. and objectives and allows REG to remain agile and responsive to the most pressing research needs in the field of real-life respiratory research.

REG Directors

The current list of REG Directors is as follows:

- Antonio Anzueto, Pulmonary/Critical Care, University of Texas Health Science Center at San Antonio, USA
- Sinthia Bosnic-Anticevich, School of Medical Sciences, University of Sydney, Australia
- Walter Canonica, Chairman of Dept of Medical Specialties at the University Hospital S. Martino Genoa, Italy
- Alan Kaplan, Department of Family and Community Medicine, University of Toronto, Toronto, Ontario, Canada
- Nikos Papadopoulos, Professor of Allergy and Paediatric Allergy, University of Manchester, UK
- Nicolas Roche, Pneumologie et soins intensifs respiratoires, groupe hospitalier Cochin, Assistance publique-Hôpitaux de Paris, and Université Paris Descartes, France
- Omar Usmani, Reader in Respiratory Medicine and Consultant Physician at the National Heart and Lung Institute (NHLI), Imperial College London & Royal Brompton Hospital (RBH).

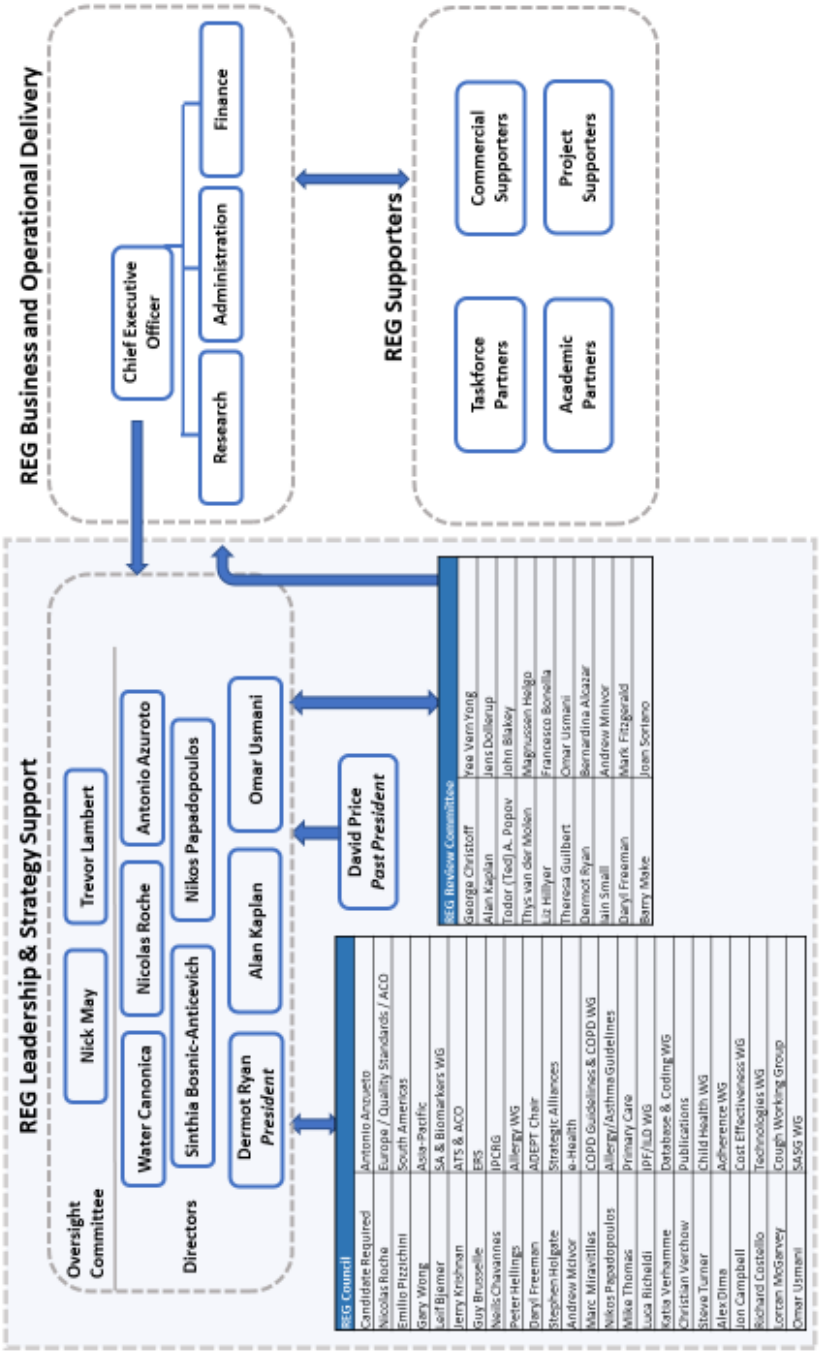
The Directors reflect the high calibre of our collaborators and offers wonderful clinical and research expertise with broad geographical reach:

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

The considerable interest and involvement we have had from supporters and collaborators alike in this important restructure of REG's governance holds great promise for REG's future success.

