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## Health Psychology Review

Publication details, including instructions for authors and subscription information:

<http://www.tandfonline.com/loi/rhpr20>

### Patient-oriented interventions to improve antibiotic prescribing practices in respiratory tract infections: a meta-analysis

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Available online: 24 May 2011

To cite this article: Bart Thoolen, Denise de Ridder & Gerty van Lensvelt-Mulders (2012): Patient-oriented interventions to improve antibiotic prescribing practices in respiratory tract infections: a meta-analysis, *Health Psychology Review*, 6:1, 92-112

To link to this article: <http://dx.doi.org/10.1080/17437199.2011.552061>

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## Patient-oriented interventions to improve antibiotic prescribing practices in respiratory tract infections: a meta-analysis

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(Received 16 August 2010; final version received 3 January 2011)

Antimicrobial resistance is a major public health issue and despite the growing awareness of this problem, antibiotic consumption remains common. Interventions geared towards the patient may be an effective means to reduce antibiotic overuse. The present study examines the effectiveness of patient-oriented interventions to promote more prudent use of antibiotics. Meta-analysis was used to evaluate the results of 28 studies describing patient-oriented intervention in terms of cognitive outcomes (attitudes and knowledge about antibiotics), use of antibiotics (self-reported by patients, prescription or dispensation rates), and patient satisfaction with treatment. Our findings demonstrate relatively small but consistent positive effects on cognitive outcomes, which were not moderated by any intervention characteristic (e.g., intervention setting or type of education materials). Findings also show moderate to large positive effects on the use of antibiotics: especially interventions promoting delayed or refused prescription proved very effective in decreasing the use of antibiotics. In contrast, interventions using other methods (any type of education) to decrease the inappropriate use of antibiotics were not effective at all. Interestingly, delayed or refused prescription did not affect patient satisfaction with treatment in a negative manner. Based on these results, it is concluded that the promotion of more prudent use of antibiotics in patients is better achieved by encouraging health professionals to delay or refuse the prescription of antibiotics rather than by educating patients about the negative aspects of antibiotics.

**Keywords:** antibiotic use; patient-oriented intervention; meta-analysis

Antimicrobial resistance is a major public health issue, and despite the growing awareness of this problem, antibiotic consumption remains common (Akkerman, Kuyvenhoven, Van der Wouden, & Verheij, 2005; Gonzalez, Malone, Maselli, & Sande, 2001). The vast majority of antimicrobial agents are prescribed to patients in primary care with (upper) respiratory and urinary tract infections (Akkerman et al., 2005; Gonzalez et al., 2001). These conditions are generally self-limiting viral infections, which can be treated with common over the counter medication. Nevertheless, many physicians continue to prescribe antibiotics for these conditions (Coenen & Goossens, 2007), despite the evidence that antibiotics are only marginally effective and can have considerable detrimental effects, including adverse effects on the patient, development of antibiotic resistant bacteria and increased health costs

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(Butler, Rollnick, Kinnersley, Jones, & Stott, 1998). In part, this over-prescription reflects a lack of knowledge and conviction on the part of the physician that antibiotics are not always a suitable line of treatment (Pontes & Pontes, 2003). From this perspective, interventions are needed which educate physicians in the more prudent use of antibiotics. From another perspective, however, overprescribing may also reflect the influence of patients in the medical consult. It has often been cited that family physicians may be under considerable pressure to prescribe antibiotics (Britten & Ukoumunne, 1997). Major contributing factors are explicit patient expectations and demands for antibiotics (André et al., 1997; Britten & Ukoumunne, 1997; Cockburn & Pit, 1997) and the physician's perception that patients expects antibiotics (i.e., implicit norms) (Arroll, Goodyear-Smith, Thomas, & Kerse, 2002; Palmer & Bauchner, 1997). Interventions geared towards the patient may therefore be an effective means to reduce antibiotics overuse, increasing patients' awareness of the negative aspects of antibiotics and thereby minimising the pressure on the physician.

