Research and development

The Joint Programming Initiative

Translate research into policy and regulation

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JPI-AMR
The Joint Programming Initiative on Antimicrobial Resistance

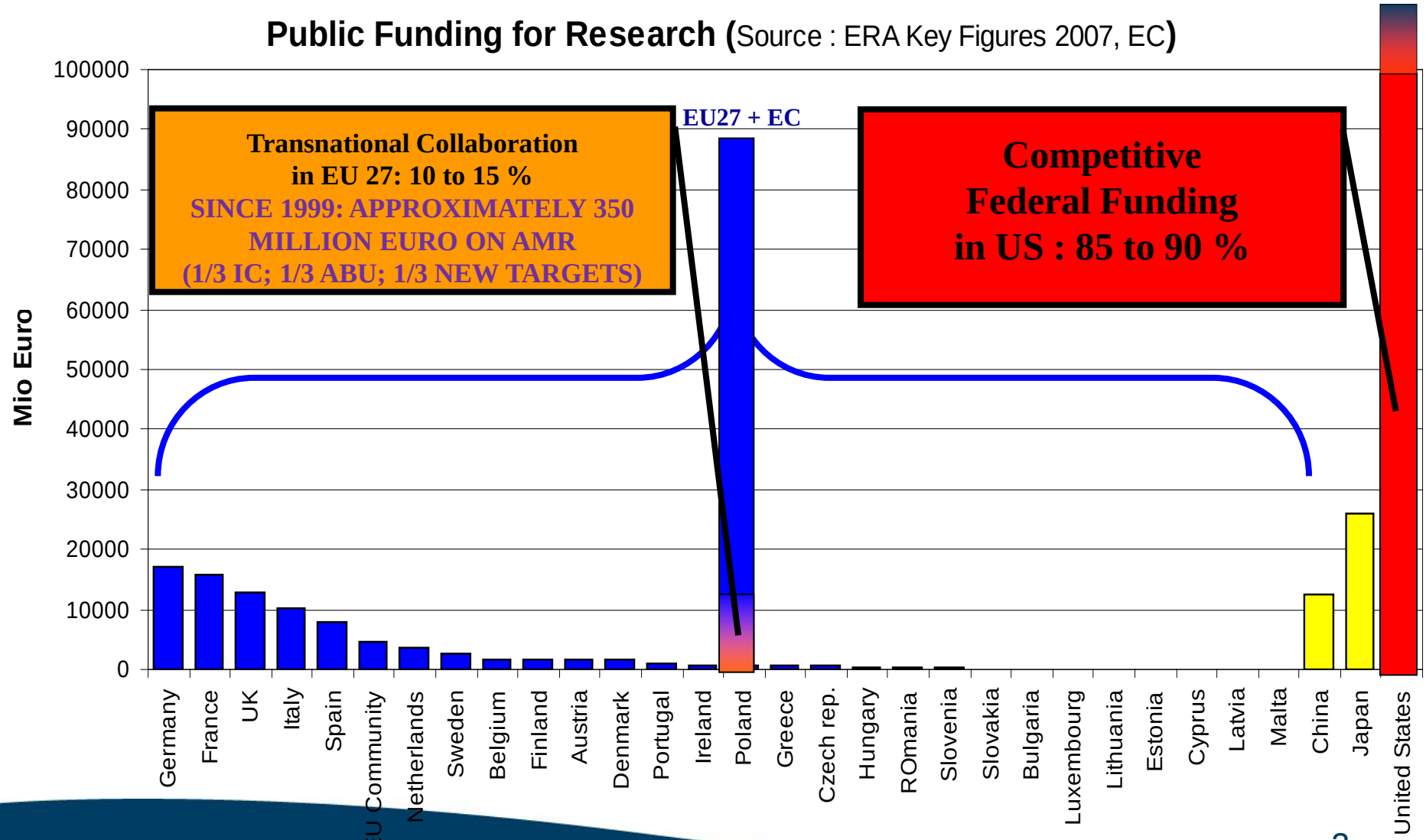
What is Joint Programming?

Aim:
To pool national research efforts in order to make better use of Europe's public R&D resources and to tackle common European challenges more effectively in a few key areas.

Objective:
Overcome the fragmentation of national research programmes to address global challenges.

Action:
European Member States agree, on a voluntary basis and in a partnership approach, on a common Strategic Research Agenda (SRA) to address major societal challenges which will be implemented jointly.

Why Joint Programming?



DL of FP Project, NABATIVI

Media Release

Basel, 4 November 2013

Roche and Polyphor join efforts to combat multi-drug-resistant bacterial infections

Roche licenses investigational antibiotic POL7080 from Polyphor. POL7080 targets *Pseudomonas* species with a novel mode of action. This "superbug" bacterium is commonly found in hospitals and has evolved to become resistant to many antibiotic treatments.

JPI-AMR 19 Participating Countries

Belgium
Denmark
Finland
France
Greece
Israel
Italy
The Netherlands
Norway
Poland
Romania
Switzerland
Spain
Sweden
Czech Republic
Turkey
Germany
The United Kingdom
Canada
EU Commission

Malta (obs.)

SRA priority topics (current draft)

