Effectiveness of physician-targeted interventions to improve antibiotic use for respiratory tract infections

Alike W van der Velden, Eefje J Pijpers, Marijke M Kuyvenhoven, Sarah KG Tonkin-Crine, Paul Little and Theo JM Verheij

Background
Antibiotic use and concomitant resistance are increasing. Literature reviews do not unambiguously indicate which interventions are most effective in improving antibiotic prescribing practice.

Aim
To assess the effectiveness of physician-targeted interventions in primary care, and to identify intervention features mostly contributing to intervention success.

Design and setting
Analysis of a set of physician-targeted interventions in primary care.

Method
A literature search (1990–2009) for studies describing the effectiveness of interventions aiming to optimise antibiotic prescription for respiratory tract infections (RTIs) in primary care, and to identify intervention features mostly contributing to intervention success.

Results
This study included 58 studies, describing 87 interventions of which 60% significantly improved antibiotic prescribing. Intervention features mostly contributing to intervention success were calculated. Association between intervention features and intervention success was analysed in multivariate regression analysis.

Conclusion
This review emphasises the importance of physician education in optimising antibiotic use. Further research should focus on how to provide physicians with the relevant knowledge and tools, and when to supplement education with additional intervention elements. Feasibility should be included in this process.

Keywords
antibiotics; primary health care; education; respiratory tract infections.

INTRODUCTION
Misuse of antibiotics is an urgent, progressive and worldwide public-health problem. Overuse of antibiotics in general and excessive use of broad spectrum antibiotics, have contributed to development of antimicrobial resistance.1 Non-indicated use of antibiotics is furthermore related to unnecessary exposure to adverse effects, costs and patients’ re-consultation.2–6 There is growing concern that therapeutic options become limited if resistance rates continue to rise. The most effective strategy for combating antimicrobial resistance is decreasing antibiotic use.4

The vast majority of antibiotics are used by primary care patients, mainly for respiratory tract infections (RTIs): otitis media, sinusitis, rhinitis, tonsillitis, pharyngitis, and bronchitis.5 RTIs are mostly viral and self-limiting, and therefore treatment effects of antibiotics are modest to negligible.6,7 Nonetheless, antibiotics are often prescribed for RTIs,7 while for the majority of patients watching waiting for the disease to run its natural course is the best approach.

In improving antibiotic use, primary care physicians and their patients are potential targets for intervention. For physicians, many guidelines have been published on appropriate treatment of RTIs. These appeared not to be sufficient enough to decrease antibiotic prescribing; implementing guidelines into daily clinical practice is hampered by factors like habits, lack of knowledge, and patients’ behaviour.5,11

Numerous interventions have been carried out, mainly in Europe and the US, with the aim to improve antibiotic prescribing practice. These are summarised in four qualitative and semi-quantitative reviews.10–12 However, there is still ambiguity whether multiple interventions are more effective than focused clinician education. In particular, the additive effect of audit/feedback, patient information material, involving other healthcare providers, remains unclear. By clarifying which intervention features mostly benefit, the complexity of implementing comprehensive interventions may be reduced.

The most recent review identified studies up to 2006,13 but there have been important studies since. As problems related to antibiotic overuse are still increasing there is a need for insight in effectiveness of interventions. As part of the European CHAMP project (Changing behaviour of Healthcare professionals And the general public towards a More Prudent use of antimicrobial agents) the study analysed an updated set of physician-targeted interventions. The study thereby aims to assess overall effectiveness and identify intervention features mostly contributing to a positive intervention outcome. The set contains a broad range of study designs and is limited to interventions concerning RTIs.

AW van der Velden, PhD, assistant professor; EJ Pijpers, MSc, PhD student; MM Kuyvenhoven, PhD, associate professor; TJM Verheij, MD, PhD, MRCGP, professor of general practice, Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, the Netherlands. SKG Tonkin-Crine, MSc, research fellow; P Little, MD, MRCP, FRCP, professor of primary care research, Primary Care and Population Sciences, Faculty of Medicine, University of Southampton, Southampton.

Address for correspondence
Alike W van der Velden, Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht (STR & 103), Heidelberglaan 100, 3584 CX Utrecht, the Netherlands.

