The potential role of computerized decision support systems to improve empirical antibiotic prescribing

Peter Davey*

Health Informatics Centre, Division of Community Health Sciences, Mackenzie Building, Kirsty Semple Way, Dundee DD2 4BF, UK

Prudent antibiotic prescribing is a cornerstone of efforts to control the emergence and spread of antimicrobial resistance and to reduce the occurrence of Clostridium difficile associated diarrhoea, and is also currently the subject of a joint Working Party of the British Society for Antimicrobial Chemotherapy and the Hospital Infection Society. An article in this issue of the Journal describes a cluster randomized trial of an intervention to improve antibiotic prescribing using TREAT, a computerized decision support system. The results from this trial provide a significant contribution to the development of evidence-based prescribing of antibiotics.

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Prudent antibiotic prescribing is a key component of efforts to control antimicrobial resistance and Clostridium difficile associated diarrhoea. In this issue of the Journal, Paul et al. report the results of a cluster randomized trial of TREAT, a computerized decision support system. This is a pivotal trial seen from the perspective of the joint BSAC and HIS Working Party on Appropriate Antibiotic Prescribing in Hospitals. We reviewed the literature on interventions to change prescribing published up to November 2003. Sixty-six studies were included that met the eligibility and quality criteria of the Cochrane Effective Practice and Organisation of Care Group. The key issue in our discussion of this evidence base was validity, which is commonly divided into internal validity, external validity and construct validity. The 66 studies that were included in the review used study designs that had internal validity because they provided some protection against bias and confounding. External validity is concerned with the extent to which results can be applied or generalized to people, settings or times other than those that were the subject of the study. Multicentre studies provide reassurance that the intervention effect is not dependent on the structure or staffing of a particular hospital. Only five of the interventions were tested in multiple hospitals and only one of these multicentre studies was of an intervention to reduce antibiotic prescribing. The other four multi-hospital interventions aimed to improve the effective management of patients with bacteraemia or pneumonia. Finally, construct validity is concerned with the relationship between the study results and a theoretical construct of prudent prescribing. The main flaw in construct validity was that very few studies provided any reassurance about the unintended adverse consequences of interventions. For example, clinical outcomes were only reported for nine (16%) of the 57 interventions that primarily aimed to reduce antibiotic prescribing. The lack of clinical outcome data fundamentally weakens any estimates of cost-effectiveness. A second flaw in construct validity was that only one of the 66 studies addressed the decision to prescribe an antibiotic and the aim of this study was to increase the proportion of women who received prophylaxis for caesarean section.

The article by Paul et al. addresses all of these issues. The authors performed a cluster randomized trial of TREAT in three hospitals in Germany, Israel and Italy. The outcomes included length of hospital stay and 30 day mortality with the null hypothesis that the introduction of TREAT would not have adverse clinical consequences. The costs and benefits of the intervention are compared in Appendix II of the article. The intervention aimed to improve decision making by junior doctors, including the decision about whether or not to start antibiotics.

What were the results? The trial was preceded by an observational cohort study that established the impact that TREAT might have if it was used in clinical practice. For infections with an identified bacterial pathogen the empirical regimens recommended by TREAT were found to be appropriate in 70% of patients compared with 57% of the regimens prescribed by physicians. At the same time TREAT advised no antibiotic treatment for 23% of patients, whereas physicians gave antibiotics to all but 19% of patients. In the randomized trial TREAT significantly improved the probability that patients received appropriate antibiotics [odds ratio (OR) 1.48, CI 1.03–2.11]. Antibiotic costs and length of stay were significantly reduced in two of the three sites. There was no significant difference in 30 day mortality overall or within each site for all patients, those...
with infectious diagnoses or those with microbiologically documented infections. All of these results were based on intention-to-treat analysis, despite the fact that TREAT was used to manage only 134 (49%) of 273 patients in the intervention arm. In a per-protocol analysis (restricting the analysis to cases in which physicians prescribed an antibiotic identical to TREAT advice) patients in the intervention arm were much more likely to receive appropriate antibiotics than patients in the control arm (OR 3.40, CI 1.96–5.90).

What is the next step? TREAT is an example of a complex intervention in health care, which is built up from a number of components that include behaviours and methods of organizing and delivering those behaviours [e.g. type(s) of practitioner, setting and location]. In 2004, the UK MRC Health Services and Public Health Research Board published a framework for the evaluation of complex interventions. They proposed four phases to the evaluation of these interventions, analogous to the phases of drug development. The first two phases involve modelling and exploratory clinical evaluation, which have both been completed for TREAT. Phase III is the main randomized controlled trial to evaluate a complex intervention, analogous to the definitive pre-licensing trials in drug development. Phase IV, the final step in the evaluation of a complex intervention is a separate study to establish the long-term and real-life effectiveness of the intervention outside of a research context in an observational study. The next step for TREAT must therefore be observational studies in clinical practice. The randomized trial clearly shows that experience with TREAT is going to vary between hospitals; the more hospitals that can evaluate TREAT and report their experience the more we will learn.

The publication of this trial is timely. The public health importance of prudent antimicrobial prescribing rises as deaths from C. difficile associated diarrhoea increase. The BSAC/HIS Working Party will be revising its systematic review of interventions to improve antibiotic prescribing to hospital inpatients in November 2006. This trial of TREAT will make a significant new contribution to the evidence base.

Transparency declarations
The author is currently in negotiation with Judex, the company who developed TREAT, with a view to undertaking further evaluation of the system, but has no commercial or financial interest.

References