A. Development of novel **antibiotics** and alternatives for antibiotics – from basic research to the market

B. Design strategies to improve treatment and prevention of infections by developing new **diagnostics**.

C. Implementation of a publicly funded **global** antibiotic resistance **surveillance** program.

D. **Transmission** Dynamics

E. The role of the **environment** and sewage as a source for the emergence and spread of antimicrobial resistance

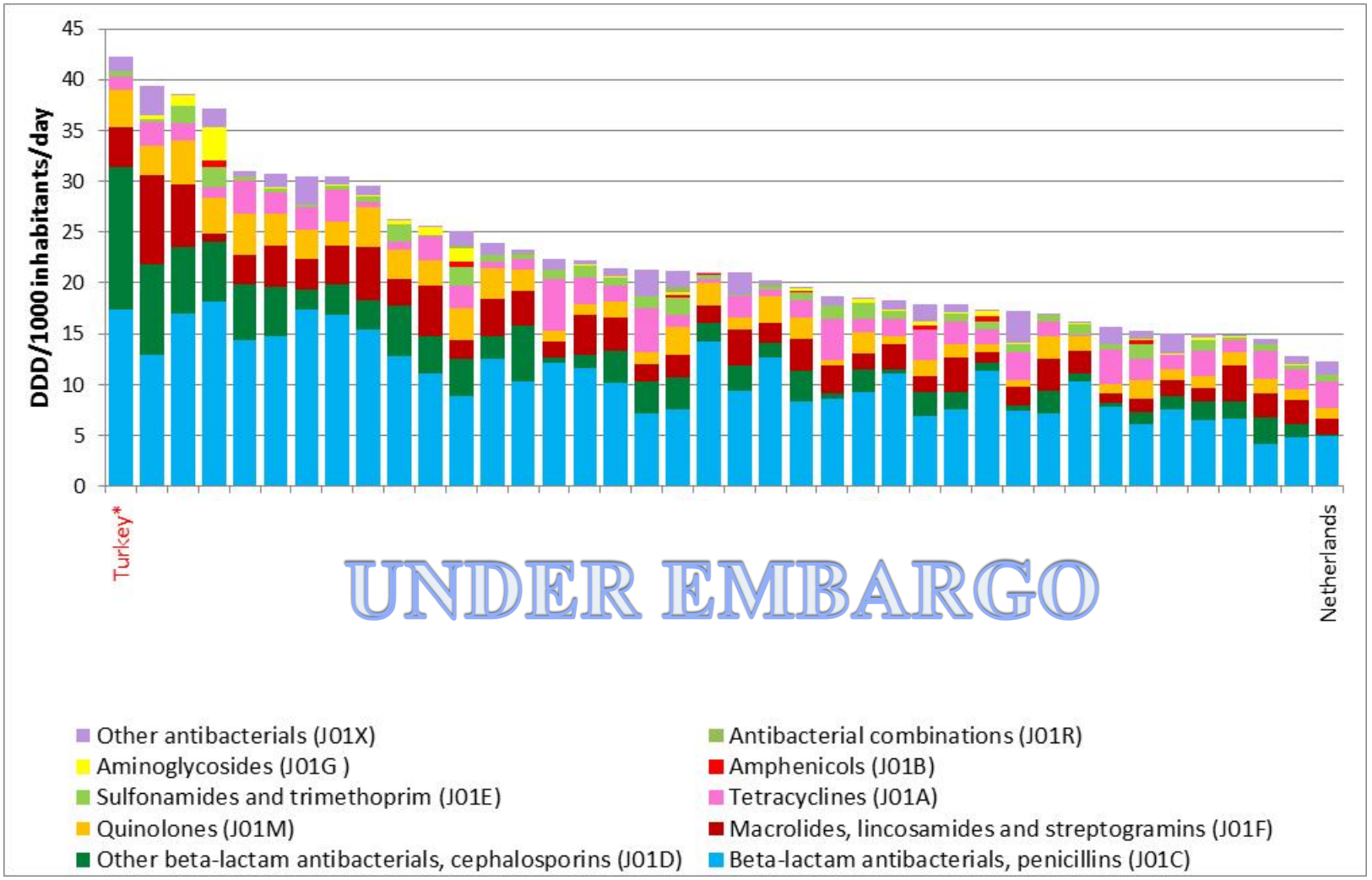
F. Designing and testing **interventions** to prevent acquisition, transmission and infection caused by antibiotic-resistant bacteria.

Next Steps

- Final approval of the Strategic Research Agenda by the Management Board of JPI-AMR, developed by the SAB
- Finish mapping of AMR research funding, by the MS and the EC
- Launch of the JPI-AMR Strategic Research Agenda (3 April 2014 in Brussels?)
- First call in early 2014 with Canada (about EUR 20 million on topic A: discovery of a new pipeline):
  - A dozen JPI-AMR countries have preliminary agreed to participate
  - Pre-announcement is planned for 15 November (EAAD event)
- Prepare an ERA-net in 2015

Translate research into policy a and regulation

Total antibiotic use in DID in 11 WHO/EURO-ESAC countries, Kosovo° and 28 ESAC-Net countries



* Countries reporting only outpatient antibiotic use
° in accordance with Security Council resolution 1244 (1999).

Versporten et al , LID, under review

Targets set by National Action Plan 2013- 2017

Indicator	2013	2014	2015	2016	2017
J01 DDD/1000 inhabitants/ per day	42	40	38	36	35

T.C. Sağlık Bakanlığı
Türkiye İlaç ve Tıbbi Cihaz Kurumu

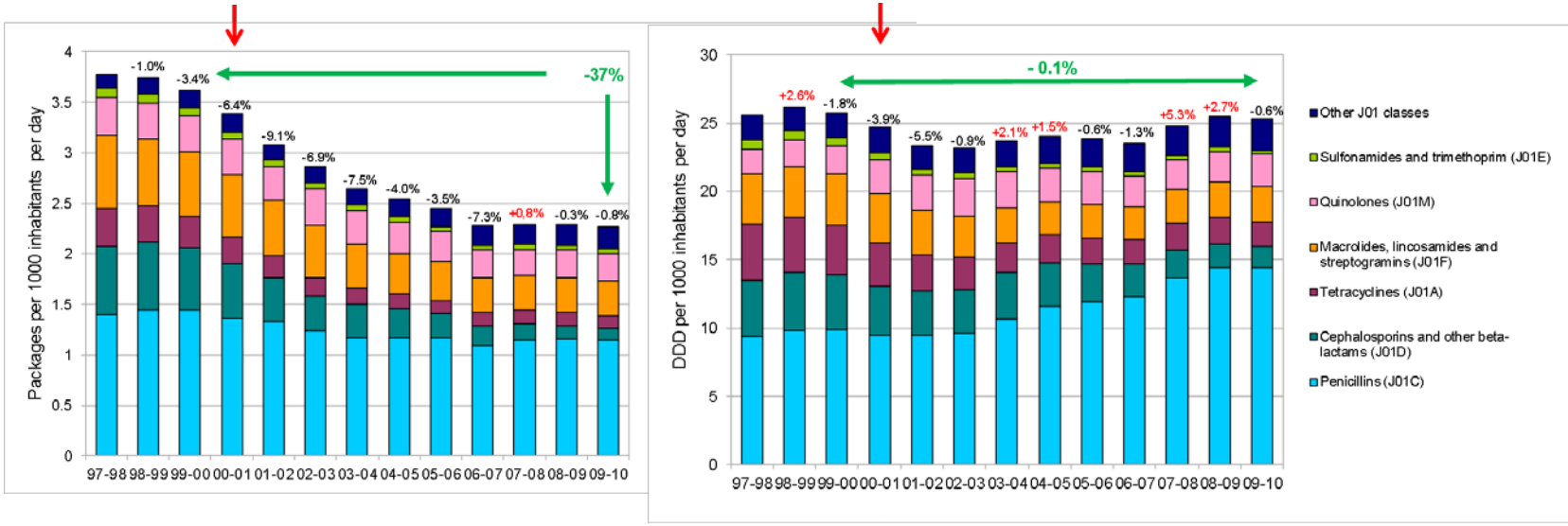
New Patient Safety Act January 1st 2011

- Antibiotic prescribing indicator: increased adherence to treatment guidelines for infections in outpatient care, and thereby a decrease in antibiotic prescribing.
  - Long term target for **2014: 250 prescriptions/1000 inhabitants** and year
  - Target for 2011: decrease by 10% of the difference between current level and long term target

