

Editorial

TRACE launch

TRACE (Translational Research on Antimicrobial resistance and Community-acquired infections in Europe) was launched on Thursday June 16 2011, in Antwerp, supported by the European Science Foundation (ESF), 17 GRACE (www.grace-irti.org) and 5 other partners. This Research Networking Programme (RNP) will receive more than the 600,000 Euros originally budgeted and has funding until 2016. TRACE aims to consolidate the expertise integrated in several research programmes, in particular within the GRACE Network of Excellence, beyond EC funding, and to apply it to steer ongoing and to deploy new research activities, and to disseminate its results.

In the beautifully restored premises of the oldest campus of the University of Antwerp, ESF Science Officer Kirsten Steinhausen welcomed this new RNP, saying that we can be very proud about the selection given the very strong competition. She also complimented TRACE for the contributions from other partners than the ESF Member Organisation, even partners outside Europe (Australia and Hong Kong). Herman Goossens, the coordinator of GRACE, was approved as Coordinator (Chair) and Samuel Coenen as Manager. Currently, the TRACE Steering Committee consists of 25 members representing all contributors to TRACE from 16 countries. But, people can still join.

TRACE will produce a brochure, this newsletter and a website. At www.esf.org/trace more information on TRACE will become available, e.g. the electronic version of TRACE News and information on the science meetings that will be organized. To disseminate the results of GRACE, but also of other EU funded projects like CHAMP (www.champ-antibiotics.org) and HAPPY AUDIT (www.happyaudit.org), train-the-trainer courses will be organised. For that purpose, we are also very grateful that the European Respiratory Society (ERS) is willing to maintain the GRACE e-learning platform, established with the support of both the European Society of Clinical Microbiology and Infectious Diseases Europe (ESCMID) and ERS.

Together with our partners in the EU, our partners in Australia and Hong Kong, and pending partners in South Africa and the US, we truly hope that TRACE will succeed in sustaining the translational research on antimicrobial resistance and community-acquired infections in Europe and beyond.

Samuel Coenen



Kirsten Steinhausen, ESF Science Officer





Genomics to combat Resistance against Antibiotics in Community-acquired LRTI in Europe

GRACE

Spreading Excellence in Respiratory Tract Infections

news

August 2011, Volume 6 (2)

Editorial

GRACE, where did we make the difference?

At the kick-off meeting in Brussels on March 17, 2006, my very first slide showed a picture of Laurel and Hardy, with one of their famous quotes "This is another nice mess you've gotten me into...". This is how I felt towards my colleagues because the challenges were enormous and the objectives hugely ambitious.

"GRACE wrote history". These were however my last words at the 'final GRACE meeting' in Antwerp on June 18, 2011, and "the 'final GRACE meeting' will turn out to be a milestone in the history of primary care research on respiratory tract infections" I continued.

Overstatement? Just have a look at some of the facts and figures presented at this meeting:

- We successfully recruited more than 20,000 subjects, and close to 80,000 forms were collected from these subjects;
- GRACE conducted the largest study ever done in the world in primary care:
 - In the observational studies, we investigated 2,986 controls and 3,109 patients;
 - In the intervention study, we included 6,774 patients in baseline and 4,348 inclusions from 246 GP surgeries;
- We managed the huge logistical challenges: 8,555 kits with 31,823 samples were transported from the primary care networks participating in GRACE to the central laboratory in Antwerp.

Moreover, a lot of novel ideas and new partnerships were born at the GRACE meetings, which resulted in successful EU funded research projects, such as MOSAR, CHAMP, TheraEDGE, TRACE, SATURN, RAPP-ID, and R-GNOSIS. The GRACE materials will be used for primary care research in many other parts of the world, such as the US, China, Australia, and South Africa.

So, after many years of working closely together, the question remains: why was GRACE so successful? I think that we created the right and healthy environment for developing not only professional but also personal relationships (and had a lot of fun). We focused on interests, not positions, and managed to separate people from the problems. But above all, we benefited from the knowledge of highly competent researchers spanning their interest from genes to patients, and eventually ... became a real FAMILY.



The main outstanding challenge will be the translation of the scientific results generated by the amazing GRACE into educational output to effectively change practice and antibiotic prescribing in primary care.

Therefore, the real impact of GRACE will only be apparent in another 5 to 10 years...

