

## Editorial

## THE FIRST EUROPEAN ANTIBIOTIC AWARENESS DAY AFTER A DECADE OF IMPROVING OUTPATIENT ANTIBIOTIC USE IN BELGIUM

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The launch of the First European Antibiotic Awareness Day by the European Centre for Disease Prevention and Control (ECDC; <http://antibiotic.ecdc.europa.eu>) on November 18 this year, shows that antimicrobial resistance is still a priority for the EU and its member states.

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More than 10 years ago 'The Microbial Threat' was the first of a series of invitational EU conferences making antimicrobial resistance an official EU issue. (1) Its recommendations initiated the European Antimicrobial Resistance Surveillance System (EARSS; [www.rivm.nl/earss](http://www.rivm.nl/earss)), the European Surveillance of Antimicrobial Consumption (ESAC; [www.esac.ua.ac.be](http://www.esac.ua.ac.be)), and the establishment of antimicrobial National Focal Points like, for Belgium, the Belgian Antibiotic Policy Coordination Committee (BAPCOC; [www.health.fgov.be/antibiotics](http://www.health.fgov.be/antibiotics)). EARSS and ESAC data identified Belgium as one of the countries with high consumption and resistance, two characteristics significantly associated at an ecological level in Europe, (2) as well as showing a cause-effect relationship in a randomised controlled trial with healthy volunteers. (3) And since for humans most antibiotics are being consumed in ambulatory care, during the last decade several measures were adopted in Belgium at the national level to improve antibiotic use in ambulatory care. And these measures did not miss their effect on both outpatient antibiotic use and antimicrobial resistance.

### MEASURES TO IMPROVE OUTPATIENT ANTIBIOTIC USE IN BELGIUM

In Belgium, several national projects aiming to promote the prudent use of antimicrobials in ambulatory care were launched, ranging from national media campaigns to sensitise the public about the problem to the development of materials for all ambulatory care physicians.

*National public campaigns:* In December 2000, BAPCOC launched a media campaign, running three consecutive winter seasons and concentrating on simple messages that were conveyed through booklets, hand

outs, posters, prime-time television spots, and websites, like "Use antibiotics less frequently, but better", "Save antibiotics, they may save your life", and "Talk to your doctor, talk to your pharmacist". In November 2004, a new media campaign was launched, now using the slogan "Antibiotics are ineffective for common cold, acute bronchitis and flu" and running until last winter season.

*Professional interventions:* Up till now BAPCOC produced evidence-based guidelines using a state of the art methodology for the appropriate use of antibiotics in ambulatory care for acute sore throat, acute otitis media, acute cystitis in women, acute rhino-sinusitis, acute lower respiratory tract infections in adults, and acute exacerbation of COPD. All BAPCOC guidelines were disseminated among all relevant physicians (generalists and specialists) in ambulatory care in Belgium.

The guideline recommendations were supplemented by conclusions of systematic literature reviews to produce an antibiotic guide to support the antibiotic prescribing decision of physicians in ambulatory care. All general practitioners received a copy of the first antibiotic guide in 2006. A copy of the second edition will be distributed among all primary care physicians in November (4).

A consortium, including among others the Belgian National Service for Medical and Disablement Insurance (RIZIV), scientific colleges for general practitioners (Domus Medica and Société Scientifique de Médecine Générale (SSMG)), the Federal Knowledge Centre for Healthcare (KCE) and medical professional defence organisations, called Platform for Quality Promotion, has provided all general practitioners with feedback reports on their antibiotic prescribing behaviour in 2001, 2003 and 2006 in 2003, 2004 and in 2007, respectively. Paediatricians, ear-nose-throat specialists, lung specialists and urologists active in ambulatory care received 2002 data in 2004. All these primary care physicians were invited to discuss these feedback reports with their peers in so-called peer review groups under the expert guidance of animators, trained by the scientific colleges. Proof of such discussions and of a clear decreasing trend in antibiotic prescribing were set as conditions for an increase in the fee for service of general practitioners. The Platform for Quality Promotion also distributed three editions of a newsletter, Medflash, on antibiotics among all primary care physicians, in 2004, 2005 and 2006, respectively. The feedback documents and newsletter are available at the RIZIV website. (5)