- The indicator was based on calculations from a diagnosis-prescribing study about respiratory tract infections in primary care

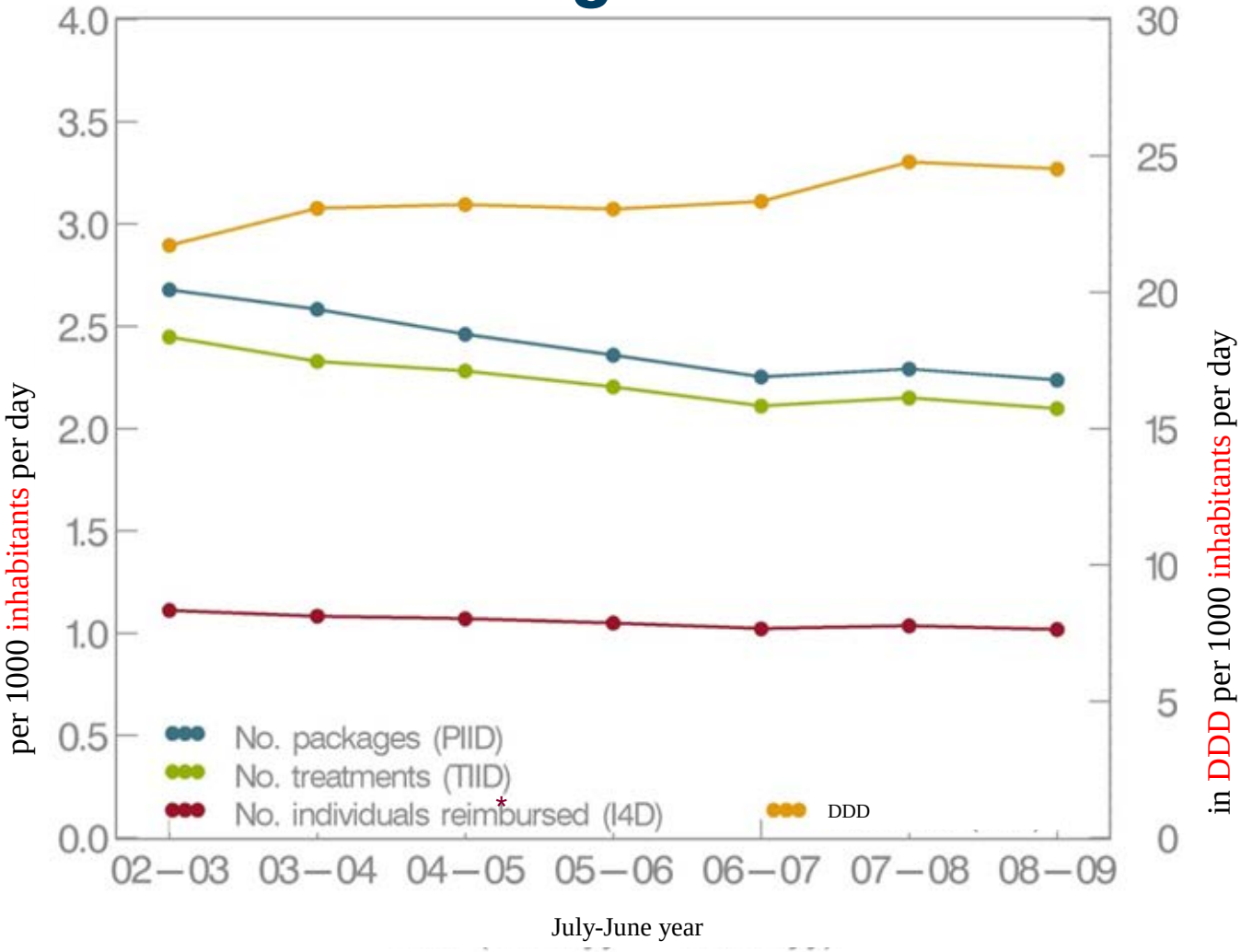
Which Indicator to Measure Antibiotic Use?