E-mail: a.w.vandervelden@umcutrecht.nl

Submitted: 4 July 2012; Editor’s response: 28 July 2012; Final acceptance: 29 August 2012.

©British Journal of General Practice

This is the full-length article (published online 26 Nov 2012) of an abridged version published in print. Cite this article as: Br J Gen Pract 2012; DOI: 10.3399/bjgp12X522958
METHOD

Search and screening
A search in MEDLINE, EMBASE, and the Cochrane Library was performed from January 1990 to July 2009, using several combinations of the keywords (and synonyms of): antibiotic, primary care, intervention, respiratory tract infection, and the specific RTI diagnoses. In addition, reference lists were screened. Inclusion criteria were: an ‘intervention’ primarily targeted at ‘physicians’ in a ‘primary care’ setting aiming to ‘improve antibiotic prescription’ for ‘RTIs’, conducted in a ‘high-income country’, presenting a ‘standardised outcome’ of ‘(first choice) prescription’ measured in ‘defined daily dosage, prescriptions or rates’, and ‘published in the English language’.

Studies were screened on relevance using title, keywords, and abstract, and subsequently using the full texts, independently by two reviewers; disagreement was resolved by consensus or by arbitration of a third person. The main reasons for exclusion were a lack of standardised outcomes or a clear description of intervention features.

Data extraction
Study data were extracted using a structured form (based on the Cochrane Data Collection Checklist of the Effective Practice and Organisation of Care group) containing the following domains: study design, intervention characteristics (type – single/multiple/multi-target-, targets – physician, patients, others-, patients’ age, setting, targeted diagnoses), the elements the intervention was composed of, and outcome parameters.

Intervention elements were categorised into: distribution of educational material (for the physician, patients presenting with a RTI, all practice patients, or the general public), educational meetings, consensus procedure, educational outreach visits, local opinion leaders, near-patient information, audit and feedback, reminders, financial incentives, and communication skills training.

Analyses
Intervention effectiveness was calculated in terms of percentages: 1) the difference of differences (δδ) for interventions with a before and after measurement and a control group, 2) the difference (δ) for interventions with a before and after measurement without a control group, or 3) the difference in after measurement for interventions with a control group but without a before measurement.

For transparency and logistic regression analysis, effectiveness was categorised into ‘plus’ (a statistically significant decrease in total prescription, or increase in first choice prescription), ‘plus/minus’ (a non-significant decrease in prescription, or increase in first choice prescription), or ‘minus’ (interventions without an effect, or with a negative effect). Associations between effectiveness (‘plus’ interventions versus the rest) and intervention features were analysed in logistic regression analysis; characteristics and elements used in at least 15 interventions were used. Statistics were calculated using SPSS (version 17.0).

RESULTS

Description of included interventions
This review comprises 58 studies, describing a total of 87 interventions aiming to optimise antibiotic prescription for RTIs. The designs used most often were a controlled before after design (41%), and a randomised controlled trial (29%). The remaining studies were RCTs without baseline measurements, or had an interrupted time series-like design with one before and one after measurement.

Of the interventions, 59 (68%) aimed to decrease total prescription of antibiotics, and 28 (32%) to increase prescription of first choice antibiotics, 77% were multiple (intervention consisting of more than one element), and 40% targeted other groups besides the physician. The 87 interventions comprised 281 intervention elements (Table 1); educational material for the physician (n = 61), educational meeting (n = 49), and audit/feedback (n = 32) were most often used.

Effectiveness of the interventions
Overall, 60% of the interventions significantly decreased antibiotic use for RTIs.
improved antibiotic prescribing (Table 2), with interventions aimed at decreasing overall prescription being more frequently effective (73%) than interventions aimed at increasing first choice prescription (32%) (diff: 0.41; 95% confidence interval [CI] = 0.28 to 0.54).