REG Council, Leads, Oversight and Executive Committees

We would like to thank the REG Council, the Oversight and Executive Committees and all our Collaborators who ensure REG continues to grow from strength to strength.



Thank You to our Supporters

We would like to extend sincere thanks to our supporters without whom REG's work would not be possible. Our activities are supported by three principle funding streams:

1. Core funding grants that enable us to undertake activities and to address research needs aligned with our central strategy as an independent research and advocacy group.

2. Working Group Grants that allow REG to undertake research aligned to the needs identified by a particular Working Group

3. Targeted project grants that allow our supporters to direct their support at specific activities proposed by REG collaborators; those that resonate with their own research priorities.

Together, these grants fund a portfolio of research that helps to:

- Develop new and strengthen existing research collaborations among our network of international experts;
- Address questions of "quality in real-life research"
- Improve understanding of current prescribing practices;
- Explore the safety and long-term implications of therapeutic interventions;
- Understand how to better target therapies to optimal effect;
- Understand the natural history of respiratory diseases and identify opportunities for earlier diagnosis, or predictors of future risk;
- Validate methodologies in real-life research;
- Test the external validity of RCT findings and generate hypotheses for future trial programs

Supporting REG through core and/or targeted grants not only helps to address these important research realities, but also:

Ensures quality and value of research - through our network of expert collaborators and links with global database and research organisations, REG can deliver high-quality research effectively, efficiently and cost-effectively. All research ideas stemming from (and funded through) the group are endorsed in terms of their clinical value by the best researchers in the field.

Underpins patient-centric care - by improving understanding of disease course and differential therapeutic outcomes across different patient groups, REG helps generate data that allows better targeting of available therapies.

Develops the research conversation - REG takes an inclusive approach, inviting input from a wide range of expert stakeholders (e.g. Industry, Medical, Academia, etc.). We work to defragment activity and build consensus approaches that will form a robust infrastructure for the rapidly-growing field of real-life research.

List of Supporters

Adelphi	Aerocrine	Astrazeneca
Boehringer Ingelheim	Chiesi	Cipla
Kyorin	Meda	Novartis
Optimum Patient Care	Observational Pragmatic Research Institute	Roche
Theravance	Three Lakes Partnership	

Projects Seeking Funding

Asthma-COPD Overlap: Comparability of Population Definitions within and between Global Databases

There is currently no standard definition for use in observational studies. This project will identify a number of possible definitions of ACO and explore the implications of these different "starting points" for observational ACO studies in terms of ACO prevalence within and between global databases.

Future phases of the work will characterise different potential population definitions and provide standard definitions and tools, to inform future ACO research.

Study Team

Study Co-Leads: Jerry Krishnan, Nicolas Roche:
Steering Committee
Alan Kaplan, Akki Niimi, Claus Vogelmeier, David Price, Dirkje Postma, Eric Bateman, Emilio Pizzichini, Eric van Ganse, Guy Brusselle, James Bailey, Janwillem Kocks, Job van Boven, Leif Bjermer, Marc Miravitlles, Mark Small, Miguel Roman, Richard Costello, Richard Martin, Ronald Dandurand, Victoria Carter
Budget: £120k (excluding any database costs)

Characterising the Asthma and COPD Overlap (ACO)

Following initial REG research to agree a consensus definition of ACO and given evolving knowledge around the risks of inhaled corticosteroid use; ACO patients require different management given the more severe patient outcomes than patients with COPD alone. The aim of this four-stage project is to produce a tool for primary care to help identify patients with ACO with the goal of optimising short and long term management.

1. Identify the prevalence and incidence of patients diagnosed as having ACO;
2. Identify the burden and cost of ACO compared with COPD and asthma populations;
3. Assess respiratory and cardiovascular outcomes in ACO, COPD, asthma treated with inhaled corticosteroids, inhaled corticosteroid/long acting beta agonists and long acting beta agonists alone;
4. Compare the characteristics in patients diagnosed with ACO to produce a tool for diagnosis.