This study reviews the content and effectiveness of interventions aimed at patients to reduce their antibiotic use. The last 10–15 years has seen a large number of such interventions implemented at both the community and individual level. It has been argued that a multifaceted approach is needed which targets the medical professional, the general public and specific patient groups, employing public relation campaigns, clinic-based education and community outreach programmes (Belongia & Schwartz, 1998). Increasing the public knowledge is generally seen as the key element of such interventions, with most intervention designs stressing the importance of clear, consistent messaging and the use of a mix of communications. This is not the first review to evaluate these interventions. Arnold and Strauss (2005), for example, did a systematic review of the effectiveness of professional and patient-based interventions in improving the selection, dose and treatment duration of antibiotics prescribed by health care providers in outpatient settings. They found that patient-based interventions were effective (small to moderate effects), particularly in the form of multifaceted interventions involving physician, patient and community education. In addition, their review demonstrated that interventions which used delayed prescription of antibiotics as the primary tool were the most effective. This particular review included only 12 studies with a patient- or community-based component, however. Similarly, a review by Raebel (2005) also found that patient-based interventions were variably effective, but again, the number of studies considered was limited. Neither review could identify underlying effective elements of such interventions. Another review (Spurling, Del Mar, Dooley, & Foxlee, 2007) specifically focussed on the effect of prescribing strategies on patients antibiotic use and found that delaying or avoiding antibiotics rather than providing them immediately reduces antibiotic use for acute respiratory infections, but can also reduce patient satisfaction. Finally, Homedes and Ugalde (2001) focussed on interventions in third world countries and found that patient-based interventions generally have only a small effect if at all but also points to the different situation in these countries in which antibiotic prescriptions are often acquired over the counter. Taken together, these reviews indicate that patient-based interventions can be effective, but it remains unclear which elements are effective.

The present review expands upon these previous reviews in three ways. First, it focuses on patient-oriented interventions to reduce antibiotic use. This review

thereby aims to provide more insight into the content and potentially effective elements of this specific group of interventions. In the second place, this review not only examines effectiveness in terms of antibiotic use, but also evaluates changes in cognitive outcomes such as knowledge, attitudes and satisfaction in patients, which are often the primary outcomes of such interventions. Finally, because of this, this review includes considerably more studies and therefore has more potential to identify effective elements. The main objective of this study is to systematically analyse the literature of interventions aimed at primary care patients in terms of their specific features and outcomes. Specific features in this meta-analysis include the target population, setting, interventionist, format, materials and conceptual basis of the intervention. Outcomes include antibiotic use and cognitive outcomes, including knowledge, attitudes, and satisfaction with treatment. The secondary objective of this review is to identify specific features of an intervention which are more or less effective in inducing change. The literature on interventions promoting a more prudent use of antibiotics advocates a multifaceted approach which targets both the general public and specific patient groups and includes a wide variety of interventions including public campaigns, community outreach programmes, and educational programmes in primary care (e.g., Belongia & Schwartz, 1998). This diversity calls for a critical assessment of which intervention components are the most effective. We will consider the following intervention moderators.

#### **Immediate vs. delayed or no prescription**

Instructing primary care physicians to refuse or give delayed prescriptions would appear an obvious and effective means of reducing antibiotic use. One may argue that interventions that manipulate the prescription of antibiotics by physicians are not truly patient-oriented intervention. However, previous studies have demonstrated that delaying or not giving a prescription can in itself change patient attitudes and appears to be equally effective as providing the patient with information (Arroll, Kenealy, & Kerse, 2003). Although the exact reason is unclear, it seems justified to assume that when a physician refuses or delays antibiotics, a certain amount of explanation will be given to the patient and that this information is well received by the patient at the very moment that he or she wants medical help. In the present meta-analysis, the effects of delayed or no prescription will be compared to interventions that directly aim at patient behavioural change and with knowledge and attitudes, antibiotic use, and patient satisfaction as outcomes.

#### **Patients/community with or without additional physician training**

Previous studies typically have found that multifaceted interventions targeting both the physician and the patient are more effective than interventions focusing solely on the patient and/or community (Arnold & Strauss, 2005). In the present meta-analysis, we will compare interventions aimed at patients (or the community) with interventions aimed at patients (or the community) that are supplemented by some kind of education for physicians on how to communicate information about antibiotics to patients. As antibiotic use is in part determined by the way physicians deal with patient expectations about antibiotics, one would expect interventions which help physicians in their communication with patients to be more effective.

