TRACE
Translational Research on Antimicrobial resistance and Community-acquired infections in Europe

TRACE news

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Editorial

TRACE involved in exciting new research proposals

Since its launch June 2011, TRACE has organized several ESF Science Meetings aiming to disseminate the results of GRACE (Genomics to combat Resistance against Antibiotics in Community-acquired LRTI in Europe; www.grace-lrti.org, 2006-2011) and TRACE related research as well as to develop new translational research on antimicrobial resistance and community-acquired infections in Europe and beyond. During the last WONCA Europe Conference "The art & science of general practice" held in the Austria Center Vienna, July 2012, a very well attended symposium was held in collaboration with EGPRN (European General Practice Research Network) and GRIN (General practice Respiratory Infections Network), and supported as ESF Science Meeting. The symposium informed the clinical management of respiratory tract infections in primary care with results from GRACE studies on the etiology, diagnosis, prognosis and treatment of LRTI, and on strategies to reduce antibiotic prescribing. The last GRIN Meeting in Bristol, September 2012, was an ESF Science Meeting as well and applied to discuss the development of new research proposals involving TRACE in response to the current most recent 7th Framework Programme Call Innovative health research 2013 of the European Commission.

Meanwhile two out of three proposals involving TRACE and submitted in response to the most recent FP7 Health Call have passed Stage 1 and were invited to submit a full proposal for Stage 2 of the evaluation by 6 February 2013. This really is a huge success for TRACE. PREPARE (Platform foR European Preparedness Against (Re-)emerging Epidemics) was submitted on time as a full proposal in response to HEALTH.2013.2.3.3-1. "Clinical management of patients in severe epidemics". TAILORED (Targeted and tailored Antibiotic treatment in older people with Lower Respiratory tract infectious Disease) was submitted in response to HEALTH.2013.2.3.1-2. "Stratified approaches to antibacterial and/or antifungal treatment". The two most recent ESF Science Meetings of TRACE involved the respective partners of these two proposals and allowed them to make great progress in the research and proposal development. The outcome of the evaluations of both PREPARE and TAILORED is to be expected in April 2013.

The involvement of TRACE entails the engagement of several TRACE partners and that both proposals build on the primary care research infrastructure developed by the FP6 funded Network of Excellence GRACE, sustained by ESF through TRACE. This remarkable research infrastructure sets Europe apart as the location of choice, world-wide, for acute infections research in the community in resource rich settings, and will uniquely enable any ambitious primary care infections research programs to confidently, efficiently and rapidly deliver the required patient recruitment and data collection to highest international standards. The GRACE and TRACE results presented in this newsletter support this strong statement.

Samuel Coenen

News

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 ran 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. The results show that internet training to use either a CRP POCT, or an enhanced communication skills plus interactive patient information booklet, achieved important reductions in antibiotic prescribing for RTIs, and the combined intervention performed best.
To estimate what the longer term consequences are of the interventions, a follow-up audit of antibiotic use was performed in the autumn of 2011, i.e. when EC funding for GRACE had ended and ESF supported the infrastructure and research activities through TRACE. Recruitment into the follow up trial was very successful. Over 4000 patients were recruited to the follow up audit (October 2011 to May 2012) in 8 networks (Table 1). Over 200 GP surgeries participated. During this period note reviews of the patients particpating in the intervention audit were carried out and GPs were asked to complete an end of study questionnaire to elucidate feedback from the interventions.

Paul Little

	Follow up
Cardiff	500
Southampton	861
Utrecht	400
Barcelona	840
Antwerp	359
Lodz	493
Szczecim	502
SemFYC	945
Total	4900