Study Team

Primary Investigator: David Price, Nicolas Roche
Steering Committee
tbc
Budget: £160k

Deployment of Oscillometry in Community Practice and Validation in Healthy Controls

The aim of this project is to test the hypotheses that:

• Oscillometry is feasible to use in community practice;

• Using oscillometry will have a significant impact on the management of patients with asthma and COPD.

This proposed routine application of oscillometry to the entire practice would be a first in Canada and likely, in North America. This descriptive feasibility study has the potential to gather data that could justify larger randomized control or cross-over design pharmacology trials. The goal for the project is to:

• Better phenotype patients with established asthma and COPD in order to more personalize their pharmacologic treatment and in turn, improve their clinical outcomes, and;

• Effect early detection and disease prevention in those with pre -clinical obstructive lung disease both through the application of oscillometry in the community setting.

Study Team

Primary Investigator: Ronald J. Dandurand
Steering Committee
Rafel Bordas, Jean Bourbeau, Peter Calverley, Tomas Carroll, David H. Eidelman, Raul San Jose Estepar, Geoffrey Maksym, Paul O'Byrne, Omar Usmani
Budget: £110k

Standardization of Oscillometry Results Across All Five Commercially Marketed Devices: Proof of Concept Study

Oscillometry has the potential to change the way both asthma and COPD are currently treated by providing the information necessary to optimize inhaled drug airway deposition by matching drug particle size to size of obstructed airway. There are five commercial oscillometry devises on the market. While the principles behind each of these machines is the same, the details of how they generate the small subsonic pressure waves and process the collected data differs, and results in systematic differences between devices when measuring the same patient. This proof of concept study aims to:

• quantify the extent to which oscillometry results differ between devices; and

• develop a methodology to achieve an acceptable degree of reproducibility of all six oscillometry parameters when using any of the five commercial oscillometry machines.

Study Team

Primary Investigator: Jason Bates
Steering Committee: Ron Dandurand, Rafaelle Delle-ca, Guy Drapeau, Raul San Jose Estepar, Sebastien Jutras, Hajime Kurosawa, Larry Lands, Jean-Pierre Lavoie, Geoff Maksym, Paolo Paredi, Thomas Schuessler, Salman Sid-diqui, Omar Usmani, Simon Young, Zofia Zysman-Colman.
Budget: £140k

Development of a real-life respiratory database checklist - Towards Optimum Reporting of Pulmonary Effectiveness Databases and Outcomes (TOR-PEDO) a REG/UNLOCK initiative

The aim of the TORPEDO project is to support the development of a real-life respiratory database checklist to provide a strong foundation for future research. The first phase created a list with optimum variables for an ideal respiratory database from a Delphi study conducted with a carefully selected and well-balanced international expert panel (+/- 30 members) with expertise in one or more specific respiratory fields (asthma, allergy, COPD, IPF/ILD, primary care, health economics and/or databases) – initial results of this first phase will be presented at the REG Summit 2017.

A second phase providing recommendations for a minimum set of variables depending on specific disease and study design / aim. The final output in Phase III will be the provision of an inventory of respiratory databases around the globe, characterised by the TORPEDO-checklist to ease comparison and stimulate data merging as well as guide the design of new respiratory databases.

Study Team

Project Co-Leads: Job van Boven, Jon Campbell
Steering Committee
Katia Verhamme, Niels Chavannes, David Price,
Budget: £80 -100k

Implications of ICS Withdrawal in the Real-Life Management of COPD

Guidelines recommend the use of inhaled glucocorticosteroids (ICS) as maintenance treatment for patients with COPD. Recent evidence from a large (n=2485) ICS withdrawal trial— the Withdrawal of Inhaled Steroids during Optimized Broncho-dilator Management (WISDOM) trial—has cast some doubt on studies which have traditionally concluded that, once initiated, withdrawal of ICS therapy is associated with: an increase in exacerbations and symptoms, a reduction in health-related quality of life and an acceleration in lung function decline. The results of the WISDOM study, including the differential implications of gradual rather than acute withdrawal of ICS, warrant further investigation and their clinical interpretation would benefit from the availability of complementary evidence from a real-world study.

The aim of the study is to evaluate the effect of ICS withdrawal (evaluated as dose reduction and cessation) on real-world clinical outcomes in patients with confirmed COPD who are adherent to ICS therapy (medication possession ratio [MPR] ≥70%).