*Herman Goossens, GRACE Coordinator
VAXINFECTIO - University of Antwerp*

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GRACE INTRO: Follow up

GRACE INTRO is a practice based trial assessing the impact of internet based training packages in communication skills and the use of CRP to modify antibiotic prescribing for patients presenting with LRTI in primary care. The trial has been running in 8 networks in 6 European Countries (Spain, Poland, England, Wales, Netherlands, and Belgium). The baseline audit was completed in December 2010, GPs were trained in the communication skills and CRP interventions in Jan 2011 and the post-intervention audit was completed in June 2011. Patient and GP interviews were carried out in June 2011 and note reviews were carried out in July 2011.

The communication package was based on previous qualitative work performed for CHAMP, and was informed by previous trials that had looked at communication skills for antibiotic prescribing (e.g. EQUIP/STAR/IMPACT). The internet training package covered topics including presentation of the evidence for prescribing, natural history of LRTI, and the effectiveness of antibiotics for treatment. This information was also incorporated into a glossy booklet to be shared with the patients. GP communication skills training were included in the internet package and a forum with a facility to ask questions to the research team. The video clips were tailored to the individual, and country. Practices also undertook practice-based discussion on a few recent prescribing cases and brief audits of their prescribing.

The CRP groups received a web based training package in the use of CRP which was underpinned by previous research from the IMPACT trial to derive evidence based +/- consensus cut off points to implement CRP tests and Standard Operating Procedures (Jochen Cals and Hasse Melbye).

CHAMP WP7, a process evaluation consisting of qualitative work, ran alongside GRACE INTRO. The aim of the process evaluation was to determine whether the web-based intervention, INTRO, was viewed as acceptable and feasible by GPs in the five countries of interest.

The process evaluation consisted of three parts; exploring GPs' views of the pilot intervention, exploring GPs' views of taking part in the trial and exploring patients' views of their consultations as part of the trial.

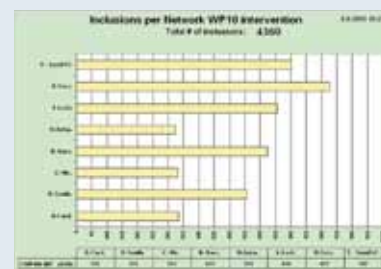
In the summer and autumn of 2010, 30 interviews were carried out with GPs across 5 countries. GPs were shown a pilot version of the web-based intervention and asked about their views and opinions on viewing and using it. GPs indicated that the format and content of the intervention were acceptable to them, although some wanted additional country-specific examples to fit better with usual practice in countries. The results of the first section of the process evaluation allowed the intervention to be improved in order to be acceptable to GPs in the countries in which it was implemented.

The later sections of the process evaluation were carried out following the completion of the RCT. 62 patient interviews were carried out within one month of the initial consultations for acute cough. Interviews asked about patient experiences of their consultation and views about the CRP test and/or patient booklet. All GPs who took part in the trial were asked to complete an online survey to capture their views on taking part in the intervention and 84 participated in interviews to explore their view's further and to explore any changes in prescribing practices as a result of the intervention. Data is currently being analysed and results are expected to be reported in 2012.

Recruitment into the GRACE INTRO trial has been very successful. 6774 patients were recruited to the baseline audit (September 2010 to January 2011) in 8 networks (GRACE News 2011;6:2). 246 GP surgeries were randomised into either: Communication + NoCRP; No Communication + CRP; Communication + CRP; No Communication + No CRP. 4360 patients were recruited to the intervention audit (February 2011 to June 2011; see figure), giving a total of 11,000 patients. Analysis has been taking place over the summer and we wait to see whether there are any significant differences between the groups in their prescribing rates.

A follow-up audit of antibiotic use will be performed in the autumn of 2011, to estimate what the longer term consequences are of the interventions. After the trial participating practices will have access to the intervention(s) not randomized to in the trial.