Table 1. Overview recruitment in 8 primary care networks

GRACE PhD

On November 2012, Saskia van Vugt successfully defended her PhD thesis "Caring for cough: guiding diagnosis in primary care", which is entirely based on GRACE data.
Accurate diagnosis in patient presenting to primary care with the most common reason for encounter, i.e. acute cough, or other symptoms suggesting a lower respiratory tract infection (LRTI), allows primary care clinicians to adequately treat and inform their patients about the expected course of their disease. This presentation can be caused by potentially life-threatening conditions like pneumonia and influenza, other, often self-limiting, bacterial or viral infections, and underlying obstructive lung diseases. The challenge in primary is to identify whether it concerns indeed a self-limiting condition, or a disease for which targeted treatment, e.g. antibiotics, referral, and/or follow-up are indicated.
This thesis showed that primary care clinicians' clinical judgment is very valuable to rule in, but not to rule out radiographic pneumonia, which was present in 5% of adult patients with acute cough. A diagnostic symptom and signs model had moderate clinical value in discriminating between high and low risk for radiographic pneumonia. In contrast to procalcitonin, C-Reactive Protein had added diagnostic value, merely by correctly ruling out pneumonia in the intermediate risk group. Secondly, it showed that previously unrevealed obstructive lung disorders (asthma and COPD) were not uncommon among patients presenting with acute cough, and poorly predicted by standardised brief diagnostic models using symptoms and signs derived from patients with chronic cough. In patients presenting during influenza epidemics, it confirmed the diagnostic value of the previously reported diagnostic influenza model ('Flu Score').

Despite the use of diagnostic models, that may serve as a cornerstone streamlining physicians' thoughts and considerations, the diagnostic process in LRTI patients remains complex and will challenge GPs also in the future.

If you are interested in reading further, this thesis is available by sending an email to s.f.vanvugt@umcutrecht.nl.

Saskia van Vugt

Figure 1: Discoloured sputum

Spreading excellence in respiratory tract infections

Clinical influences on antibiotic prescribing decisions for lower respiratory tract infection: a nine country qualitative study of variation in care

Lucy Brookes-Howell, Kerenza Hood, Lucy Cooper, Samuel Coenen, Paul Little, Theo Verheij, Maciek Godycki-Cwirko, Hasse Melbye, Jaroslaw Krawczyk, Alicia Borras-Santos, Kristin Jakobsen, Patricia Worby, Herman Goossens, Christopher C Butler. BMJ Open 2012;2:e000795. doi:10.1136/

There is variation in antibiotic prescribing for lower respiratory tract infections (LRTI) in primary care that does not benefit patients. This study aimed to investigate clinicians' accounts of clinical influences on antibiotic prescribing decisions for LRTI to better understand variation and identify opportunities for improvement.

The multi country primary care qualitative interview study was based on semi-structured interviews using open-ended questions and a patient scenario. Data were subjected to five-stage analytic framework approach (familiarisation, developing a thematic framework from the interview questions and emerging themes, indexing, charting and mapping to search for interpretations), with interviewers commenting on preliminary reports. 80 primary care clinicians were randomly selected from primary care research networks based in nine European cities.

The interviewed clinicians reported four main individual clinical factors that guided their antibiotic prescribing decision: auscultation, fever, discoloured sputum (Fig. 1) and breathlessness. These were considered alongside a general impression of the patient derived from building a picture of the illness course, using intuition and familiarity with the patient. Comorbidity and older age were considered main risk factors for poor outcomes. Clinical factors were similar across networks, apart from C reactive protein near patient testing in Tromsø. Clinicians developed ways to handle diagnostic and management uncertainty through their own clinical routines.

In conclusion, the clinicians emphasised the importance of auscultation, fever, discoloured sputum and breathlessness, general impression of the illness course, familiarity with the patient, comorbidity, and age in informing their antibiotic prescribing decisions for LRTI. As some of these factors may be overemphasised given the evolving evidence base, greater standardisation of assessment and integration of findings may help reduce unhelpful variation in management. Non-clinical influences will also need to be addressed.

Chris Butler

Severity assessment for lower respiratory tract infections: potential use and validity of the CRB-65 in primary care

Nick A Francis, Jochen W Cals, Christopher C Butler, Kerenza Hood, Theo Verheij, Paul Little, Herman Goossens, Samuel Coenen on behalf of the GRACE Project Group. Prim Care Respir J 2012; 21: 65-70.

The aim of this study was to explore the potential use of the CRB-65 rule (based on Confusion, Respiratory rate, Blood pressure and age >65 years) in adults with lower respiratory tract infection (LRTI) in primary care.