Study Team

Primary Investigator: Marc Miravitlles, David Price
Steering Committee
Marc Miravitlles, David Price, Helgo Magnussen, Dermot Ryan, Ronald Dandurand, Jens Dollerup, Alberto Papi, Nicolas Roche, Jennifer Quint, Therese Lapperre, Caroline Gouder, Richard Costello, Juan José Soler-Cataluña, Faisal Yunus, Bernardino Alcazar Navarrete, David Halpin, Akio Niimi,
Budget: £60-80k

Development of a Longitudinal Asthma Treatment Step Algorithm and Association with Asthma Outcomes

Based on asthma management guidelines (British Thoracic Society and Global Initiative for Asthma), the aim of this project is to develop pharmacy utilization treatment step algorithms using a quality controlled, primary care research data-base from the United Kingdom. The study will also examine longitudinal pharmacy utilization treatment step patterns and associate them with patient characteristics.

From this, it will be possible to characterize patients within a large-scale primary care research database in terms of their asthma management guideline-based treatment step, track how patients' treatment steps change over time, and relate treatment steps and changes to various patient characteristics.

A second phase of the project will compare asthma outcomes by treatment step utilization patterns within age categories. This will allow the team to test for differences in the likelihood of achieving

asthma control and the risk of exacerbation by commonly observed treatment step patterns, adjusting for differences in patient characteristics across patterns.

Study Team

Primary Investigator: Jonathan Campbell
Steering Committee
Alexandra Dima
Budget: £80k

Development and Database Validation of a Small Item set COPD Management Tool (EX-ACT-S) for Potential use in Telehealth

Through analysis of existing datasets utilising the EXerbAtions of Chronic Pulmonary Disease Tool (EXACT), to develop a reduced (approximately five-item) questionnaire that is sufficiently sensitive and specific to be a practical clinical tool for identifying the onset of exacerbations of chronic obstructive pulmonary disease (COPD).

The aim of the project is to use an existing EXACT database to develop a reduced (approximately five-item) questionnaire that is sufficiently sensitive and specific to be a practical clinical tool for identifying the onset of exacerbations of chronic obstructive pulmonary disease (COPD), and to validate the instrument in a second database.

Study Team

Primary Investigator:
EXACT-S Steering Committee
Paul Jones, Dermot Ryan, Hilary Pinnock, Nancy Leidy
Budget: £140k

Patients Hospitalised for Asthma: Characteristics and Disease Management

Hospitalizations remain a major issue in asthma management given their detrimental consequences for patients and their induced societal costs. Characteristics of hospitalizations and identification of specific profiles of admitted patients are poorly documented. A historical dynamic cohort will be conducted using French claims data. Twelve months of management will be investigated before index hospitalization.

The main objective of the project is to describe asthma-related hospitalizations, and primary care management in the 12 months before admission. The study will consider patient baseline characteristics and their reimbursed medical resource utilisation in the 12 preceding months. These data will be of interest for prevention, in view of optimizing asthma management.

Study Team

Study Co-Leads: Nicolas Roche, Alexandra Dima
Steering Committee
Eric Van Ganse, Laurent Laforest, Marine Ginoux, Sandrine Herbage, Manon Belhassen
Budget: £120k

Exhaled Breath Temperature (EBT) in Obstructive Lung Diseases Monitoring

The X-halo Home EBT monitor is designed for individual daily use, operates through an app on smartphones and tablets, provides the measurement results within less than 10 breaths, draws a chart

with the measured values positioned on a floating average of 10 days with calculated green, yellow and green zones based on standard deviations. It also documents information on asthma control, and prescribed treatment. The data can be uploaded on a specialized site and transmitted to the treating physician at the discretion of the patients. The aim of this project is to assess the ability of X-halo Home to differentiate / characterize different airway obstructive states. The hypothesis is that EBT decreases over the Asthma - COPD spectrum in stable disease proportional to the reduction of the airways vascular bed. However, fluctuations in diseases activity over time will be different between the two extremes (Asthma & COPD) in terms of variability of the daily measurements (similar to peak expiratory flow (PEF)-metry) and during exacerbations; intermediate group(s) of patients may shape up corresponding to intermediate (ACOS) phenotype(s). This project will consider whether daily measurement of EBT under standardized ICS-LABA treatment will help to identify intermediate phenotypes along the asthma – COPD spectrum.