Packages or Defined Daily Doses or …



Outpatient antibiotic use in Belgium 1997 – 2010 July – June years

Outpatient Antibiotic Use in Belgium



* Excluding self-employed workers; insured only since '08

Coenen S et al. **JAC** 2013;68: online

Quality of Antibiotic Use

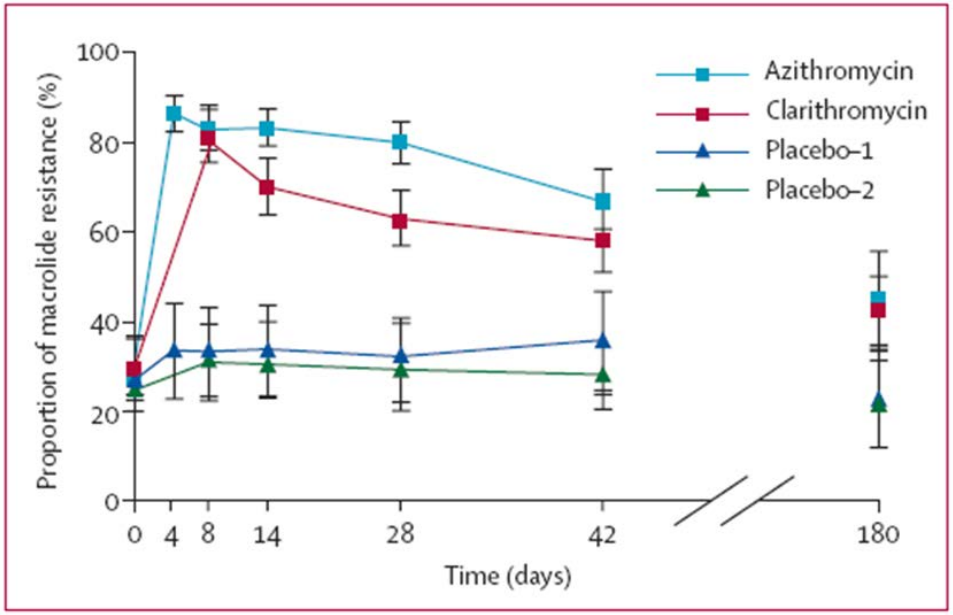
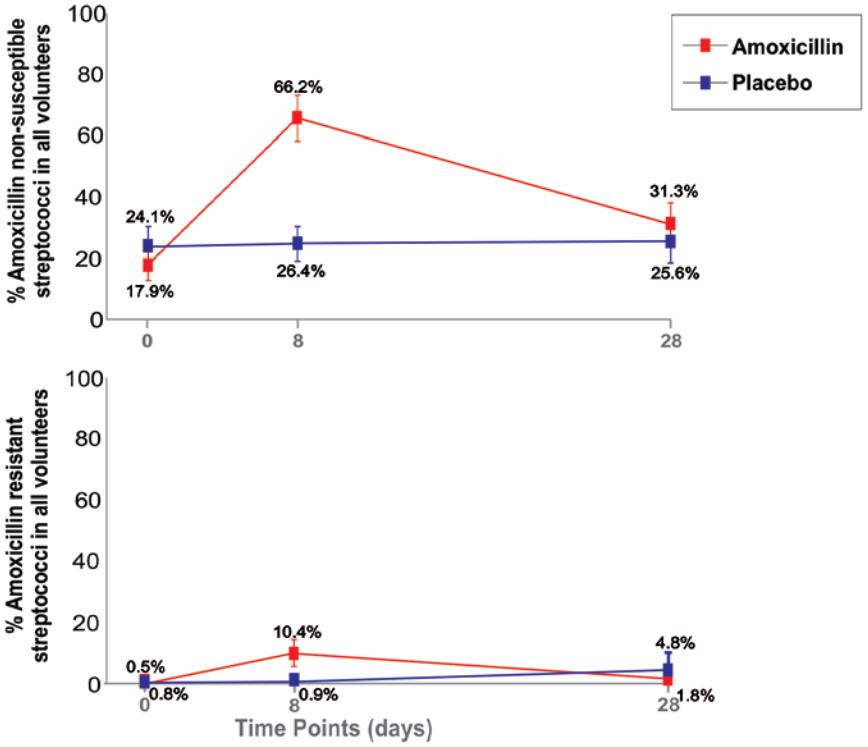


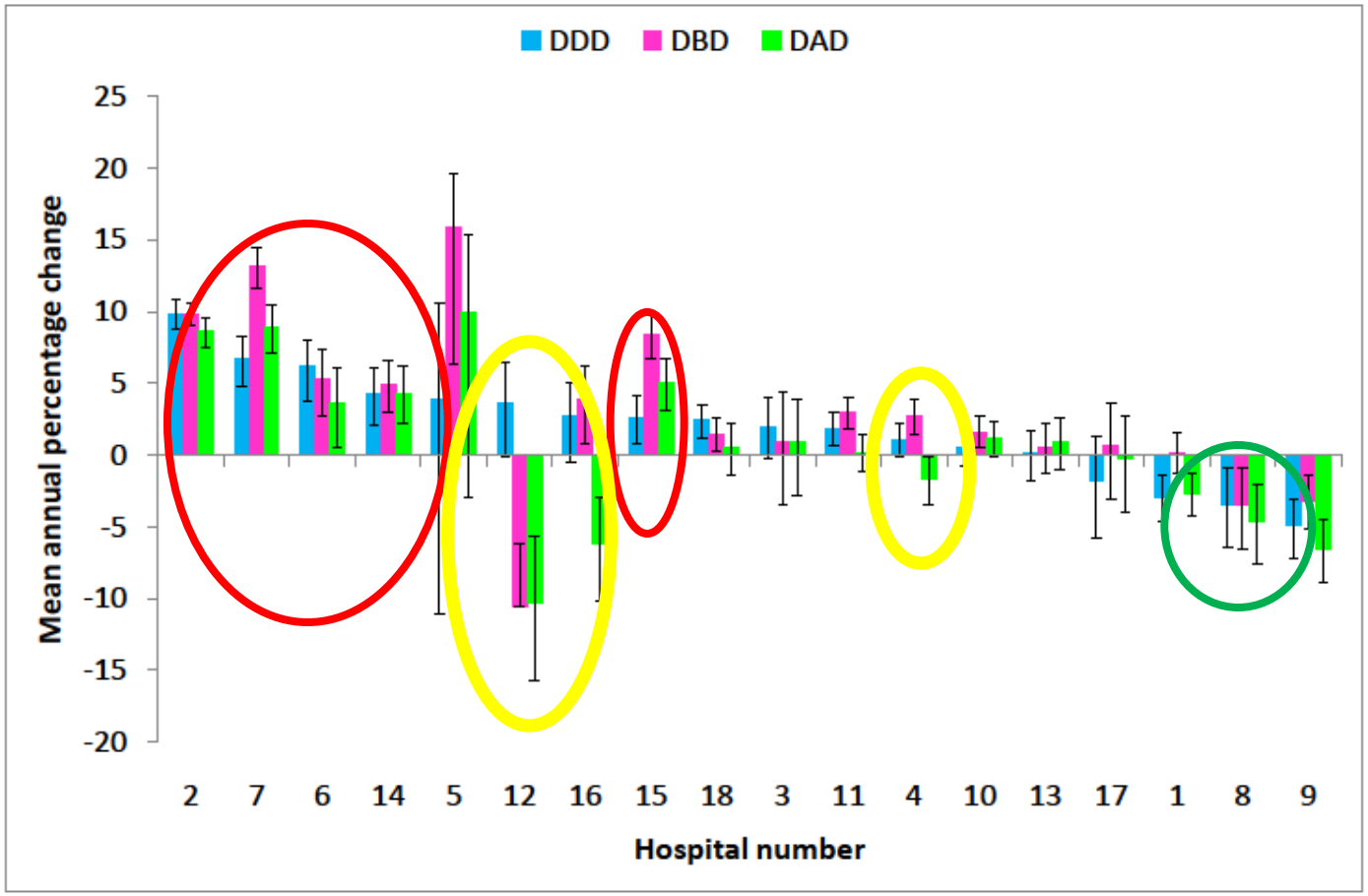
Figure 2: **Temporal changes in the proportion of macrolide-resistant streptococci after azithromycin and clarithromycin use**
Data shown are for all 204 volunteers followed through to day 42, and for 99 volunteers followed through to day 180. Error bars are 95% CI.