Primary care clinicians in 13 European countries recorded antibiotic treatment and clinical features for adults with LRTI. Patients recorded daily symptoms. Multilevel regression models determined the association between an elevated CRB-65 score and prolonged moderately severe symptoms, hospitalisation, and time to recovery. Sensitivity analyses used zero imputation. The model controlled for antibiotic prescribing.

Respiratory rate and blood pressure were recorded in 22.7% and 31.9% of patients, respectively. A total of 2,690 patients completed symptom diaries. The CRB-65 could be calculated for 339 (12.6%). A score of >1 was not significantly associated with prolonged moderately severe symptoms (odds ratio (OR) 0.42, 95% CI 0.04 to 4.19) or hospitalisations (OR 3.12, 95% CI 0.16 to 60.24), but was associated with prolonged time to self-reported recovery when using zero imputation (hazard ratio (HR) 0.75, 95% CI 0.64 to 0.88) (Table 2).

	CRB-65 >1
Logistic regression models	**Odds ratio (95% CI)**
Model 1: Prolonged moderately severe illness, complete case (N=334, GPs=36)	0.42 (0.04 to 4.19)
Model 2: Prolonged moderately severe illness, zero-imputed (N=2,613, GPs=80)	1.17 (0.76 to 1.81)
Model 3: Hospitalisations, complete case (N=326, GPs=35)	3.12 (0.16 to 60.24)
Model 4: Hospitalisations, zero-imputed (N=2,545, GPs=80)	2.93 (0.77 to 11.17)
Survival analysis models	**Hazard ratio (95% CI)**
Model 5: Time to recovery, complete case (N=322, GPs=35)	0.67 (0.41 to 1.11)
Model 6: Time to recovery, zero imputed (N=2,468, GPs=78)	0.75 (0.64 to 0.88)†

Table 2: Associations between CRB-65 score and antibiotic prescribing, and prolonged illness, hospitalisations, and rate of recovery.

In conclusion, respiratory rate and blood pressure were infrequently measured in adults with LRTI. No evidence was found to support using the CRB-65 rule in the assessment of LRTI in primary care. However, it is unclear whether it is of value if used only in patients where the primary care clinician suspects pneumonia.

Nick Francis

Predicting benign course and prolonged illness in lower respiratory tract infections: a 13 European country study

Saskia F van Vugt, Chris C Butler, Kerenza Hood, Mark J Kelly, Samuel Coenen, Herman Goossens, Paul Little and Theo J Verheij. Fam Pract 2012; 29:131–8

Clinicians and patients are often uncertain about the likely clinical course of community-acquired lower respiratory tract infection (LRTI) in individual patients. A study was set out to develop a prediction rule to identify patients at risk of prolonged illness and those with a benign course.

The signs and symptoms were set out that predicted prolonged illness (moderately bad symptoms lasting >3 weeks after consultation) in 2690 adults presenting in primary care with LRTI in 13 European countries by using multilevel modelling.

212 (8.1%) patients experienced prolonged illness. Illness that had lasted >5 days at the time of presentation, >1 episode of cough in the preceding year, chronic use of inhaled pulmonary medication and diarrhoea independently predicted prolonged illness. Applying a rule based on these four variables, 3% of the patients with < 1 variable present (n = 955, 37%) had prolonged illness. Patients with all four variables present had a 30% chance of prolonged illness (n = 71, 3%) (Fig. 2).

It was concluded that most patients with acute cough (>90%) recover within 3 weeks. A prediction rule containing four clinical items had predictive value for the risk of prolonged illness, but given its imprecision, appeared to have little clinical utility. Patients should be reassured that they are most likely to recover within three weeks and advised to re-consult if their symptoms persist beyond that period.

