ADVANCES IN... REAL-LIFE RESPIRATORY MEDICINE

The Respiratory Effectiveness Group Newsletter: Spring 2013 – New Beginnings

Welcome and introduction

Edinburgh's famous New Year fireworks!

Welcome to 2013 and to the first issue of ***Advances in Real-life Respiratory Medicine*** – the newsletter of the **Respiratory Effectiveness Group** (**REG**).

The aim of this quarterly newsletter is to keep everyone who is part of REG, (or interested in our work) a quick update of our current and future activities.

The newsletter will be emailed to all members and also posted on our website (to be launched Jan/Feb 2013): **www.effectivenessevaluation.org**

Please send the newsletter on to any colleagues or friends you think may be interested, and please contact, Alison Chisholm (REG Implementation Manager) if:

- You're interested in **collaborating** on any of the current, or planned activities
- Your have any **comments and suggestions** – on the newsletter and/or activities for the group
- You're not a member, but are be interested in getting involved.

Email:
alison@effectivenessevaluation.org

Who is the Respiratory Effectiveness Group and what are we trying to achieve?

David Price, REG founding member and Professor of Primary Care Respiratory Medicine at The University of Aberdeen

Classical randomised controlled trials (RCTs) have long been considered the gold standard in evaluating the safety and efficacy of new therapies. Their position at the core of the evidence base and necessity for drug licensing is without doubt, but there are limitations to what a RCT can tell you about treating real patients in routine care.

Classical RCTs are designed to identify clear cause-and-effect between an intervention and an outcome. As such, they involve tightly-controlled, well-characterised patient populations so as to minimise confounders and avoid loose causality relationships. Yet the resultant highly-characterised population included in RCTs represents only a subgroup of the broadly heterogeneous respiratory patient population treated in everyday clinical practice. Thus, the extent to which RCT efficacy can be accurately extrapolated to reflect long-term effectiveness of respiratory therapies (in diverse, chronic patient populations) is limited.

Real respiratory patients are not optimally adherent to their medication; nor are they all nonsmokers of normal weight and aged between 18-60 years. Seldom do they fall within RCT lung function and reversibility criteria, or manage to perform perfect, consistent inhaler manoeuvres. Indeed, frequently they have comorbid conditions and challenging lifestyles that can exacerbate their respiratory condition, and/or lead to poly-pharmacy challenges, and more.

While RCTs evaluate a treatment's **efficacy** (i.e. its ability to achieve a beneficial effect under highly favourable circumstances), real-life studies evaluate **effectiveness** — a treatment's ability to improve patient outcomes in the gamut of patients treated in routine care across a wide spectrum of practice settings (see **p4** for a further exploration of these definitions).

In recent years there has been growing recognition of the need to look beyond RCTs, and to real-life data, when appraising the full clinical evidence base.

Through international collaboration, REG aims to take the field of real-life respiratory research to the next level.

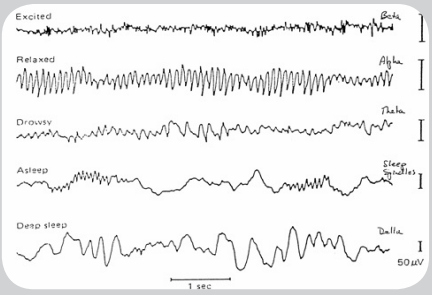
ERS Session Proposal

ERS hot-topic submission

REG has submitted a real-life themed Hot Topic session proposal for this year's European Resipratory Society (ERS) annual congress. The congress would provide a great platform to present and discuss the important issues in real-life respiratory research.

We should know by February if the proposal has been accepted.

What's in a name...?



How EEG became REG ?

The Effectiveness Evaluation Group seemed like the perfect name for the research initiative, but then... Find out more on **page 3.**

NEW BEGINNINGS...

Membership of the Respiratory Effectiveness Group

Who else is part of the initiative and what does it mean...?