Malhotra-Kumar S, et al. Lancet. 2007;369:482-490.

Malhotra-Kumar S, et al. Lancet. submitted

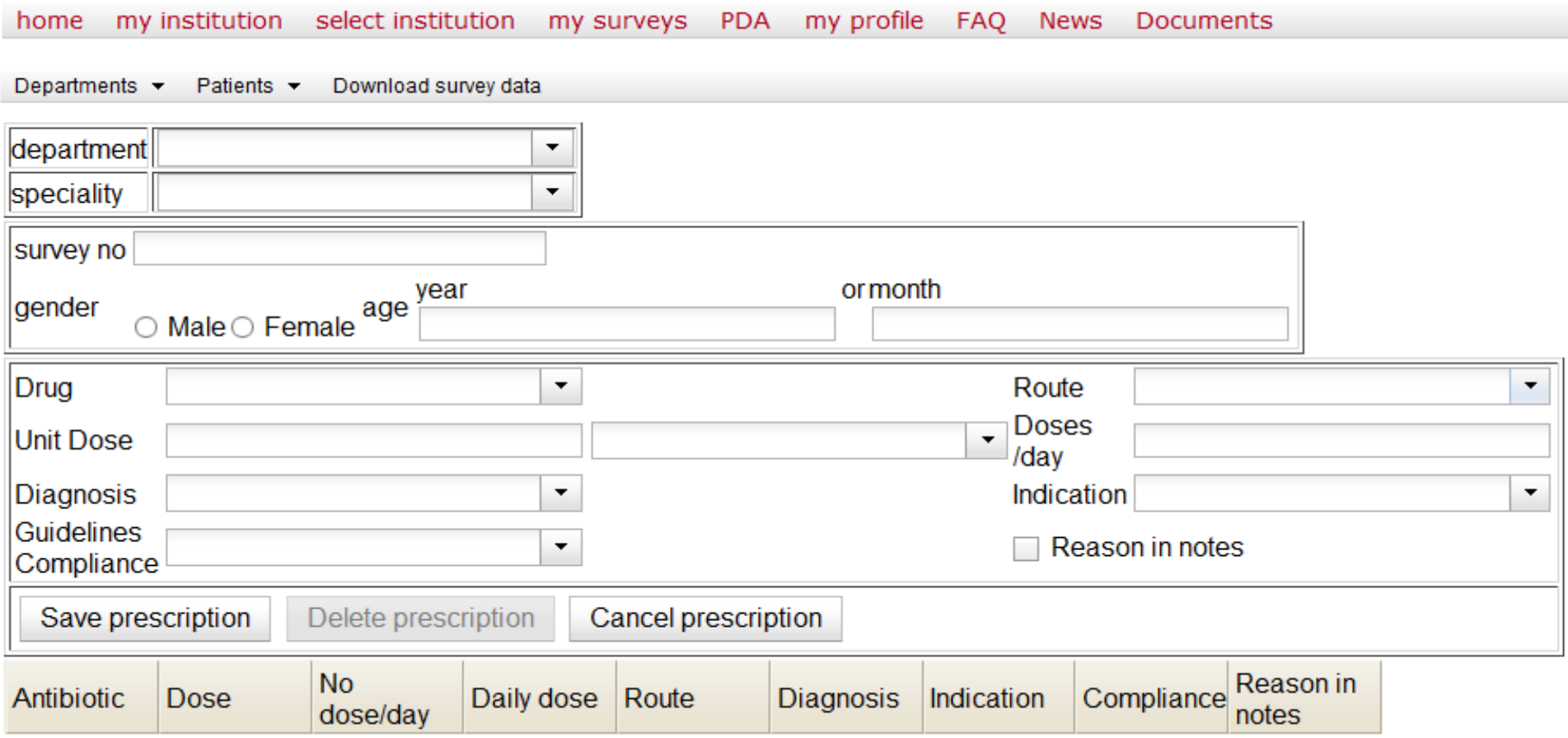


DDD, DBD & DAD



Ansari et al . **JAC** 2010; 65:2685-91

Web-Based Data entry

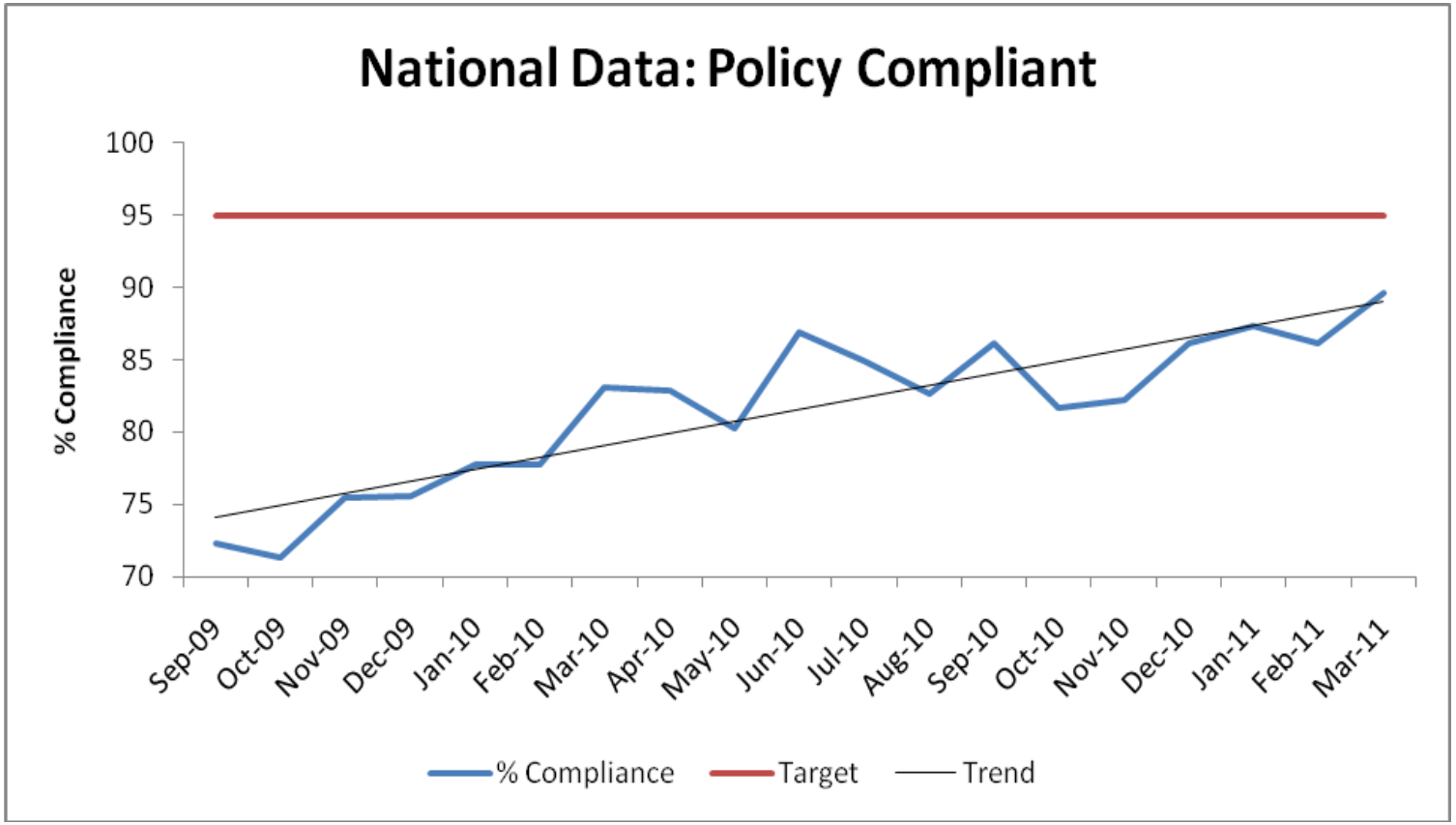


Scottish ESAC 2009 PPS

- Hospitals included: 31
- Patients included: 8,732
- Treated patients: 28%
- Areas of good practice:
  - Greater use of narrow spectrum antimicrobials compared to the rest of Europe
- Areas where improvement is required:
  - Indication documented: 76% (target: 95%)
  - Compliance with NHS Board guidelines: 58% (target: 95%)
  - Surgical prophylaxis greater than one day: 30%
  - Treated patients: 28%