Theo Verheij

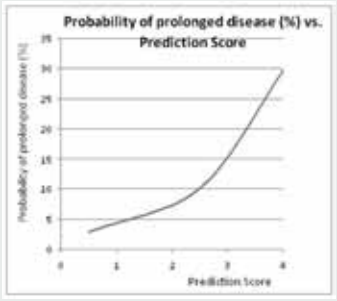

Figure 2: Plot showing relation between the probability of prolonged illness as a function of the score based on the new prediction rule. The new prediction rule consists of four items from medical history: illness that had lasted >5 days prior to the first consultation, more than one episode of cough lasting more than 1 week in the preceding year, chronic use of inhaled pulmonary medication and diarrhoea. For each score, the probability of prolonged illness was computed by counting the actual patients with prolonged illness in the total population. The risk of prolonged illness markedly increased with a higher score.

General practitioners' views on the acceptability and applicability of a web-based intervention to reduce antibiotic prescribing for acute cough in multiple European countries: a qualitative study prior to a randomised trial

Sibyl Anthierens, Sarah Tonkin-Crine, Elaine Douglas, Patricia Fernandez-Vandellos, Jaroslaw Krawczyk, Carl Llor, Jochen WL Cals, Nick A Francis, Lucy Yardley, Samuel Coenen, Theo Verheij, Herman Goossens, Paul Little and the GRACE INTRO study team. BMC Fam Pract 2012;13:101.

Interventions to promote prudent antibiotic prescribing by general practitioners (GPs) have often only been developed for use in one country. We aimed to develop an intervention which would be appropriate to implement in multiple European countries in order to offer greater benefit to practice whilst using fewer resources. The INTRO (INternet TRaining for antibiOtic use) intervention needed to deliver training to GPs in the use of C-Reactive Protein (CRP) near patient tests to help diagnose acute cough and in communication skills to help explain prescribing decisions to patients. We explored GPs' views on the initial version of INTRO to test acceptability and potentially increase applicability for use in multiple countries before the start of a randomised trial.

30 GPs from five countries (Belgium, England, the Netherlands, Poland and Spain), were interviewed using a "think aloud" approach. GPs were asked to work through the intervention and discuss their views on the content and format in relation to following the intervention in their own practice (Fig. 3). GPs viewed the same intervention but versions were created in five languages. Data were coded using thematic analysis.

GPs in all five countries reported the view that the intervention addressed an important topic, was broadly acceptable and feasible to use, and would be a useful tool to help improve clinical practice. However, GPs in the different countries identified aspects of the intervention that did not reflect their national culture or healthcare system. These included perceived differences in communication style used in the consultation, consultation length and the stage of illness at which patient typically presented.

An online intervention to support evidence-based use of antibiotics is acceptable and feasible to implement amongst GPs in multiple countries. However, tailoring of the intervention to suit national contexts was necessary by adding local information and placing more emphasis on the fact that GPs could select the communication skills they wished to use in practice. Using think aloud methods to complement the development of interventions is a powerful method to identify regional contextual barriers to intervention implementation.

Figure 3: Screenshot of the GRACE INTRO intervention website

Sibyl Anthierens

Sensitive Assay for Virus Discovery in Respiratory Clinical Samples

Michel de Vries, Martin Deijs, Marta Canuti, Barbera D. C. van Schaik, Nuno R. Faria, Martijn D. B. van de Garde, Loes C. M. Jachimowski, Maarten F. Jebbink, Marja Jakobs, Angela C. M. Luyf, Frank E. J. Coenjaerts, Eric C. J. Claas, Richard Molenkamp, Sylvie M. Koekkoek, Christine Lammens, Frank Leus, Herman Goossens, Margareta Ieven, Frank Baas, Lia van der Hoek. PLoS ONE 6(1): e16118.

In 5–40% of respiratory infections in children, the diagnostics remain negative, suggesting that the patients might be infected with a yet unknown pathogen. Virus discovery cDNA-AFLP (VIDISCA, Fig. 4) is a virus discovery method based on recognition of restriction enzyme cleavage sites, ligation of adaptors and subsequent amplification by PCR.

However, direct discovery of unknown pathogens in nasopharyngeal swabs is difficult due to the high concentration of ribosomal RNA (rRNA) that acts as competitor.