**Community vs. primary care setting**

This specific factor raises the question where interventions can best take place, in the primary care setting or in the wider community. Community-based interventions can reach more people, but it is questionable whether the majority attend to the message when it is not relevant to them (i.e., when they are not ill). Interventions targeting the wider community have been found to be effective in changing attitudes about antibiotic use, but changes may fade before they can become effective (when patients consult the physician for a condition potentially requiring antibiotics) (Belongia et al., 2005). In contrast, interventions taking place in a primary care facility address people who are ill and potentially expecting antibiotics for a specific condition. Furthermore, as an authority figure, the physician may be more convincing than written or oral communication in the wider community. Therefore, one would expect interventions taking place in primary care to be more effective than community-based interventions.

**Written vs. oral or combined communication**

This factor examines which format is the most effective: oral interventions (e.g., group education), written interventions (e.g., brochure) or those combining the two. We expect oral interventions to be more effective than the written, as this allows more direct communication about patients' existing knowledge and attitudes. We also expect that a combination of oral and written will be the most effective, as the message is brought across in multiple ways, with more repetitions and more likely to meet individual information processing styles.

**Illness focus: general vs. specific and upper vs. lower respiratory infections.**

Based on the available studies, it will be examined whether interventions are more effective in specific categories of diseases. One could expect interventions to be more effective in upper respiratory tract infections than in lower respiratory tract infections (where antibiotics are more often necessary). One could also expect interventions to be more effective when they focus on a specific disease (e.g., otitis) rather than on respiratory tract infections or infections in general, as the information given can address specific symptoms and alternative remedies of a specific disease.

**Interventions with a theoretical basis vs. non-theoretical studies**

Theoretically based interventions are generally regarded to be more effective in changing attitudes and behaviours (Finch, Metlay, & Baker, 2004). Specifically, the potential of theoretical models such as the Stages of Change Model and Social Learning Theory has been put forward (Finch et al., 2004). Similarly, it has been argued that the model of shared decision making could introduce a theoretical perspective which could potentially make interventions more successful (Butler, 2001). Studies were regarded as having a theoretical basis when the variables that were assessed were explicitly derived from and interpreted in the context of a particular theory. It will be examined if theory-based interventions are indeed more effective than those in which information is provided without any theoretical consideration, and which theories appear most promising in the context of antibiotic use.

### **Interventions targeting parents vs. adults**

We will examine whether parents are more open to interventions when their children are involved than when they themselves are the patient. As a parent, people may be more protective of their children, visit the physician more often when their child is sick and expect antibiotics. However, they also may therefore be more open to information indicating the dangers of antibiotic treatment.

### **Sociodemographic factors**

Lower education level, ethnic background and socioeconomic background have all been linked to lower knowledge about, increased expectations for, and higher use of antibiotics. As there is more room for change in these groups we would expect intervention effects to be greater. Where possible these patient variables will be included in the analyses.

### **Method**

#### ***Selection of studies***

This review is based on recent literature, published from 1993 to 2008, and listed in the PSYCINFO, EMBASE or MEDLINE databases. Following the recommendations by Lipsey and Wilson (2001), search engines were browsed with the following terms which were combined using “AND” to limit the retrieved studies to those involving interventions and antibiotic use in the primary care setting and/or community: antibiotic\* or antimicrob\*; respiratory tract or urinary tract or sore throat or cough or otitis or bronchitis or pneumonia or tonsillitis; intervention or education or feedback or program\* or course; patient\* or outpatient or public or community or parent or general practice or ambulatory care or primary care or family practice; use or behaviour or prescription or dispensation or knowledge or expectation or belief or attitude or satisfaction. Abstracts retrieved in the search were reviewed for potential inclusion by the second author. Initial selection was lenient and based on the criteria described in the next section. Subsequently, relevant articles were retrieved and the content was analysed. In a second stage, the reference lists of eligible articles were browsed for additional studies not found via the initial search.

#### ***Criteria for including studies***

##### *Type of studies*

All randomised and quasi randomised controlled trials and controlled before and after studies were included. Studies with a single outcome following the intervention were included if a control group was present.

##### *Type of participants and settings*

As all members of a community are potentially patients in primary care, we included interventions geared to the general public in addition to those targeting patients in general practice or outpatient clinic. Interventions thus included (1) Patients in the consulting room of a primary care facility; (2) Patients in the waiting room;

(3) (Specific) populations of a primary care facility; and (4) (Specific) members of the public.