Since 1999, the Belgian Centre for Pharmacotherapeutic Information (BCFI; [www.bcfi.be](http://www.bcfi.be)) regularly pub-

lishes articles on the rational use of antibiotics in primary care in the *Folia Pharmacotherapeutica*. The information on the rational use of antibiotics in acute respiratory and urinary tract infections was based on the conclusions of RIZIV consensus meetings on these topics, the latter building on systematic literature reviews and input from experts in the field. (6)

*Other projects:* Besides all these national efforts, several other projects on the appropriate use of antibiotics have been initiated in Belgium. During the Belgian presidency of the European Union in 2001, a European conference on antibiotic use in Europe was held to kick off ESAC. At the same time the Council Recommendation on the prudent use of antimicrobial agents in human medicine was voted by the ministers of health in the European parliament. (7) In 2004, an international workshop on educational campaigns was convened in Brussels, and in 2005 a European Science Foundation workshop on antibiotic prescribing quality indicators in Antwerp.

In Belgium, large European projects like ESAC and more recently Genomics to combat Resistance against Antibiotics in Community-acquired LRTI in Europe (GRACE; [www.grace-lrti.org](http://www.grace-lrti.org)) are being coordinated. And we are also a partner in several other European projects aiming to improve outpatient antibiotic use like for example Changing behaviour of Health care professionals And the general public towards a More Prudent use of antimicrobial agents (CHAMP) and Development and dissemination of a school antibiotic and hygiene education pack and website across Europe (e-Bug; [www.e-bug.eu](http://www.e-bug.eu))

## EFFECT ON OUTPATIENT ANTIBIOTIC USE IN BELGIUM

Outpatient antibiotic use expressed in the number of reimbursed packages per 1 000 inhabitants per day decreased by more than one third between the 1997-1998 and the 2006-2007 winter season in Belgium (RIZIV data). Comparing antibiotic use during the 2000-2001 and the 2001-2002 December-March periods with the same period in 1999-2000, controlling for the influence of influenza-like illness, showed a significant decrease for the first (6.5%) and a non-significant (3.4%) one for the second campaign of antibiotic use, expressed in the number of defined daily doses (DDD) sold (IMS-Health data). (8) That the decrease is less pronounced in DDDs than in packages (both RIZIV data) is due to the increase of the number of DDDs per package in the last decade. (9, 10) More recent work also showed that

the decrease in antibiotic use in packages, not in DDD, was significantly more pronounced since the start of the campaigns in Belgium, i.e. in 2000. (11)

While antibiotic use decreased, the proportional use of amoxicillin-clavulanate and of the so-called 'respiratory' quinolones showed a transient increase soon after the start of the public campaigns in Belgium. At this point, a substantial proportion of the amoxicillin-clavulanate and 'respiratory' quinolones use seems to have been replaced by the use of amoxicillin, as recommended in guidelines and the antibiotic guide.

### EFFECT ON ANTIMICROBIAL RESISTANCE IN BELGIUM

While penicillin, tetracycline and macrolide resistance in *S. pneumoniae* expressed as the proportion of non-susceptible isolates increased up to the year 2000, it has decreased substantially since then, from 18% to 10%, 32% to 23%, and 36% to 25%, respectively (data from the UZ Leuven Reference centre for *S. pneumoniae*). In the latter period macrolide resistance in *S. pyogenes* is decreasing as well, and it is currently estimated to be less than 2% (data from the University of Antwerp Reference centre for *S. pyogenes*).

Despite the spectacular decrease in the last decade of both outpatient antibiotic use and antimicrobial resistance of *S. pneumoniae* and *S. pyogenes* in Belgium, some questions however still need an answer.

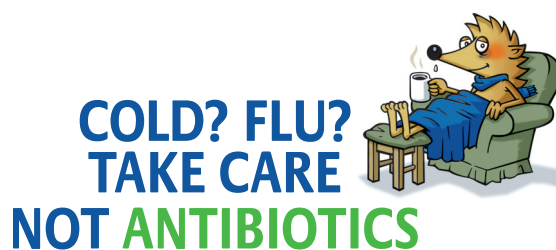
### UNANSWERED QUESTIONS

Do the data on antimicrobial resistance provide a valid estimate of the resistance problem in primary care? Although these data result from a selected group of patients sampled in both ambulatory care and in hospitals, they currently represent the best estimate. On the other hand, the data on outpatient antibiotic use for Belgium are considered to be valid, albeit that it is suggested to look at different outcome measures at the same time. After all, use expressed in DDD provided a quite different picture from use expressed in packages - the best proxy for prescriptions in Belgium.