Central to the success of the Respiratory Effectiveness Group is the quality of our members. Every member of the group is an expert in some area of respiratory medicine and has either show a past interest in real-life and health outcomes research, or has indicated an interest in finding out more about the field.

The positive response to REG has been overwhelming. Almost a 100% of invitations to join the initiative have been accepted and we hope this reflects the growing interest in real-life research and the timeliness of the initiative.

A founding principle of REG is that it will be owned and run by its members. The work we undertake will be the work our members feel is of greatest value to the field. We welcome suggestions from you all for: **studies**, **communication opportunities**, **educational activities**, and **anything else** you think could be a valuable use of the group's expertise and resource. The influence and credibility of the initiative will depend on your quality insights to make sure REG's work:

- Improves the profile and quality of real-life research
- Sets standards to encourage quality among others working in this field
- Effectively communicates the value of real-life data, and
- Improves understanding of how real-life data should be used to inform guidelines, clinical practice, licensing and safety monitoring.

Management Group	Affiliation
David Price (Founder)	**University of Aberdeen, UK**
Leif Bjermer	Lund University, Sweden
Guy Brusselle	Ghent University Hospital, Belgium
Jon Campbell	University of Colorado, USA
Stephen Holgate	University of Southampton, UK
Elliot Israel	Brigham and Woman's Hospital, Harvard, USA
Jerry Krishnan	University of Illinois, USA
Richard Martin	National Jewish, USA
Andrew McIvor	McMaster University, Canada
Marc Miravitlles	Hospital Universitari Vall d'Hebron, Barcelona, Spain
Nikos Papadopoulos	University of Athens, Greece
Alberto Papi	University of Ferrara, Italy
Nicolas Roche	Hôtel-Dieu, Paris, France
J. Christian Virchow	University Clinic Rostock, Germany
Gary Wong	Chinese University of Hong Kong, Hong Kong

The Management Group have been nominated so ensure there is a small proactive and responsive core group who will set REG's overall strategy

Steering Committee	
Alvar Agusti, Spain	Ian Pavord, UK
Antonio Anzueto, USA	Hilary Pinnock, UK
Viebeke Backer, Denmark	Theodore Popov, Greece
Peter Barnes, UK	Dirkje Postma, Netherlands
Eric Bateman, South Africa	Malcolm Sears, Canada
Synthia Bosnic-Anticevich, Australia	Ian Small, UK
Andrew Briggs, UK	Joan Soriano, Spain
Chris Brightling, UK	Helen Reddel, Australia
Peter Calverley, UK	Miguel Román Rodríguez, Spain
Henry Chrystyn, UK	Dermot Ryan, UK
Gene Colice, USA	Björn Ställberg, Sweden
Daryl Freeman, UK	Stan Szefler, USA
Andy Griggs, UK	Michael Thomas, UK
Kevin Gryffudd-Jones, UK	Stephen Turner, UK
John Haughney, UK	Omar Usmani, UK
Federico Lavorini, Italy	Wim van Aaldern, Netherlands
Karin Lisspers, Sweden	Joan Soriano, Spain
Thys van der Molen, Netherlands	Claus Vogelmeier, Germany
Teoh Oon Hoe, Singapore	

The Steering Committee has been selected for their expertise and interest in real-life research and "subteams" will collaborate on different REG activities. Study and activity suggestions are encouraged from all.

To ensure the group is dynamic and proactive we've appointed a Management Group, led by our founding member **David Price**. The Management Group will set the agenda and lead on the overall strategy for the group but all members will share in the work of the group. Everyone who contributes their time and efforts to REG will be recognised as **authors of that work.**

If you have any questions about membership or any colleagues you'd like to recommend as additional members, please contact Alison Chisholm, REG Implementation Manager: **alison@effectivenessevaluation.org**

Membership benefits

Members enjoy being part of a group that will help lead, shape and direct real-life research, but what else...?

Each year, REG will undertake a series of studies selected by the Management Group from a selection of suggestions put forward by the wider REG membership.