#### *Types of interventions*

Interventions were included if they addressed the knowledge, attitudes and/or behaviours of patients or public with regard to antibiotic use. These included (1) Different prescription styles (no or delayed prescription or watchful waiting versus immediate prescription); (2) Distribution of education materials (brochures, posters, newspaper, television, internet or other audio-visual), which may have been delivered personally or through mass mailings; (3) Individual oral sessions with physicians or nurses; or (4) Educational (group) meetings (in general practice, school, day care, or other facility). An important objective of the present meta-analysis was to determine which concepts derived from psychological theories on behaviour change would contribute to the effectiveness of interventions. Unfortunately, most studies did not report adequately on the concepts that were used or employed scales that were specifically designed for that particular study, making it impossible to categorise outcome variables in terms of well-defined concepts, such as attitudes, outcome expectancies, risk beliefs, subjective norms, or perceived control.

#### *Type of outcomes*

Effects of interventions were evaluated in terms of (1) knowledge and attitudes about antibiotic use, (2) antibiotic use, measured in terms of prescription rates, dispensation by pharmacy or self-reported by the patient, and (3) satisfaction with treatment.

#### *Statistical information*

To be included, studies required at the minimum a pre–post test outcome and/or a control group when outcomes were measured only after the intervention. Furthermore, to calculate effective sizes (if not given), outcomes had to be reported in terms of either percentages or means, and include either a standard deviation or specific p value (Cooper & Hedges, 1994; Lipsey & Wilson, 2001).

#### *Data coding*

Data abstraction was performed by the first two authors using a template specifically designed to assess intervention studies (Van Lensvelt-Mulders, Hox, Van der Heijden, & Maas, 2005). This detailed coding format includes information on study design (degree of randomisation and control), methodological quality (adequate description of method and intervention; sample size at baseline and, if applicable, at follow-up), participant information (sample type (clinical or community), age, gender, non-response, and drop-out), intervention characteristics (target, setting, material, length, and theory) and outcomes (description of measures, statistical measures, time interval between intervention and assessment of outcomes).

The first 10 studies were coded by two independent coders (the first two authors). The independent codings showed marginal differences which were resolved by considering the original study. Interrater agreement was very good, with an average

Cohen's kappa of about 90%. The remainder of the studies were coded by the first author (BJT).

In studies containing two experimental conditions (e.g., delayed and refused prescription), the effectiveness of each experimental condition was compared separately with the control condition (e.g., immediate prescription). Similarly, when outcomes were reported separately for two different groups of patients (e.g., adults and children), the study was treated as two separate sub-studies. Effective sizes were calculated and reported separately for each sub-study comparison.

Outcomes were recorded as presented in the study, including as much statistical information as possible. In case of multiple outcomes, for example, when knowledge was measured with separate items, we calculated wherever possible an overall score for this outcome. Where baseline results were available, pre-intervention and post-intervention means were reported for both study and control groups, and difference in absolute change from baseline was calculated along with *p* values if available. When baseline data were not available, results were expressed as relative percentage change (the difference between the intervention and the control group at post-intervention). Where trials compared more than one intervention, comparisons of each intervention to the control group were handled separately.

### *Analytic strategy*

Subsequent analyses were based on the most common form of reporting on the outcomes (antibiotic use, knowledge, and satisfaction). With regard to all outcomes, we ultimately chose to analyse the effectiveness of the intervention (and specific components) based on the post-intervention comparisons between intervention and control groups. Very few studies included both pre- and post-test scores, and we therefore limited ourselves to the latter.

The meta-analysis first assessed overall effective size and variation in effective sizes, presented in per cent difference between control and experimental condition (Cohen's *d*). Cohen's (1992) guidelines for interpreting average effective sizes were used: *d*'s about 0.20 were considered small, about 0.50 moderate, and  $>0.80$  were considered large. Next, we examined heterogeneity between conditions based on a homogeneity analysis whereby *Q* score indicates the degree of heterogeneity. When the *Q* score is significant, variation between studies cannot be explained by sampling error alone. A mixed random effects model was employed to examine potential predictors of variance. We first included study quality descriptors, including study year, country, and whether or not randomisation took place. Subsequently we included intervention moderators which we hypothesised could influence the effectiveness of the interventions. Finally, if possible, we used regression analysis to examine the relative effects of different predictors. However, as the number of studies (comparisons) was generally too small per outcome and not all predictors were reported in each study, we also had to rely on a series of ANOVAs to examine separately the potential effects of each factor.