In the current study VIDISCA was optimized by adjusting the restriction enzymes and decreasing rRNA amplification in the reverse transcription, using hexamer oligonucleotides that do not anneal to rRNA. Residual cDNA synthesis on rRNA templates was further reduced with oligonucleotides that anneal to rRNA but can not be extended due to 3′-dideoxy-C6-modification. With these modifications >90% reduction of rRNA amplification was established. Further improvement of the VIDISCA sensitivity was obtained by high throughput sequencing (VIDISCA-454). Eighteen nasopharyngeal swabs were analysed, all containing known respiratory viruses. The proper virus could be identified in the majority of samples tested (11/18). The median load in the VIDISCA-454 positive samples was 7.2 E5 viral genome copies/ml (ranging from 1.4 E3–7.7 E6).

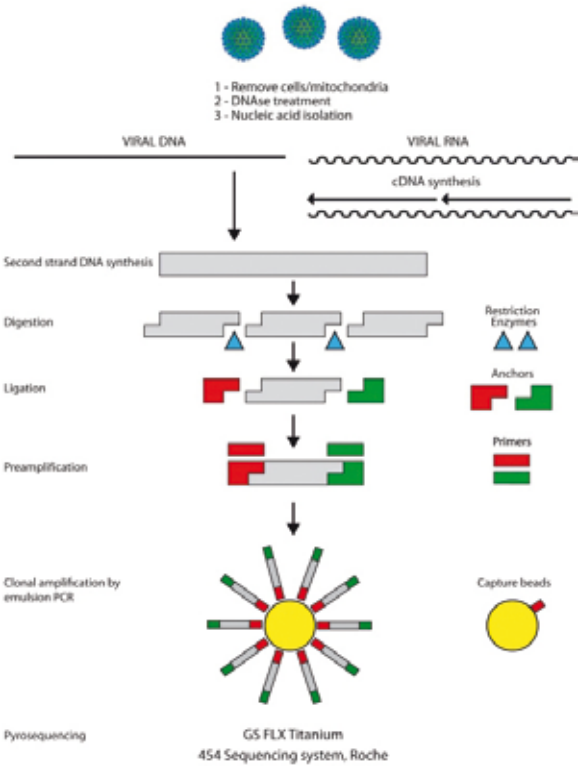

Figure 4: VIDISCA

The presented results show that optimization of VIDISCA and subsequent high-throughput-sequencing enhances sensitivity drastically and provides the opportunity to perform virus discovery directly in patient material.

Lia van der Hoek

Performance of Different Mono- and Multiplex Nucleic Acid Amplification Tests on a Multipathogen External Quality Assessment Panel

Katherine Loens, Anton M. van Loon, Frank Coenjaerts, Yvette van Aarle, Herman Goossens, Paul Wallace, Erik J. C. Claas and Margareta Ieven on behalf of the GRACE Study Group. J Clin Microbiol 2012; 50: 977–87.

An external quality assessment (EQA) panel consisting of a total of 48 samples in bronchoalveolar lavage (BAL) fluid or transport medium was prepared in collaboration with Quality Control for Molecular Diagnostics (QCMD) (www.qcmd.org). The panel was used to assess the proficiency of the three laboratories that would be responsible for examining the 6,000 samples to be collected in the GRACE Network of Excellence (www.grace-lrti.org).

The main objective was to decide on the best-performing testing approach for the detection of influenza viruses A and B, parainfluenza virus types 1 to 3, respiratory syncytial virus (RSV), human metapneumovirus, coronavirus, rhinovirus, adenovirus, *Chlamydophila pneumoniae*, *Mycoplasma pneumoniae*, and *Legionella pneumophila* by nucleic acid amplification techniques (NAATs).

Two approaches were chosen: (i) laboratories testing samples using their in-house procedures for extraction and amplification and (ii) laboratories using their in-house amplification procedures on centrally extracted samples. Furthermore, three commercially

available multiplex NAAT tests-the ResPlex (Qiagen GmbH, Hilden, Germany), RespiFinder plus (PathoFinder, Maastricht, The Netherlands), and RespiFinder Smart 21 (PathoFinder) tests-were evaluated by examination of the same EQA panel by the manufacturer.