Study Team

Primary Investigator: Todor Popov
Steering Committee
tbc
Budget: £140-£160k

Claims-based Validation of a UK COPD Clinical Risk Prediction Model

Multidimensional tools and indices do exist in COPD to assess the severity and/or risk of future exacerbations, but they typically draw on data that are not collected in routine care and so cannot be easily operationalized in community-based COPD. REG has developed a risk pre-diction tool using routinely collected primary care data from the UK to identify patients at increased risk of multiple COPD exacerbations. This study aims to:

1) Develop an equivalent model using administrative insurance claims data to identify patients at increased risk of multiple COPD exacerbations.

2) Test the external validity of the UK model by seeking to validate it in a non-UK (claims-based) healthcare setting.

Study Team

Primary Investigator: Daryl Freeman
Steering Committee
David Price, Richard Martin, Barry Make, Marjan Kerkhof, Mark Fitzgerald, Mohsen Sadatsafavi
Budget: £80-100k

Implications of Diagnosing Comorbid Obstructive Sleep Apnoea (OSA) on Asthma Control

The aim of this study is to evaluate the impact on asthma control of receiving a diagnosis (and treatment) for obstructive sleep apnoea (OSA).

Study Design:

- 1 year of baseline characterisation data before OSA diagnosis
- 1 outcome year post diagnosis
- Index date = date of OSA diagnosis

There are a range of options for analysis, including:

• Compare outcomes in patients pre / post diagnosis
• Quantifying the Scale of Undiagnosed
• Obstructive Sleep Apnoea (OSA)

There is also the potential for secondary analysis considering patients with OSA diagnosis at index date and CPAP prescribed.

Study Team

Primary Investigator: Mihaela Stefan
Steering Committee tbc
Budget: £50-60k

Quantifying the Scale of Undiagnosed Obstructive Sleep Apnoea (OSA)

OSA is grossly under-diagnosed in Primary Care with potentially important consequences. A further challenge is that diagnosis is open to "patient manipulation", e.g. potential to lie during screening for OSA. In the UK, there is an opportunity to work with dentists who have a low-tech alternative to CPAP and to set up an out of hospital services. The aim of this study is to quantify the likely burden/prevalence of OSA compared with the diagnosed burden/prevalence (i.e. quantify the scale of undiagnosed OSA). The study will evaluate the "true" burden based on known features, e.g. BMI >40, neck circumference, hypertension, etc. It will also compare "true prevalence" with "diagnosed prevalence".

Study Team

Primary Investigator: Mihaela Stefan
Steering Committee tbc
Budget: £50-60k

Steroid Sparing – quantification of oral steroid burden (focus on atopic dermatitis)

This study addresses the need to quantify the burden of cumulative steroid exposure in atopic dermatitis ± obstructive airways disease. The primary objective of the study will be to quantify the burden of maintenance steroid use and potential benefits of steroid sparing. However, prior work by REG's Small Airways Study Group also suggests that it is the total steroid exposure (cumulative dose over time) is of key concern and has metabolic implications over time. The study will examine atopic dermatitis ± asthma ± rhinitis

Study Team

Primary Investigator: David Price
Steering Committee tbc
Budget: £120-140k

Cost Implications of Oral Steroid Comorbidities

The biologics for severe asthma are having to meet increasingly high barriers to gain market access (e.g. ≥4 courses of oral steroids required before patients be-come eligible for mepo).

Sweeney et al (Thorax. 2016;71(4):339-46. Comorbidity in severe asthma requiring systemic corticosteroid therapy: cross-sectional data from the Optimum Patient Care Research Database and the British Thoracic Difficult Asthma Registry) quantified the burden of potential steroid comorbidities

in severe asthma in terms of prevalence but to date no "price tag" has been put on the cost of steroid comorbidities in severe asthma

The aim of this project is to model the cost implications of 1-2 of the most common comorbidities identified by Sweeney et al (e.g. diabetes) and develop disease models with a view to then licensing out the use of these models for a usage.

Study Team

Study Co-Leads: Jon Campbell
Steering Committee tbc
Budget: £80-100k

Validation of the REG Asthma Risk Prediction Tool

The aim of this project is to validate the REG Asthma Risk Prediction tool, which uses routine care records to predict risk of frequent (≥2 and ≥4 asthma exacerbations in a 2-year follow-up period).

The validation work would include:

- Application to CPRD (or another UK database, e.g. THIN) to secure a database to validate the OPCRD model
- Validation of the risk prediction tool in a claims database
- Address the canalisation question
- A cluster analysis to assess consistency of predictors across databases

The aim is to convert the analysis to a risk model using regression equations; one option is to develop a tool that includes all the variables that could sit within a GP system and function as a decision support tool. There is also an opportunity to item-reduce the tool to make it more practical for real-world (and patient) use; in this case the optimal risk tool will be the fewest questions that still achieve strong predictive power.