Is there a cause-effect relationship between the decreasing outpatient antibiotic use and decreasing antimicrobial resistance? To assess the effect of an intervention, the ideal study design is a randomised controlled study. To assess the effect of the public campaigns and professional intervention the interrupted time series design currently is considered to be the best, and has been applied.

What element of the public campaigns and/or professional intervention contributes most to the improvement of outpatient antibiotic use? Although this is a difficult question to answer, most likely the former have had the most dramatic effect on the quantity of antibiotic consumption, whereas only the latter have the potential to improve the quality of antibiotic use, i.e. avoid over- as well as under-prescribing, and prescribe the best choice antibiotic. (12) Furthermore, it has been demonstrated that in order to improve antibiotic use multifaceted interventions are most successful. (13) Given the evidence that both quantity and quality improved, the Belgian initiatives will have had an impact on both public and professional awareness. Moreover, the latter was assessed after the first campaigns and shown to be true. (14) In addition, it is unlikely that we overlooked any important intervention as BAPCOC is coordinating most if not all of the activities related to antibiotic policy in Belgium.

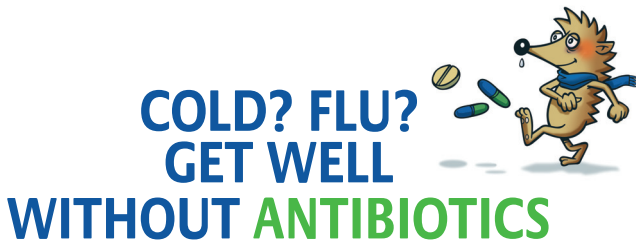
### TOWARDS A EUROPEAN ANTIBIOTIC AWARENESS DAY



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Similar initiatives have seen the light of day in France, another European country with high outpatient antibiotic use and high antimicrobial resistance. (9) The success of both France and Belgium in curbing antibiotic overuse and resistance resulted in a European initiative by ECDC, i.e. a European Antibiotic Awareness Day on November 18. (15) All countries with high outpatient antibiotic use and resistance are invited and supported to (further) improve their outpatient antibiotic use. ECDC has provided all member states with visuals (logos and slogans) tested and translated in all EU languages, key messages, guidance on how to organise a press conference to launch the day in their country (presentation slide kit, draft press release), and background material (in English only). ECDC slogans are very similar to the ones used in Belgium over the last four years: "Cold, flu? Take care, not antibiotics," "Cold, flu?"

Get well without antibiotics," but actions preferably have a special focus on young families and their children.



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## THE NEW PUBLIC CAMPAIGN IN BELGIUM

As there is still room for improvement, in Belgium a new public campaign has been launched ([www.gebruikantibioticacorrect.be](http://www.gebruikantibioticacorrect.be); [www.usagecorrectantibiotiques.be](http://www.usagecorrectantibiotiques.be)), in line with the European initiative, but taking into account the strengths and weaknesses of our previous campaigns, and the threats and opportunities for a new campaign, identified by the current members of the working group 'sensitisation' within BAPCOC coordinating the public campaigns in Belgium. TV was considered the most important medium, the content of last campaign's TV spots and website were appreciated a lot, and we believe in the success of our previous awareness campaigns and in the use of a gadget. To repeat the same message in the same way again was not an option. The special target group, the European initiative and the penetration of new media in Belgian households represent great opportunities for new campaigns, the sustainability of which could be hampered by the lack of structural funding for BAPCOC. In addition we hope we can avoid misuse of 'the microbial threat' by the pharmaceutical industry to promote use of (new) broad spectrum antibiotics as well as the difficult differentiation between viral and bacterial infections and their respective need for antibiotics. The lack of data on complications, to monitor a possible downside of reducing antibiotic use, was also acknowledged. The new campaign will thus use slogans in line with the previous campaigns as well as the ECDC visuals, and focus on antibiotic use in children. Although November 18 is a good moment to kick off the new campaign we will take into account that such a campaign is most effective during influenza epidemics. (8) We also aim to address all primary care physicians as well as the pharmacists, both with the public campaign and with scientific publications in their national journals.