Paul Little



INTRO: post-intervention inclusions per network



Spreading excellence in respiratory tract infections

Antibiotic prescribing for discoloured sputum in acute cough/lower respiratory tract infection

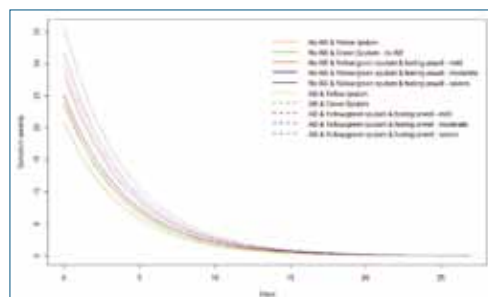
C.C. Butler, M.J. Kelly, K. Hood, T. Schaberg, H. Melbye, M. Serra-Prat, F. Blasi, P. Little, T. Verheij, S. Mölsted, M. Godycki-Cwirko, P. Edwards, J. Almirall, A. Torres, U-M. Rautakorpi, J. Nuttall, H. Goossens and S. Coenen

Prescribing antibiotics for patients with discoloured sputum caused by acute cough has little effect on alleviating symptoms and recovery, a GRACE study has found. Acute cough is one of the commonest reasons why people seek health care and accounts for a considerable proportion of antibiotics prescribed in the community.

One of the commonest manoeuvres in clinical medicine is to ask these patients about their sputum, with clinicians using phrases such as “Are you coughing anything up?” Or, “What colour is your sputum?” The rationale behind these questions is that both clinicians and patients commonly believe that yellow and green sputum production is strongly associated with a bacterial infection, which is much more likely to benefit from antibiotic treatment compared to non-productive cough or cough that produces clear sputum.

In a study published in the European Respiratory Journal, the Workpackage 8 team, including colleagues from 14 European centres, present data from an observational study of 3402 adult patients with acute cough presenting for health care in 14 primary care networks.

The research found that patients producing discoloured sputum were indeed prescribed antibiotics more frequently than those not producing sputum (OR: 3.2, 95% CI: [2.1, 5.0]), unlike those producing clear/white sputum (OR: 0.95, 95% CI: [0.61, 1.48]).



Estimated patient recorded scaled symptom severity scores over 28 days after presentation for adult patients with acute cough, sub-grouped according to sputum type, degree of feeling unwell, and antibiotic treatment (AB=antibiotic)

Crucially, however, antibiotic treatment was not associated with greater rate or magnitude of symptoms score resolution among those who: produced yellow (Coefficient: 0.00, p-value: 0.68) or green sputum (Coefficient: -0.01, p-value: 0.11). Neither was recovery among those feeling generally unwell on its own, or taken together with sputum production, associated with antibiotic treatment (see figure).

Clinicians and patients are therefore likely to both be over-interpreting the importance of the colour of sputum in the decision whether or not to prescribe, or take, antibiotics.

Chris Butler said, “One of the exciting things about this research is that our findings from this large, multi-country observational study resonate with findings from randomised trials where benefit from antibiotic treatment in those producing discoloured sputum has been found to be marginal at best or non-existent. Our findings add weight to the message that acute cough in otherwise well adults is a self-limiting condition and antibiotic treatment does not speed recovery to any meaningful extent. In fact, antibiotic prescribing in this situation simply unnecessarily exposes people to side effects from antibiotics, undermines future self-care, and drives up antibiotic resistance. This has highlighted an opportunity for enhancing the quality of care of patients with this common symptom.”

New data from the largest randomised controlled trial of antibiotics for acute cough is eagerly awaited (GRACE WP 9 and 10), which will add further to this rapidly growing evidence base improving the quality of antibiotic prescribing decisions for common conditions in primary care.

Chris Butler

Antibiotic prescribing for adults with acute cough/ lower respiratory tract infection: congruence with guidelines

J. Wood, C.C. Butler, K. Hood, M.J. Kelly, T. Verheij, P. Little, A. Torres, F. Blasi, T. Schaberg, H. Goossens, J. Nuttall and S. Coenen

One of the implicit aims of European guidelines for treating acute cough/lower respiratory tract infection (LRTI) is to reduce non evidence-based variation in antibiotic prescribing and increase the use of recommended first-line antibiotics. However, thus far, we have had little robust information on how actual clinical practice matches up to recommendations in key treatment guidelines for managing common infections. Using prospective, observational data from GRACE Workpackage 8 (WP8), we explored congruence of both antibiotic prescribing and antibiotic choice with European Respiratory Society (ERS)/European Society of Clinical Microbiology and Infectious Diseases (ESCMID) guidelines for managing LRTI.

The patients presented with new or worsening cough/LRTI of less than 28 days duration to 14 primary care research networks in 13 countries. Clinicians recorded symptoms on presentation, and their examination and management. Patients were followed up with self-complete diaries.