Conclusion: better than European data but room for improvement

Results Scotland – Policy Compliant



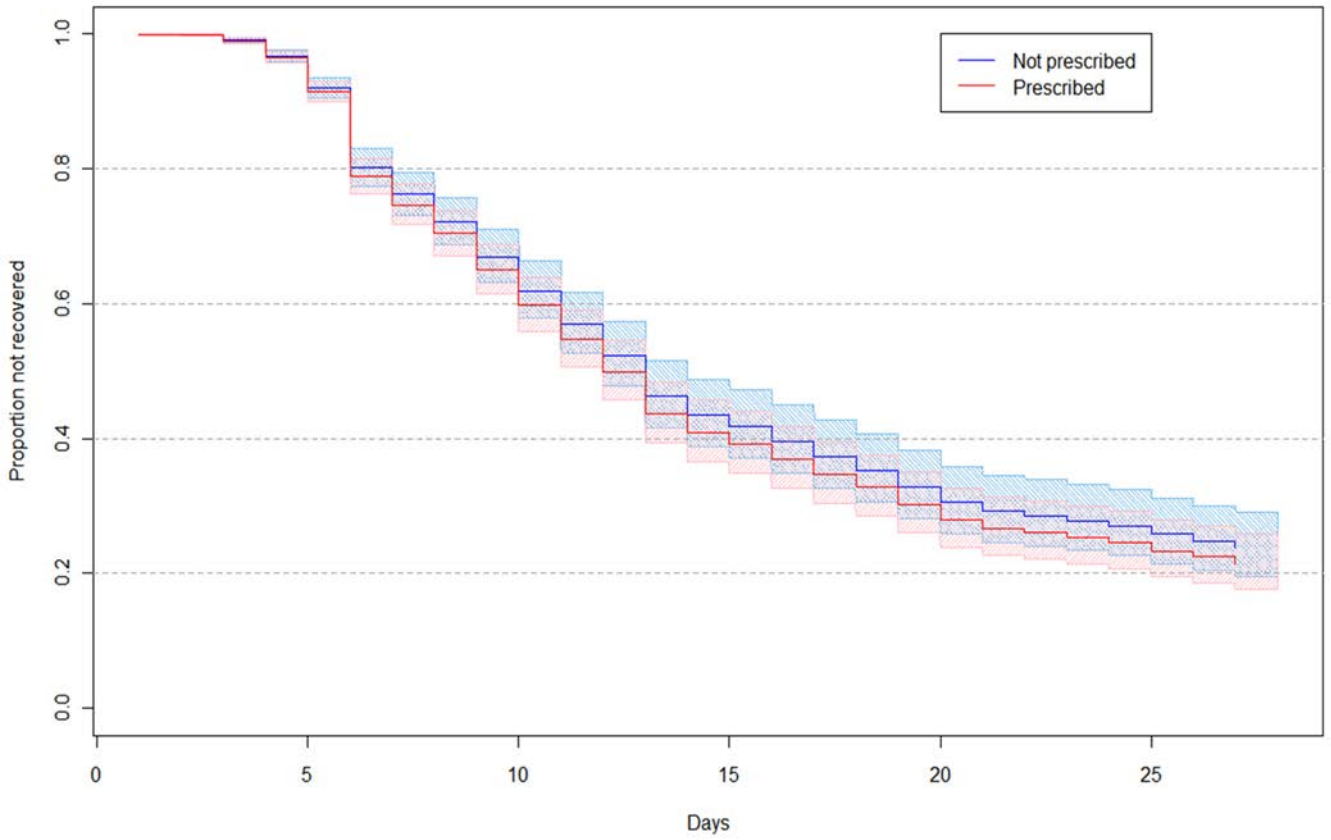
National compliance 83% and 4/14 NHS boards achieved target
2011 - need to focus on improvement

GRACE Studies (FP6 project)

- **Observational studies:**
  - About 4,200 patients consulting with acute (≤28 days duration) cough as the main symptom.
  - Antibiotic recovery, OTC, Adherence, Compliance
- **Randomised clinical trial:**
  - 2,061 adult patients with CA-LRTI
  - Interventions: amoxycillin 1 gr TID or placebo
- **Intervention trial:**
  - Baseline in 6,774 patients and 4,358 patients post-test
  - 2x2 factorial design (Communication, CRP, Usual care)