Aside from these core studies, all REG members will be given access to the **Optimum Patient Care Research Database** (see **p3**) to pursue their own research questions, either within their current research groups, or in collaboration with other REG members. OPCRD is approved for medical research subject to the Annonymised Data Ethics

NEW BEGINNINGS...

Page 2 continued...

Protocols and Transparency (ADEPT) Committee approving that an intended study is clinically valuable and well designed. If you'd like to apply for an OPCRD datacut, please submit your protocol to **Alison Chisholm** (alison@effectivenessevaluation.org) who will oversee the ADEPT approval process.

REG will help to disseminate the results of studies undertaken by its members as part of the initiative.

Optimum Patient Care Research Database

Find out more about the database at your disposal

The **Optimum Patient Care Research Database** (**OPCRD**) has been developed by Optimum Patient Care (OPC) — a social enterprise that offers free respiratory service evaluations to primary care practices. The service evaluation involves a thorough appraisal of patients' **electronic medical records** (EMRs) and associated **patient reported outcomes** (PROs) (captured through OPC's disease-specific) questionnaires. Each patient's PROs are anonymously cross-matched to their EMRs using unique patient identifiers, automatically assigned at the point of EMR extraction.

The OPC service evaluation offers participating practices patient-level and practice-level reports that characterise patients and practice populations in terms of current disease management and future risk. The reports also include clinical suggestions (in line with guideline recommendations) that may help to optimise patient outcomes and better to target practices' resource.

The EMRs and PROs captured through the OPC service evaluation are pooled within the OPC Research Database (OPCRD). The database is growing daily, but currently contains records from **over 300 (primarily UK) practices**. It has received **ethical approval** for use in medical research and has been used for academic research, Industry-funded research and also by the UK's Department of Health.

Visit: **www.optimumpatientcare.org**

What's in a name...?

Introducing the **"The Respiratory Effectiveness Group"**
(...formerly the Effectiveness Evaluations Group... EEG)

Shakespeare's Juliet declared that: "A rose by any other name would smell as sweet". She was trying to convince Romeo that their names (and feuding families) were of no consequence.

She was wrong. Names can be rather contentious things, or so we've been finding out…

The Effectiveness Evaluation Group seemed like the sort of name that would give our real-life endeavours gravitas, that would differentiate our research from trial-bound efficacy studies and reflect the group's research-driven nature. Or so we thought.

It was all going so well until the inevitable abbreviation of the name crept in. The Effectiveness Evaluation Group quickly turned into **E-E-G**... then into EEG... and then...confusion and consternation! EEG has been the shorthand for electroencephalogram since the technology was first used to map the electrical activity of the human mind in 1924, as you well know.

With the non-respiratory connotations of EEG numerous and the potential for confusion around the name ample, rumblings of dissent broke out among the Management Group.

The Group also felt the initiative's name should reflect its members' field of expertise – **respiratory medicine**. Respiratory is the ideal speciality to spearhead a more general real-life initiative. Respiratory populations, after all, are typically made up of widely heterogeneous patients,

often with comorbidities that may affect treatment outcomes, have to deal with inhaler technologies to administer their treatment and often face long-term disease management. Indeed respiratory medicine arguably presents the "**perfect real-life storm**" through its union of drug; technology; heterogeneous patients and long-term data requirements.

In light of these comments, we have decided to "re-christen" the initiative; it is now called **The Respiratory Effectiveness Group**. If the initiative extends to other specialities in the future, the "Respiratory" specification can simply be dropped, and the more generic "The Effectiveness Group" used instead.

For now, we hope the re-naming aids clarity and, importantly, avoids confusion.

What's everyone else saying...?