With respect to the absolute outcome measures, overall antibiotic prescription was reduced by 11.6% and first choice prescription increased by 9.6% upon averaging the difference measurements of the individual interventions (Table 3). The extreme value of –72% in reducing overall prescription came from a study analysing the effectiveness of near-patient testing.26 Another extreme difference in this category, –44%, resulted from a combination of communication skills training and near-patient testing.28

**Table 1. Frequencies of intervention elements used within the 87 interventions (n = 281)**

<table>
<thead>
<tr>
<th>Intervention element</th>
<th>Frequency</th>
<th>%a</th>
</tr>
</thead>
<tbody>
<tr>
<td>Educational material for the physician</td>
<td>61</td>
<td>70</td>
</tr>
<tr>
<td>Educational meeting</td>
<td>49</td>
<td>56</td>
</tr>
<tr>
<td>Audit and feedback</td>
<td>32</td>
<td>37</td>
</tr>
<tr>
<td>Educational outreach visit</td>
<td>24</td>
<td>28</td>
</tr>
<tr>
<td>Educational material for RTI patients</td>
<td>21</td>
<td>24</td>
</tr>
<tr>
<td>Educational material for practice patients</td>
<td>17</td>
<td>20</td>
</tr>
<tr>
<td>Educational material for general public</td>
<td>15</td>
<td>17</td>
</tr>
<tr>
<td>Reminders</td>
<td>12</td>
<td>14</td>
</tr>
<tr>
<td>Consensus procedure</td>
<td>9</td>
<td>10</td>
</tr>
<tr>
<td>Communication skills training</td>
<td>8</td>
<td>9</td>
</tr>
<tr>
<td>Near-patient testing</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>Local opinion leader</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>Financial incentives</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>Otherb</td>
<td>14</td>
<td>16</td>
</tr>
</tbody>
</table>

*a% of interventions containing the particular element. bFor example, national policy, group discussions between physicians and patients, visiting a microbiology lab.

**Table 2. Proportion of effective interventions (n = 87)**

<table>
<thead>
<tr>
<th>Effectiveness category</th>
<th>AB n = 59</th>
<th>FC n = 28</th>
<th>Total n = 87</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plus</td>
<td>43 (73%)</td>
<td>9 (32%)</td>
<td>52 (60%)</td>
</tr>
<tr>
<td>Plus/minus</td>
<td>12 (20%)</td>
<td>17 (61%)</td>
<td>29 (33%)</td>
</tr>
<tr>
<td>Minus</td>
<td>4 (7%)</td>
<td>2 (7%)</td>
<td>6 (7%)</td>
</tr>
</tbody>
</table>

*AB = decreasing total antibiotic prescription. FC = increasing first choice prescription. Plus = a statistically significant decrease in total prescription or increase in first choice prescription. Plus/minus = a non-significant decrease in total prescription or increase in first choice prescription. Minus = interventions without an effect or with a negative effect.

**Associations between effectiveness rates and intervention features**

Within the 59 interventions aiming to decrease overall prescription for RTIs, the associations of various intervention features with effectiveness are shown in Table 4. Multiple interventions were more frequently effective than interventions using one element (odds ratio [OR] 6.5).

With respect to the most often effective intervention element, only educational material for the physician showed an independent association with a positive intervention outcome (OR 5.5).

As multiple interventions showed to be most often effective, various combinations of elements were tested for their combined effectiveness rate. Only the combination educational material for the physician with educational meeting yielded significance (OR 3.5; 95% CI = 1.2 to 10). In a multiple-target intervention, combining physician with patient education, a non-significant added value was found from adding educational material for patients (OR 5.8; 95% CI = 1-35).

**DISCUSSION**

**Summary**

Interventions aimed at reducing overall prescription were more frequently effective (73%) and had higher effectiveness (–11.6%) than interventions aimed at increasing first choice prescription (32% of interventions were effective, with a mean increase of 9.6%). Multiple interventions, which contained at least educational material for the physician, were most often effective. Non-significant added values were found for interventions which, in addition to physician education, contained information material for patients.

**Strengths and limitations**

This broad overview of physician-targeted interventions to improve antibiotic prescribing for RTIs is part of the CHAMP project. The aim of CHAMP was to review all available evidence of the effectiveness of interventions, campaigns, and projects, to obtain a complete picture of how to promote prudent antibiotic use. In propagating initiatives to restrict antibiotic use, such combined insight is pivotal in designing the most effective intervention.