Primary Care Networks (n=20)

Proportion of adult LRTI patients not recovered against time (Kaplan-Meier)

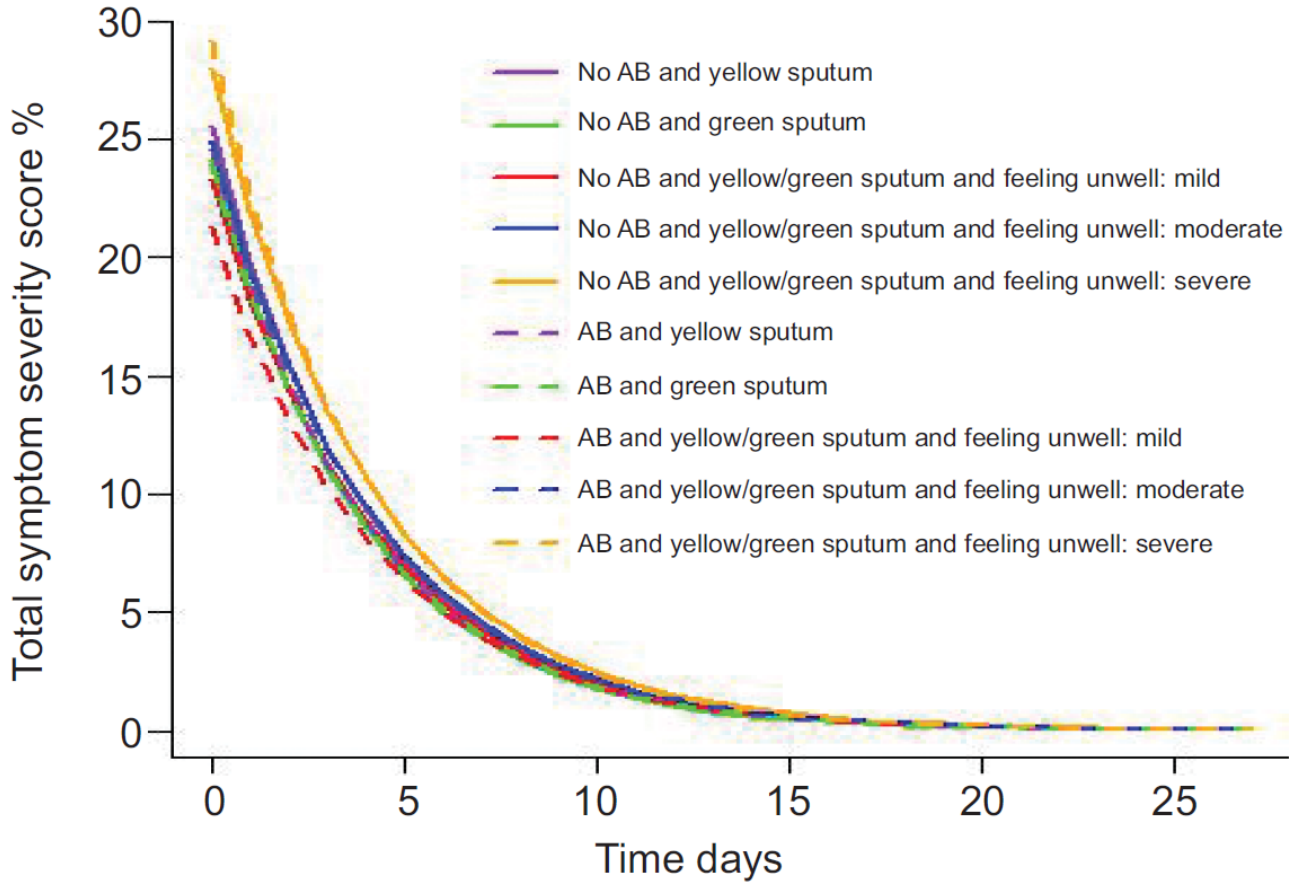


Butler C *et al.* **BMJ** 2009

Rapid response to the BMJ paper

“I am not surprised at these findings of the GRACE group …. Antibiotics in the otherwise healthy are only needed if the patient feels unwell or has purulent phlegm. ”

Proportion of adult LRTI patients not recovered against time (Kaplan-Meier)



Butler C *et al*. **Eur Res J** 2011;38:119-25

Conclusion

Discoloured sputum does influence clinician prescribing.

There was no association between antibiotic prescribing and patient recovery for any patient subgroup investigated

Antibiotic Self-Medication before Consultation by Country (n=2,530)

Belgium (n=327): 2.8%
England (n=196): 0.0%
France (n=30): 0.0%
Germany (n=171): 0.6%
Italy (n=43): 25.6%
Netherlands (n=277): 0.0%
Poland (n=506): 0.2%
Slovakia (n=130): 0.0%
Slovenia (n=130): 0.0%
Spain (n=492): 2.4%
Sweden (n=92): 0.0%
Wales (n=197): 1.0%

Hamoen et al, BJGP, submitted

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, Christopher C Butler, Maciek Godycki-Cwirko, Artur Mierzecki, Slawomir Chlabicz, Antoni Torres, Jordi Almirall, Mel Davies, Tom Schaberg, Sigvard Mölstad, Francesco Blasi, An 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

Interpretation

Our trial is the largest study so far of the use of antibiotics in acute lower-respiratory-tract infection, and adds much to the placebo-controlled evidence noted in the Cochrane review, especially data for patients aged 60 years or older.[16] Compared with placebo, amoxicillin did not significantly affect the duration of symptoms rated "moderately bad" or worse in the first few days of infection, neither overall nor in patients older than 60 years. Symptom severity also did not differ significantly between treatment groups. Amoxicillin prevented some patients from developing new or worse symptoms but the number needed to treat was high and matched by a similarly sized number needed to harm for side-effects. Our data suggest, if anything, a smaller benefit from antibiotics for symptoms and a clearer estimate of harms than did the Cochrane review. Thus, unless pneumonia is suspected, antibiotics should not be prescribed for patients with acute lower-respiratory-tract infection.

Funding European Commission Framework Programme 6, UK National Institute for Health Research, Barcelona Ciberde Enfermedades Respiratorias, and Research Foundation Flanders.