	Lab 1		Lab 2		Lab 3	Respiex		RespiFinder	
	In-house	EasyMag	In-house	EasyMag		1	2	Plus	Smart 21
Subpanel 1 (n=21)									
Nr correct results	20/21	17/21	18/21	17/21	NA	9/21	9/21	18/21	16/21
Nr false-positive	0/21	3/21	1/21	0/21	NA	2/21	4/21	0/21	0/21
Nr false-negative	1/21	1/21	2/21	4/21	NA	10/21	8/21	3/21	5/21
Subpanel 2 (n=13)									
# correct results	12/13	12/13	8/13	10/13	NA	5/13	7/13	10/13	10/13
# false-positive	0/13	0/13	3/13	0/13	NA	0/13	1/13	0/13	0/13
# false-negative	1/13	1/13	2/13	3/13	NA	8/13	5/13	3/13	3/13
Subpanel 3 (n=14)									
# correct results	14/14	NA	11/14	NA	14/14	5/14	4/14	12/14	10/14
# false-positive	0/14	NA	0/14	NA	0/14	0/14	0/14	0/14	0/14
# false-negative	0/14	NA	3/14	NA	0/14	9/14	10/14	2/14	4/14

Table 3. Summary of results

No large differences among the 3 laboratories were noticed when the performances of the assays developed in-house in combination with the in-house extraction procedures were compared. Also, the extraction procedure (central versus local) had little effect on performance. However, large differences in amplification efficacy were found between the commercially available tests; acceptable results were obtained by using the PathoFinder assays (Table 3).

Katherine Loens

The impact of using different tariffs to value EQ-5D health state descriptions: an example from a study of acute cough/lower respiratory tract infections in seven countries

Raymond Oppong, Billingsley Kaambwa, Jaqui Nuttall, Kerenza Hood, Richard D Smith, Joanna Coast. Eur J Health Econ 2011. DOI10.1007/s10198-011-0360-9

When using the EQ-5D in European cross-national studies, there is no consensus over whether the European value set (EVS), country specific value sets (CVS) or UK value set (UKVS) should be used. Data on health outcomes were collected in 7 countries. EQ-5D index scores were generated for each country using all three value sets. QALYs (Quality Adjusted Life Years) gained over 4 weeks based on EQ-5D scores were also generated in order to investigate the implications for cost-utility analysis.

EQ-5D scores obtained using the EVS were similar to values obtained using the CVS and UKVS in all countries. CVS-based EQ-5D scores were on average associated with a smaller baseline-to-week 4 change/improvement in all countries (except in Wales and Belgium) while UKVS-based EQ-5D scores showed the largest improvement over the same period for every country. There were gains in QALYs over the 4 week period and with all value sets. The difference between the QALYs derived from the different tariffs was small in most cases (Table 4). With regards to cost-utility analysis, the results suggest that in most countries (with the exception of Belgium and Finland), using different tariffs to value EQ-5D would not have made a difference to the decisions based on the results of cost-utility analysis.

Jo Coast

Country	Tariff	QUALYS over 4 weeks
Wales	EVS	0.059
	CVS	0.058
	EVS-CVS	0.001
England	EVS	0.064
	CVS	0.064
	EVS-CVS	0.000
Netherlands	EVS	0.064
	CVS	0.066
	UKVS	0.064
	EVS-CVS	-0.002**
	EVS-UKVS	0.000
	UKVS-CVS	-0.002
Spain	EVS	0.067
	CVS	0.066
	UKVS	0.067
	EVS-CVS	0.001**
	EVS-UKVS	0.000
	UKVS-CVS	0.001
Germany	EVS	0.066
	CVS	0.070
	UKVS	0.066
	EVS-CVS	-0.004
	EVS-UKVS	0.000
	UKVS-CVS	-0.004
Belgium	EVS	0.064
	CVS	0.063
	UKVS	0.065
	EVS-CVS	0.001
	EVS-UKVS	-0.001*
	UKVS-CVS	0.002
Finland	EVS	0.065
	CVS	0.064
	UKVS	0.065
	EVS-CVS	0.001
	EVS-UKVS	0.001
	UKVS-CVS	0.000

Table 4: QALYs gained over 4 weeks with different tariffs

*Significantly different at 5% level

**Significantly different at 1% level paired test

Amoxicillin for acute lower-respiratory-tract infection in primary care when pneumonia is not suspected: a 12-country, randomised, placebo-controlled trial.