Study Team

Study Co-Leads: John Blakey, Borislav Dimitriov, Mike Thomas
Steering Committee tbc
Budget: £120-140k (excluding any data costs)

Supporting Upcoming REG Projects

The continued success and impact of REG depends on the continued backing of our supporters. If you are interested in supporting any REG projects, you can work with us either as a co-supporter with other partners or select a project as an exclusive supporter.

REG also provides an option to offer a core grant, which is then distributed across the projects according to research needs and priorities as assessed by our global team of research experts.

If you would like further details on any of these projects, or have a study you would like to propose, please contact us at enquiries@effectivenesevaluation.org.

Appendices

Appendix 1: REG Collaborators

REG brings together over 300 Collaborators from more than 40 countries.

A Del Cuvillo, Spain
Aileen David-Wang, Philippines
Aji Barot, UK
Akki Niimi, Japan
Alan Kaplan, Canada
Alberto Papi, Italy
Alex Dima, France
Alexander V Emelyanov, Russia
Alexandru Corlateanu, USA
Alison Chisholm, UK
Allan Becker, Canada
Allan J Walkey, USA
Alvar Agusti, Spain
Alvaro Cruz, Brazil
Amnon Ariel, Israel
Anders Løkke, Denmark
Andrew McIvor, Canada
Andrew Menzies-Gow, UK
Andrew Wilson, UK
Anne Brunton, UK
Anthony Yii, Singapore
Antonella Muraro, Italy
Antonio Anzueto, USA
Arata Azuma, Japan
Athol U. Wells, UK
Audrey Dunn Galvin, Ireland
Bandana Saini, Australia
Barry J. Make, USA
Bassam Mahbob, Dubai
Bernard Vrijens, Belgium
Bernardino Alcazar Navarrete, Spain
Bjorn Stallberg, Sweden
Boris Klanger, Sweden
Brett McQueen, USA
Brian Casserly, Ireland
Brian Lipworth, UK
Bruno Crestani, France
Camilo Roa, Philippines
Carlo Vancheri, Italy
Carole Youakim, Lebanon
Caroline Gouder, Malta
Chantal Raherison-Semjen, France
Chen Wang, China
Chin Kook Rhee, South Korea
Chris Brightling, UK
Chris Burton, UK
Chris Goss, USA
Christer Janson, Sweden
Christine Jenkins, Australia
Christopher Ryerson, Canada
Chunxue Bai, China
Ciaran O'Neill, Ireland
Claire Hopkins, UK
Clare Murray, UK
Claudia Valenzuela, Spain
Claus Bachert, Belgium
Claus Vogelmeier, Germany
Cristina Esquinas Lopez, France
Cynthia Rand, USA
Daryl Freeman, UK
David Costa, France
David Halpin, UK
David Hui, Hong Kong
David Price, Singapore
Demosthenes Bouros, Greece
Dermot Nolan, UK
Dermot Ryan, UK
Diahn-Warng (Steve) Perng, Taiwan
Diana Church, UK
Dmitry Nonikov, Russia
Don Sin, Canada
Dragos Bumbacea, Romania
Eli Meltzer, USA
Elizabeth Hillyer, USA
Elizabeth Kern, USA
Elizabeth Regan, USA
Ellen Koster, Netherlands
Elliot Israel, USA
Emilio Pizzichini, Brazil
Eric Bateman, South Africa
Eric van Ganse, France
Erkka Valovirta, Finland
Erlina Burhan, Indonesia
Eugene Bleecker, USA
Fabrizio Luppi, Italy
Faisal Yunus, Indonesia
Federico Lavorini, Italy
Fernando J. Martinez, USA
Ferran Morell, Spain
Francesco Bonella, Germany
Francine Ducharme, Canada
Frank Accurso, USA
Fulvio Braido, Italy
Ganesh Raghu, USA
Gary Wong, Hong Kong
Gene Colice, USA
George Christoff, Bulgaria
Gianenrico Senna, Italy
Giorgio Piacentini, Italy
Giovanni Ferrara, Sweden
Gisli Jenkins, UK
Glenis Scadding, UK
Glenn Crater, USA
Göran Eriksson, Sweden
Grace Lomax, UK
Guy Brusselle, Belgium
Hae-Sim Park, South Korea
Harold Collard, USA
Helen Reddel, Australia
Helgo Magnussen, Germany
Henry Chrystyn, UK
Hilary Pinnock, UK
Hironori Sagara, Japan
Holbrook, Janet, USA
Hye Yun Park, South Korea
Iain Small, UK
Ian Glaspole, Australia
Ian Pavord, UK
Isao Kamae, Japan
J Christian Virchow, Germany
Jacqui Brereton, UK
Jaime C Sousa, Portugal
James Paton, UK
Janwillem Kocks, Netherlands
Jean Bourbeau, Canada
Jean Bousquet, France
Jeff Myers, USA
Jennifer Quint, UK
Jens Dollerup, Denmark
Jens Søndergaard, Denmark
Jerry Krishnan, USA
Joan B Soriano, Spain
Joan Sweeney, UK
Joaquim Mullol, Spain
Joaquin Sastre, Spain
Job van Boven, Netherlands
Joergen Vestbo, Denmark
John Blakey, UK
John Fenton, UK
John Haughney, UK
Jon Campbell, USA
Jonathan Grigg, UK
Jörg D. Leuppi, Switzerland
Juan José Soler, Spain
Juan Luis Garcia Rivero, Spain
Judith Garcia-Aymerich, Spain
Juliet Foster, Australia