## IN CONCLUSION

Although there are some limitations to link the decrease in outpatient antibiotic use and in antimicrobial resistance with the measures adopted in Belgium at the national level during the last decade to improve antibiotic use in ambulatory care, we believe we have a strong case that could serve as an example for other countries with high outpatient antibiotic use and resistance, as a stimulus to continue our effort to improve the quality of outpatient antibiotic prescribing in Belgium, and as an opportunity to further develop the methodology to assess the effect of public campaigns. Objectives that are all in line with the aims of the annual European Antibiotic Awareness Day.

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## REFERENCES

1. The Copenhagen Recommendation, Report from the EU Conference on the Microbial Threat; 1998.
2. Goossens H, Ferech M, Vander Stichele R, Elseviers M, and the ESAC Project Group. Outpatient antibiotic use in Europe and association with resistance: a cross-national database study. *Lancet* 2005;365:579-87.
3. Malhotra-Kumar S, Lammens C, Coenen S, Van Herck K, Goossens H. Impact of azithromycin and clarithromycin therapy on pharyngeal carriage of macrolide-resistant streptococci among healthy volunteers: a randomised, double-blind, placebo-controlled study. *Lancet* 2007;369:482-90.
4. Chevalier P, De Sutter A. Belgische gids voor anti-infectieuze behandeling in de ambulante praktijk. 2 ed. Brussels: Belgian Antibiotic Policy Coordination Committee; Federale Overheidsdienst Volksgezondheid, Veiligheid van de Voedselketen en Leefmilieu. 2008.
5. Nationale Raad voor Kwaliteitspromotie. Antibiotica feedback. [cited 24 October 2008]; Available from: <http://www.riziv.fgov.be/care/nl/doctors/promotion-quality/feedbacks/feedback-antibiotics/index.htm>
6. Comité voor de Evaluatie van de Medische Praktijk inzake Geneesmiddelen. Consensusvergaderingen - Juryrapporten [cited 24 October 2008; Available from: <http://www.riziv.fgov.be/drug/nl/statistics-scientific-information/consensus/index.htm>
7. Council recommendation of 15 November 2001 on the prudent use of antimicrobial agents in human medicine. Official Journal of the European Communities L34. 2002;45:13-6.
8. Bauraind I, Lopez-Lozano J-M, Beyaert A, et al. Association between antibiotic sales and public campaigns for their appropriate use. *JAMA* 2004;292:2468-70.
9. Goossens H, Guillemot D, Ferech M, et al. National campaigns to improve antibiotic use. *Eur J Clin Pharmacol* 2006 62:373-9.
10. Coenen S, Costers M, Goossens H. Comment on: Can mass media campaigns change antimicrobial prescribing? A regional evaluation study. *J Antimicrob Chemother*, 2007;60(1):179-80.
11. Davey P, Ferech M, Ansari F, Muller A, Goossens H, on behalf of the ESAC Project Group. Outpatient antibiotic use in the four administrations of the UK: cross-sectional and longitudinal analysis. *J Antimicrob Chemother* doi:10.1093/jac/dkn386: in press.
12. Coenen S, Van Royen P, Michiels B, Denekens J. Optimizing antibiotic prescribing for acute cough in general practice: a cluster-randomized controlled trial. *J Antimicrob Chemother* 2004;54: 661-72.
13. Arnold SR, Straus SE. Interventions to improve antibiotic prescribing practices in ambulatory care. *Cochrane Database of Systematic Reviews*. 2005, Issue 4. Art. No.: CD0035539. DOI: 10.1002/14651858. CD003539 Pub2.
14. Bauraind I, Vanden Bremt I, Bogaert M, et al. Evaluation of the Impact of a Public Campaign for a More Rational Use of Antibiotics in Belgium. 41st Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) [this conference was organized by the American Society for Microbiology {ASM} ]; 2001 December 16-19; Chicago, Ill; 2001.
15. Watson R. Multidrug resistance responsible for half of deaths from healthcare associated infections in Europe. *BMJ* 2008 June 7, 2008;336:1266-a-7.