A potential pitfall of making searches as complete as possible by including a broad variety of study designs is decreasing overall quality. The study rated the quality of all included studies,26 which offered the possibility to limit the analyses to moderate and high quality interventions; this did not
Table 3. Effectiveness outcomes of the interventions (n = 87)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Total AB, mean [range], %</th>
<th>n</th>
<th>First choice, mean [range], %</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>δδ</td>
<td>–8.7 [–27 to 18.8]</td>
<td>33</td>
<td>9.2 [–2 to 27.2]</td>
<td>15</td>
</tr>
<tr>
<td>δδ</td>
<td>–12.3 [–37 to 4.3]</td>
<td>16</td>
<td>11.1 [–5 to 41]</td>
<td>11</td>
</tr>
<tr>
<td>diff i-a</td>
<td>–20.3 [–72 to –1]</td>
<td>10</td>
<td>3.6 [0 to 5.1]</td>
<td>2</td>
</tr>
</tbody>
</table>

δδ = difference of differences for interventions with a before and after measurement and a control group. δ = difference for interventions with a before and after measurement without a control group. diff i-a = difference in after measurement for interventions with a control group but without a before measurement.

Table 4. Associations between intervention features and effectiveness rates (n = 59)

<table>
<thead>
<tr>
<th>Intervention features</th>
<th>n</th>
<th>Crude OR (95% CI)</th>
<th>AOR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>More RTI diagnoses*</td>
<td>42</td>
<td>1.7 (0.6 to 4.9)</td>
<td>2.5 (0.7 to 8.9)</td>
</tr>
<tr>
<td>More targets*</td>
<td>28</td>
<td>1.7 (0.7 to 4.7)</td>
<td>1.4 (0.4 to 4.7)</td>
</tr>
<tr>
<td>Multiple intervention*</td>
<td>46</td>
<td>7.6 (2.4 to 24)</td>
<td>6.5 (1.9 to 22)</td>
</tr>
<tr>
<td>Educational material physician</td>
<td>41</td>
<td>5.6 (2 to 16)</td>
<td>5.5 (1.7 to 18)</td>
</tr>
<tr>
<td>Educational meeting</td>
<td>35</td>
<td>2.4 (0.9 to 6.4)</td>
<td>2.1 (0.7 to 6.8)</td>
</tr>
<tr>
<td>Outreach visit</td>
<td>16</td>
<td>2.1 (0.4 to 6.8)</td>
<td>1.2 (0.3 to 4.5)</td>
</tr>
<tr>
<td>Educational material RTI patients</td>
<td>15</td>
<td>1.9 (0.6 to 6.2)</td>
<td>0.8 (0.2 to 3.3)</td>
</tr>
<tr>
<td>Educational material practice patients</td>
<td>16</td>
<td>1.9 (0.6 to 6.2)</td>
<td>1.4 (0.4 to 4.8)</td>
</tr>
<tr>
<td>Audit and feedback</td>
<td>20</td>
<td>0.9 (0.3 to 2.4)</td>
<td>0.5 (0.2 to 1.8)</td>
</tr>
</tbody>
</table>

AOR = adjusted odds ratio. OR = odds ratio. *Interventions targeted at more than one RTI diagnosis. *Interventions targeting other groups besides the physician. *Interventions consisting of more than one element. Multivariate regression analysis on interventions aiming to decrease overall antibiotic prescription. ±Statistical significance.

Funding
This work was supported by the Sixth Framework Programme of the European Commission in the context of the international collaborative CHAMP study: Changing behaviour of Healthcare professionals And the general public towards a More Prudent use of antimicrobial agents (reference: SP5A-CT-2007-044317).

Provenance
Freely submitted; externally peer reviewed.

Competing interests
The authors have declared no competing interests.

Acknowledgements
We thank our colleagues of the CHAMP consortium.

Discuss this article
Contribute and read comments about this article on the Discussion Forum: http://www.rcgp.org.uk/bjgp-discuss

Influence the conclusions (data not shown). Other possible limitations of combined effectiveness calculations are language selection, publication bias, and selection bias of participants. The study cannot rule out that it missed interventions, those reported in non-English, or unpublished ones, for instance because of negative or unwanted results. It is likely that physicians participating in the included interventions were motivated to learn and change their behaviour. For a broader implementation towards a possibly less motivated population, presented effects may be an overestimation.