Julio Ancochea, Spain
Jürgen Behr, Germany
Justus Dezeeuw, Germany
Kaissa DeBoer, USA
Karen Ward, UK
Karin Lisspers, Sweden
Katerina Antoniou, Greece
Katia Verhamme, Netherlands
Ken Ohta, Japan
Kevin Brown, USA
Kevin Flaherty, USA
Kevin Gruffydd-Jones, UK
Kirsten Beyer, Germany
Kjell Alving, Sweden
Klaus Rabe, Germany
Koichiro Kamio, Japan
Konstantinos Kostikas, Greece
Lara Fairall, South Africa
Lars-Olaf Cardell, Sweden
Le Thi Tuyet Lan, Vietnam
Leif Bjermer, Sweden
Len Bacharier, USA
Liam Chong Kin, Malaysia
Liam Heaney, UK
Louis-Philippe Boulet, Canada
Luca Richeldi, Italy
Ludger Klimek, Germany
Luke Barry, Ireland
Lynn Josephs, UK
Maarten Van Den Berge, Netherlands
Magnus Skold, Sweden
Magnus Wickman, Sweden
Manon Belhassen, France
Manuela Funke-Chambour, Switzerland
Marc Miravitlles, Spain
Marcia Pizzichini, Brazil
Marcia Vervloet, Netherlands
Margaret Williamson, Australia
Maria Molina, Spain
Maria Ospina, Canada
Mariano Mazzei, Argentina
Marijn de Bruin, UK
Mariko Koh Siyue, Singapore
Mark Fitzgerald, Canada
Martin K Church, UK
Martin Kolb, Canada
Massimo Triggiani, Italy
MD Ibanez, USA
Michael Keane, Ireland
Michael Kreuter, Germany
Michelle Nuttal Eakin, USA
Miguel Román Rodríguez, Spain
Mihaela S Stefan, USA
Mike Thomas, UK
Ming-Cheng Chan, Taiwan
Miriam Barrecheguren Fernandez, France
Mohammad Osman Yusuf, Pakistan
Mohsen Satafadasavi, Canada
Moises Selman, Mexico
Mona Bafadhel, UK
Mónica Monteagudo, Spain
Myrna Dolovich, Canada
N S Zhong, China
Neil Kendle, UK
Nemr Eid, USA
Nick May, UK
Nicolas Roche, France
Niels Chavannes, Netherlands
Nikos Papadopoulos, Greece
Nina Castillo-Carandang, Philippines
Omar Usmani, UK
Paola Rottoli, Italy
Pascal Chanez, France
Pascal Demoly, France
Patrick Flume, USA
Patrick Soverein, Netherlands
Pete Smith, Australia
Peter Barnes, UK
Peter Calverley, UK
Peter Hellings, Belgium
Peter Lange, Denmark
Phil Lieberman, USA
Piyameth (Ning) Dilokthornsakul, Thailand
Rachel Jordan, UK
Ralph Mosges, Germany
Randall Brown, USA
Ratko Djukanovic, UK
Renaud Louis, Belgium
Richard Costello, Ireland
Richard Harvey, Australia
Richard Iles, UK
Richard Martin, USA
Richard Russell, UK
Robert Lemanske, USA
Robert Wise, USA
Rohit Katial, USA
Roland Buhl, Germany
Ronald Dahl, Denmark
Ronald Dandurand, Canada
Ruby Pawankar, Japan
Rupert Jones, UK
Sakae Homma, Japan
Sam Sonnappa, India
Samantha Walker, UK
Samy Suissa, Canada
Sang-Heon Cho, South Korea
Scott Sagel, USA
Sean Higgins, Ireland
Serg Avdeev, Russia
Shigeo Muro, Japan
Simon Carney, Australia
Simon Walsh, UK
Sally Singh , UK
Sinthia Bosnic Anticevich, Australia
Sita Andarini, Indonesia
Soko Setoguchi-iwata, USA
Sonia Buist, USA
Stan Szefler, USA
Stefano Graziadei, UK
Stephen Holgate, UK
Stephen Peters, USA
Stephen Turner, UK
Steve Montefort, Malta
Steven Nathan, USA
Sundeep Salvi, India
Tamera Corte, Australia
Tan Tze Lee, Singapore
Teoh Oon Hoe, Singapore
Thao Le, Australia
Theresa Guilbert, USA
Therese Sophie Lapperre Stevens, Singapore
Thomas Geiser, Switzerland
Thys van der Molen, Netherlands
Tjard Schermer, Netherlands
Toby Maher, UK
Todor Popov, Bulgaria
Tony D'Urzo, Canada
Torsten Zuberbier, Germany
Trevor Lambert, UK
Triya Damayanti, Indonesia
Ulrich Costabel, Germany
Vibeke Backer, Denmark
Victoria Carter, UK
Vincent Cottin, France
Walter Canonica, Italy
Wanda Phipatanakul, USA
Warner Carr, USA
William (Bill) Busse, USA
Wim van Aalderen, Netherlands
Wytske Fokkens, Netherlands
Yee Vern Yong, Malaysia
Zafar Zafari, Canada
Zhong Nanshan, China
Zuzana Diamant, Sweden