1,776 (52.7%) patients were prescribed antibiotics. Given patients' clinical presentation, clinicians could have justified an antibiotic prescription for 1,915 (71.2%) patients according to the ERS/ESCMID guidelines. 761 (42.8%) of those who were prescribed antibiotics received a first-choice antibiotic (i.e. tetracycline or amoxicillin; see figure). Ciprofloxacin was prescribed for 37 (2.1%) and cephalosporins for 117 (6.6%). However, some of those patients that did not receive a prescription for amoxicillin or tetracycline received a narrower spectrum agent such as penicillin V, so some guideline incongruent prescribing may have been better quality prescribing from the perspective of containing antimicrobial resistance.

A first-choice antibiotic in the guidelines was prescribed to the minority of patients who received an antibiotic prescription.

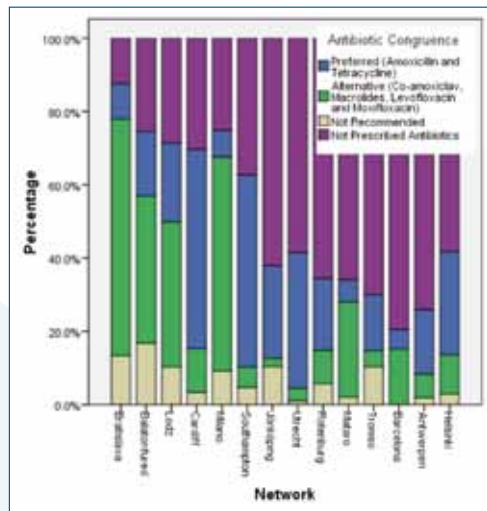
Our exploratory analysis suggested that a lack of specificity in definitions in the ERS/ESCMID guidelines could have enabled clinicians to justify a higher rate of antibiotic prescription. More studies are therefore needed to produce specific clinical definitions and indications for treatment.

In an editorial in the European Respiratory Journal accompanying both of these papers, Mark Woodhead asked why practice differed so widely from the recommendations in the guidelines?¹ Dr Woodhead pointed out that there was limited empirical evidence on which the to base the guidelines. These recommendations had to rely on consensus rather than robust data. As more findings emerge from the GRACE clinical studies, guideline developers will have a stronger empirical basis for their recommendations. This study is a good illustration of why the GRACE Network of Excellence first set out to describe current practice (WP8) in order to identify opportunities for improving care, and then went on to undertake diagnostic, prognostic, etiological and intervention studies to demonstrate how care can be improved.

Chris Butler

Reference

1. Woodhead M. Prescribing and guidelines: both must improve to combat antimicrobial resistance. *European Respiratory Journal*. 2011;38:9-11.



Stacked bar chart of the percentages of antibiotics grouped according to ERS-ESCMID guideline recommendations prescribed by network

Final GRACE Meeting

Yesterday

Yesterday
All our knowledge seemed so far
Full Resistant bugs were here to stay
Oh, insight seemed so far away

Suddenly
There was a very good idea
A pretty girl came walking down the street
O GRACE my dear so suddenly

Why she
Has to go
We don't know, We love her so
We will name her TRACE
She will stay for ever more

Antwerp town
was the place where it all started up
Herman Goossens he just cannot stop
Oh, Herman do you ever rest?

GRACE my dear
You grew up so fast and beautiful
Meetings, site visits you name it all
Oh, were we ever back at home?

chorus

Inclusion rate
who did best - there was always debate
in the meantime it was getting late
oh coughing patients where are thou

On the phone
More than family we just said it all
ACT conferencing spring to fall
Oh, please give me another call

chorus

GRACE some day,
Money was not easy game to play
Some funny problems sure came on our way
Oh, Brussels, please, could you now pay?

Infection
will we ever find the holy grail
does it work -the drug- or does it fail
Oh, tell where does our science sail?

chorus

GRACE meetings
We saw each other every year two times
to show results and to set out new lines
O we shall miss the evening wines

Finally,
3 thousand patients were a fact
nobody had expected that
A network of real excellence!

chorus

Thank you all
For your friendship and your expertise
And forgive us our Dutch English please
Ad infini-tum TRACE repeat
mmm-mmm-mmm-mmm-mmm-m-m

*Lidewij Broekhuizen
Saskia van Vugt
Theo Verheij*



Colophon

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