First, we will report descriptive data of the studies included in the analysis. Next, we will describe about the outcomes of interventions in three sections, addressing attitudes and knowledge about antibiotics, antibiotic use, and satisfaction with treatment respectively.

## Results

### *Description of retrieved and selected studies*

The result of the initial search in the electronic databases was 1922 hits in MEDLINE, 238 in EMBASE and 233 in PSYCINFO.<sup>1</sup> Based on the abstracts, the initial search uncovered 194 studies which focused on patient-related outcomes in relation to antibiotic use. Of these, 166 studies were excluded as these were not intervention studies ( $n = 123$ ) or intervention studies which did not include a patient-oriented component ( $n = 22$ ), did not report clearly on the effectiveness of the intervention ( $n = 8$ ), did report on patient medical outcomes only ( $n = 2$ ), gave inadequate or unclear statistical information or had a poor design without a control group ( $n = 11$ ). This resulted in 28 articles which were deemed fit for further analysis.

### *Study characteristics*

The 28 retrieved studies were published between 1997 and 2008, the majority having been conducted in the USA ( $n = 16$ ) and the UK ( $n = 6$ ). In 18 studies, the control group received usual care. In the other 10 studies, patients in the control group also received what could be considered an intervention (e.g., information). With regard to randomisation, 19 studies used some form of randomisation, either at the patient level ( $n = 9$ ) or at the practice or community level ( $n = 10$ ). Studies varied considerably in their sample size, from less than 100 participants ( $n = 2$ ) to entire communities or states ( $n = 9$ ).

### *Participant and intervention characteristics*

There was considerable variation in the types of population which were targeted: 20 studies focused on patients within the primary care setting and eight studies approached specific groups in the community. Most studies reported on patient-oriented interventions without an additional GP component ( $n = 16$ ); the remainder reported on patient-oriented interventions that were supplemented by some kind of education for physicians ( $n = 12$ ). Half of the interventions ( $n = 15$ ) targeted parents, 13 targeted adults or did not focus on a specific age group. With regard to illness-focus, 15 studies addressed antibiotic use in upper RTI (of which eight a specific illness, such as otitis or sore throat), six focused on lower RTI, five on RTI in general, and two on infections in general. Only four studies described an explicit theoretical background of the intervention. Studies generally gave a poor description of the sample, often not indicating age groups, gender or socioeconomic background of participants, making comparisons of participant features impossible. Table 1 provides an overview of the associations between the main moderator variables, showing that, in general associations between intervention characteristics were modest. There was a significant correlation, however, between prescription style (whether or not the prescription of antibiotics was refused or delayed) and the inclusion of a GP component in the intervention. In addition, prescription style also varied with the intervention setting (primary care facility vs. community) and the types of materials used (written vs. oral or a combination of materials), albeit not significantly. These associations between intervention characteristics are not surprising and mostly relate to the setting of the intervention which is associated

Table 1. Correlations between moderators.

	1	2	3	4	5
1 Setting					
2 Materials	0.32				
3 Illness focus	0.21/0.23	0.28/0.26			
4 Age focus	0.05	0.08	0.05/0.08		
5 GP component	0.34	0.30	0.19/0.16	0.09	
6 Prescription	0.40	0.35	0.27/0.25	0.10	0.41*

\* $p < 0.05$ ; significance levels may vary per correlation due to the different number of studies reporting on the specific intervention characteristic.

Note: Setting (primary care vs. community); Materials (oral or combined vs. written only); Illness focus (URT vs. LRT/generic vs. specific); Age focus (parents vs. all age groups); GP component (either or not GP training); Prescription (refused/delayed prescription vs. immediate prescription).

with a number of other intervention characteristics that are also determined by setting (e.g., an additional training for the GP can only be delivered when the intervention takes place in the primary care setting). We will address the potentially moderating effects of intervention characteristics separately to determine which factors matter most.