Quotations from some of (respiratory) medicine's great and good

- "' Real-world studies should be funded and results used to inform guidelines." (The Brussels' Declaration. Holgate S, et al. *Eur Respir J.* 2008;32:1433–42)
- "Hierarchies place RCTs on an undeserved pedestal... [they] should be replaced by accepting – indeed embracing – a diversity of approaches... avoid adopting entrenched positions about the nature of evidence... the interpretation of evidence requires judgement." (Sir Michael Rawlins, *Harveian Oration*, 2008)
- Asthma control should be evaluated using composite measures and validated in both clinical trials and in: "large, prospective studies in 'real-world' settings ...to ensure they provide content validity as well as reflect clinically meaningful outcomes." (ATS/ERS Taskforce. *Am J Respir Crit Care Med*. 2009;180:59–99)
- "A combination of observational studies, pragmatic trials and RCTs should be used because all have advantages and drawbacks and each is designed to answer a different question." (ARIA and GA2LEN. *Allergy*. 2010;65:1212–21).

NEW BEGINNINGS...

Defining a common language

You say tomato; I say tomato; You say "comparative effectiveness", I say "real-life…"

REG plans to improve clarity around various aspects of real-life research through validating methodologies and endpoints; setting standards, and working towards a unified approach to real-life research.

In a similar vein, we'd like to use a few inches of this first newsletter to offer clarity around some of the terminology used in real-life research.

The following "definitions" are largely based on (although slightly adapted from) a very useful publication from the Lung Diseases Division of the National Heart, Lung, and Blood Institute (NHLBI) – the output of one of the group's workshops. The full paper citation is: Lieu TA, et al. *Am J Respir Crit Care Med*. 2011; 184: 848–856.

Efficacy: the efficacy of a treatment refers to its ability to improve patient outcomes in a population likely to respond to the treatment, with strict adherence to the treatment protocol, in specialised centers and with highly motivated providers seeking to answer the question:
"Can this intervention achieve a beneficial effect under highly favourable circumstances?"

Effectiveness: the effectiveness of a treatment refers to its ability to improve patient outcomes in the gamut of patients treated in routine care, in real-world settings – a far more heterogeneous population than the RCT population, with a the normal spectrum of disease, comorbid illness, ethnicity, and/or age, with average compliance with treatment protocols and medications, and/or in a wider spectrum of practice settings.

Real-life data: some argue that all patient data is real-life because it comes from real patients, but the terms real-life, or real-world (the two are interchangeable), typically refer to the continuum of data collected in naturalistic settings, outside the tightly-controlled RCT environment.

Real patients are not a homogeneous group, they are a widely varying group of individuals with different disease severities and individual characteristics that can affect treatment effectiveness

Comparative Effectiveness: the terms "**comparative effectiveness**" and "**relative effectiveness**" are interchangeable, the first is more common in the US; the second more so in Europe.

Comparative Effectiveness Research lies within the continuum of effectiveness research and is particular to the study of **two or more interventions** using a variety of study designs, which allows comparative evaluation of the effectiveness of these interventions in real-world settings, for diverse patient populations and subgroups, assessing a full range of outcomes.

Not all effectiveness research is ***comparative effectiveness research***. An RCT conducted in real-life conditions that compares a medication to placebo may constitute effectiveness research, but not ***comparative effectiveness***.

Comparative effectiveness research must:

1. Compare interventions or implementation strategies in real-world settings
2. Assess a comprehensive array of health-related outcomes
3. Include diverse patient populations and attention to important subgroups
4. Use a variety of observational or experimental methods.

New beginnings

Starting 2013 with a new logo and a new website!

REG's now has a logo (see right) and our website (**www.effectivenessevaluation.org**) will be launched in early 2013!

The website will develop over time, but we want it to become a central repository for information about real-life respiratory research. You'll be alerted when it goes live in the next few weeks and we'll welcome your comments and suggestions to make sure it's a really valuable resource that offers information about REG activities; links to useful real-life assessment tools; presentation materials and much more.

Logo explained: the linked curves capture our ethos of collaboration and the shape repetition reflects the principle of mirroring real-life conditions in research

Submit your real-life research ideas today:
Email Alison Chisholm at: alison@effectivenessevaluation.org