Paul Little, Beth Stuart, Michael Moore, Samuel Coenen, Chris C Butler, Maciek Godycki-Cwirko, Artur Mierzecki, Slawomir Chlabicz, Antoni Torres, Jordy Almirall, Melanie Davies, Tom Schaberg, Sigvard Mölstad, Francesco Blasi, Ann De Sutter, Janko Kersnik, Helena Hupkova, Pia Touboul, Kerenza Hood, Mark Mullee, Gilly O'Reilly, Curt Brugman, Herman Goossens, Theo Verheij; on behalf of the GRACE consortium. Lancet Infect Dis 2013;13:123-9

Lower-respiratory-tract infection is one of the most common acute illnesses managed in primary care. Few placebo-controlled studies of antibiotics have been done, and overall effectiveness (particularly in subgroups such as older people) is debated. This study aimed to compare the benefits and harms of amoxicillin for acute lower-respiratory-tract infection with those of placebo both overall and in patients aged 60 years or older.

Patients older than 18 years with acute lower-respiratory-tract infections (cough of ≤28 days' duration) in whom pneumonia was not suspected were randomly assigned (1:1) to either amoxicillin (1 g three times daily for 7 days) or placebo by computer-generated random numbers. The primary outcome was duration of symptoms rated "moderately bad" or worse. Secondary outcomes were symptom severity in days 2-4 and new or worsening symptoms. Investigators and patients were masked to treatment allocation. This trial is registered with EudraCT (2007-001586-15), UKCRN Portfolio (ID 4175), ISRCTN (52261229), and FWO (G.0274.08N).

1038 patients were assigned to the amoxicillin group and 1023 to the placebo group. Neither duration of symptoms rated "moderately bad" or worse (hazard ratio 1·06, 95% CI 0·96-1·18; p=0·229) nor mean symptom severity (1·69 with placebo vs 1·62 with amoxicillin; difference -0·07 [95% CI -0·15 to 0·007]; p=0·074) differed significantly between groups (Fig. 5). New or worsening symptoms were significantly less common in the amoxicillin group than in the placebo group (162 [15·9%] of 1021 patients vs 194 [19·3%] of 1006; p=0·043; number needed to treat 30). Cases of nausea, rash, or diarrhoea were significantly more common in the amoxicillin group than in the placebo group (number needed to harm 21, 95% CI 11-174; p=0·025), and one case of anaphylaxis was noted with amoxicillin. Two patients in the placebo group and one in the amoxicillin group needed to be admitted to hospital; no study-related deaths were noted. The authors noted no evidence of selective benefit in patients aged 60 years or older (n=595).

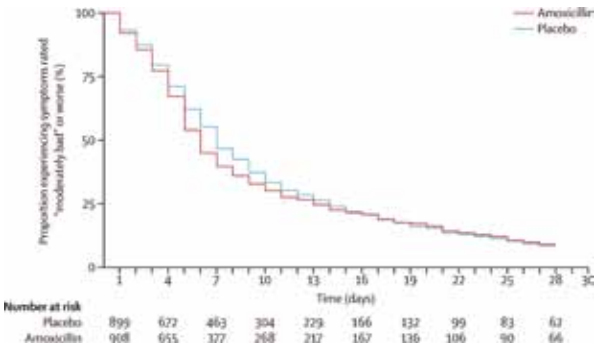

Figure 5: Kaplan-Meier estimates for duration of symptoms rated "moderately bad" or worse

In conclusion, when pneumonia is not suspected clinically, amoxicillin provides little benefit for acute lower-respiratory-tract infection in primary care both *overall and in patients aged 60 years or more, and causes slight harms.*

Paul Little

Announcement

TRACE Steering Committee Meeting:

Friday October 4, 2013
Nice, France.

This meeting is preceeding the GRIN-meeting October 4 and 5, 2013.

Colophon

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