Appendix 2: Financial Summary

Profit & Loss		
Respiratory Effectiveness Ltd Trading as REG [Respiratory Effectiveness Group]		
1 January 2017 to 31 December 2017		
	31 Dec 17	**31 Dec 16**
Income		
Restricted Income	£287,988.30	£463,863.49
Unrestricted income	£127,688.92	£253,137.83
Total Income	**£415,677.22**	**£717,001.32**
Less Cost of Sales		
Research Costs	£202,729.09	£449,492.04
Summit Costs	£80,461.92	£67,760.54
Total restricted costs	**£283,191.01**	**£517,252.58**
Administrative costs	£126,369.75	£194,234.52
Total Cost of Sales	**£409,560.76**	**£711,487.10**
Net Profit	**£6,116.46**	**£5,514.22**

Balance Sheet		
Respiratory Effectiveness Ltd Trading as REG [Respiratory Effectiveness Group]		
As at 31 December 2017		
	31 Dec 2017	**31 Dec 2016**
Assets		
Bank		
BARC EUR	£2,247.09	£54,204.19
BARC GBP	£62,691.00	£19,151.66
BARC USD	£41,269.33	£193,466.02
PYPL USD	£0.00	£584.21
Total Bank	**£106,207.42**	**£267,406.08**
Current Assets		
Accounts Receivable	£226,561.29	£179,995.84
Loans	£0.00	£14,085.81
Prepayments	£51,197.66	£16,709.05
Total Current Assets	**£277,758.95**	**£210,790.70**
Fixed Assets		
Office Equipment - accumulated depreciation	-£62.69	£0.00
Office Equipment - at cost	£586.33	£0.00
Total Fixed Assets	**£523.64**	**£0.00**
Total Assets	**£384,490.01**	**£478,196.78**
Liabilities		
Current Liabilities		
Accounts Payable	£55,777.38	£84,957.25
Accruals	£4,250.00	£2,818.55
Deferred Revenue	£307,586.85	£377,652.77
PAYE & NIC Control	£2,822.19	£0.00
Pension Fund	£124.15	£0.00
REG Barclaycard	£112.29	£0.00
VAT Control	£2,853.23	£5,708.20
Total Current Liabilities	**£373,526.09**	**£471,136.77**
Total Liabilities	**£373,526.09**	**£471,136.77**
Net Assets	**£10,963.92**	**£7,060.01**
Equity		
Accumulated Surplus	£4,847.45	£1,161.28
Current Year Earnings	£6,116.46	£5,898.73
Total Equity	**£10,963.91**	**£7,060.01**