The set of included studies is homogeneous with respect to primary target group (physician), indication (RTI), setting (primary care), and aim (optimise antibiotic prescribing). However, the authors are aware of heterogeneity with respect to outcome variables, baseline prescribing, intensity of interventions, and geographic location. Especially due to differences in outcome measures (for example, prescriptions or DDD per consultation, episode, patient, or inhabitant), absolute outcomes cannot be compared in a meaningful way, and this study therefore focused on significance of effectiveness. Logistic regression on a binary outcome was used to identify the intervention features which are associated with intervention success, to provide insight for an effective basic intervention which can be broadly applied. Given the inclusion criteria, it is obvious that the majority of interventions use educational material and/or meetings, of which only educational material appeared to be associated with intervention success. On the other hand, 40% of interventions also targeted patients with information material, and although effectiveness rates of these multitarget interventions were increased, this appeared not to be significant. This review thereby emphasises the central role of physician education and currently indicates less priority for extending these interventions with education directly delivered at patients.

Comparison with existing literature
Compared to the review of Arnold and Straus, this study specifically focused on physician-targeted interventions and RTIs, thereby identifying a new set of interventions; only 10 of the same studies appeared in both reviews. By the study’s specific search, a more homogeneous set of studies is obtained which facilitates comparability and quantitative analyses. Arnold and Straus concluded that interventions aimed at reducing overall prescription are less often effective than interventions aimed at increasing first choice prescription, while this study found the opposite. However, they included some less effective interventions aimed at decreasing antibiotic prescription for asthma, diarrhoea, and skin infections. The finding that multiple interventions are more often effective than single interventions is corroborated by others. However, two reviews concluded that multifaceted interventions, combining physician- and patient-targeted elements, are even more effective, and should be the approach to resolve antibiotic-related problems. The study’s finding that targeting patients besides the physician did not significantly increase effectiveness rates is remarkable. One may expect that increasing patients’ knowledge and awareness by offering information material, positively affect prescribing behaviour by decreasing pressure on physicians. A review of public campaigns to decrease antibiotic use suggested an effect of public education. However, all but one campaign targeted the public and physicians simultaneously, and it is therefore unclear whether the effects were
attributable to behaviour of physicians, patients, or both. The results are in line with a meta-analysis concluding that patient-oriented interventions have a very modest effect on antibiotic use, and that this effect was only due to delayed prescription by the physician.78

**Implications for clinical practice**

The conclusion that physician education is effective in decreasing antibiotic use relevant for primary care practice. However, the current situation shows that just delivering guidelines is not enough to restrict antibiotic prescribing. This review shows the need to intensify educational material by adding another element to create a multiple intervention. Which specific element to add will probably depend on the local situation, but various elements can be considered to adequately increase the impact of an intervention.

An educational meeting appeared more effective than audit/feedback and written patient information, but, on the other hand, is more labour intensive. Most studies indicate that patients are quite satisfied not receiving antibiotics as long as they are taken seriously, are being examined and get a proper explanation.76–80 The authors therefore hypothesise that it is more effective when patients receive explanation, reassurance, and antibiotic-related information from their own physician, specific to their own situation, instead of from written material. Time constraints and miscommunication between physician and patients about expectations of the consultation are thought to lead physicians to prescribe against their better judgement.81 Therefore, communication training, providing physicians with succinct and understandable arguments to communicate with their patients, should help to decrease antibiotic use. The few interventions using communication skills training appeared very effective.28,82 Another relatively new intervention element, near-patient testing, showed high effectiveness.26,28 Testing decreases diagnostic uncertainty of the physician, and concomitantly provides the physician with communication tools helping to explain treatment decisions to their patients.

These results emphasise the central role of physician education in decreasing antibiotic use. Ideally, a patient-centred element, teaching physicians how to efficiently communicate a clear take-home message and how to deal with patients’ concerns and pressure, should be included. Research is needed on how to broadly deliver education, and to identify the essential elements for an effective and versatile intervention.
REFERENCES