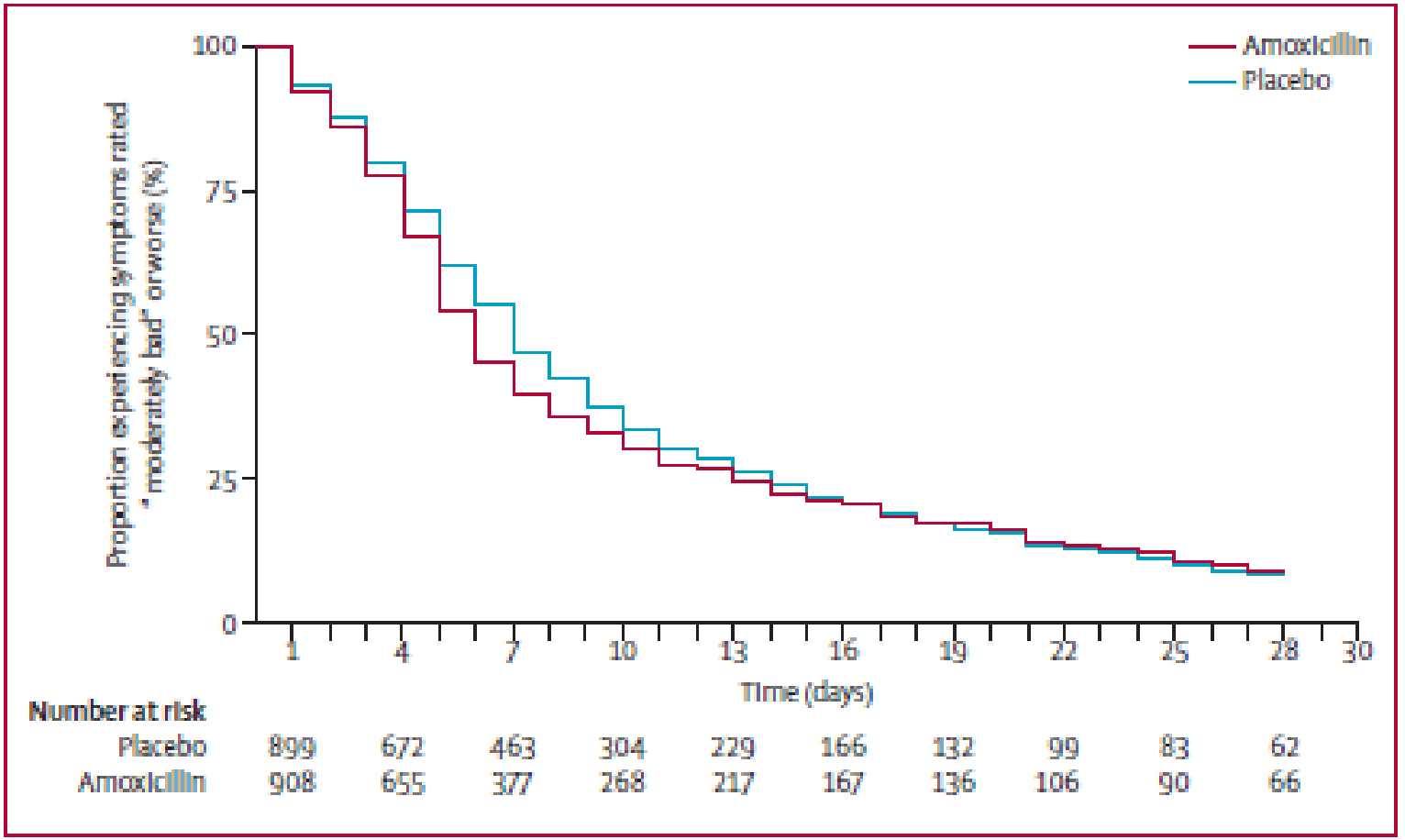


Figure 2: Kaplan-Meier estimates for duration of symptoms rated "moderately bad" or worse

Effects of internet-based training on antibiotic prescribing rates for acute respiratory-tract infections: a multinational, cluster, randomised, factorial, controlled trial

Paul Little, Beth Stuart, Nick Francis, Elaine Douglas, Sarah Tonkin-Crine, Sibyl Anthierens, Jochen W L Cals, Hasse Melbye, Miriam Santer, Michael Moore, Samuel Coenen, Chris Butler, Kerenza Hood, Mark Kelly, Maciek Godycki-Cwirko, Artur Mierzecki, Antoni Torres, Carl Llor, Melanie Davies, Mark Mullee, Gilly O'Reilly, Alike van der Velden, Adam W A Geraghty, Herman Goossens, Theo Verheij, Lucy Yardley, on behalf of the GRACE consortium

Funding European Commission Framework Programme 6, National Institute for Health Research, Research Foundation Flanders.

Little et al, Lancet 2013

GRACE Professional Intervention

- National implementation in Belgium
- Expand to other countries, other infections, children, choice of antibiotics

	Usual care	Communication
Usual care	Usual care 58%	Communication training 41%
CRP	CRP training 35%	CRP + Communication training 31%

MOSAR Studies (FP6 Project)

Interventions to reduce colonisation and transmission of antimicrobial-resistant bacteria in intensive care units: an interrupted time series study and cluster randomised trial

Lennie P G Derde, Ben S Cooper, Herman Goossens, Surbhi Malhotra-Kumar, Rob J L Willems, Marek Gniadkowski, Waleria Hyrniewicz, Joanna Empel, Mirjam J D Dautzenberg, Djillali Annane, Irene Aragão, Annie Chalfine, Uga Dumpis, Francisco Esteves, Helen Giamarellou, Igor Muzlovic, Giuseppe Nardi, George L Petrikkos, Viktorija Tomic, Antonio Torres Martí, Pascal Stammet, Christian Brun-Buisson, Marc J M Bonten*, on behalf of the MOSAR WP3 Study Team*

Interpretation Improved hand hygiene plus unit-wide chlorhexidine body-washing reduced acquisition of antimicrobial-resistant bacteria, particularly MRSA. In the context of a sustained high level of compliance to hand hygiene and chlorhexidine bathings, screening and isolation of carriers do not reduce acquisition rates of multidrug-resistant bacteria, whether or not screening is done with rapid testing or conventional testing.

Funding European Commission.

Conclusion

- The EU has funded many research projects which provided great evidence for better use and regulation of antibiotics
- However, translation of these scientific results into educational output to effectively change practice and antibiotic prescribing is a major challenge!

- And I honestly don’t know how to do that!