### ***Effects on knowledge and attitudes***

Eleven studies assessed the knowledge and attitudes about antibiotics of (potential) patients. There was considerable variation in the measurement of outcomes. For example, what one study labelled knowledge, another study considered to be beliefs in effectiveness, making it impossible to categorise variables in terms of more sophisticated psychological constructs). Furthermore, many studies failed to report on the psychometric qualities of these scales. Overall, the most common outcome was a single post-intervention measurement of knowledge or attitudes comparing an experimental condition with another condition. Effective sizes were calculated based on the difference between the control and intervention groups after the intervention. Some studies included multiple comparisons and were thus treated separately in the analyses. Overall, 11 studies were examined in 15 comparisons encompassing 28 conditions. As can be seen in Table 2, seven comparisons primarily investigated the effects of no or delayed prescription versus immediate prescription of antibiotics on patient knowledge and attitudes. The other eight comparisons involved interventions employing information provision in the form of brochures or leaflets ( $n = 2$ ), video ( $n = 2$ ), group course ( $n = 2$ ) or multiple modes of information provision ( $n = 2$ ). In each case, the control group did not receive any intervention.

The overall effective size was significant but small ( $d = 0.23$ ,  $p < 0.001$ ), indicating that the knowledge and attitudes in the experimental conditions slightly improved compared to the control condition after the intervention. Effective sizes  $d$  ranged from 0.00 to 0.42, with five studies showing small to moderate effects (0.30–0.50), five studies showing small effects between 0.20 and 0.30 and the remainder showing negligible effects  $< 0.20$ . The  $Q$  score of 220.31 ( $df = 15$ ,  $p < 0.001$ ) revealed considerable heterogeneity between studies, indicating that the variance could not

Table 2. Content and effectiveness of the interventions investigating effects on knowledge and attitudes about antibiotics in patients.

Study	Control condition	Experimental condition	ES <i>d</i>
Arroll et al., 2002 (New Zealand)	Immediate prescription	Delayed prescription (3 days)	0.00
Bauchner, Osganian, Smith, and Triant, 2001 (USA)	No intervention	Video and brochure	0.27
Cebatorenco and Bush, 2008 (Moldavia)	No intervention	Student (aged 12–13) taught group education.	0.24
	No intervention	Adult group education, multiple materials	0.42
Croft et al., 2007 (UK)	No intervention	Child care (brochure)	0.38
Dowell, 2001 (UK)	Immediate description	Delayed prescription (7 days)	0.07
Huang et al., 2007 (USA)	No intervention	Combination of home- and office-based materials	0.03
Little et al., 1997 (UK)	Immediate prescription + advice	Delayed prescription (3 days) + advice package	0.27
		No prescription + advice package	0.32
Little et al., 2001 (UK)	Immediate prescription + advice	Delayed prescription (3 days) + standard oral advice	0.30
Little et al., 2005 (UK)	Immediate prescription	Delayed prescription (3 days)	0.35
	Immediate prescription No leaflet (prescription varied)	No prescription Information leaflet (prescription varied)	0.28 0.02
Trepka et al., 2001 (USA)	No intervention	Intervention for general practitioner plus Multiple materials and presentations for patients	0.07
Wheeler et al., 2001 (USA)	No intervention	Video and leaflet	0.23

be explained by sampling error alone. For this reason, we chose for a mixed random effects model to examine potential predictors of variance in effective sizes. We first included quality descriptors including study year, country (USA vs. other) and whether or not randomisation took place. Subsequently, we examined intervention characteristics including where the intervention took place (practice or community setting), the kind of information materials involved, the theoretical basis of the intervention, whether or not the physician had received a training on how to deliver information to patients, the age group of participants (parents vs. adults vs. all ages) and type of illness which the intervention focused on (upper vs. lower RTI and specific illnesses vs. general infections). Neither the quality indicators nor the

intervention characteristics explained a significant proportion of the variance. Singular regressions of each individual variable also had no effect with  $p$  values  $>0.35$ .

### *Summary*

Most interventions appeared to be moderately successful in improving knowledge or attitudes, but results varied considerably and were generally quite small. We were not able to identify variables which could explain differences between studies. A more detailed examination of the most effective interventions does not clarify the findings. This is in part due to the poor description of the interventions. It must be noted that the only study alluding to theory was the most successful in changing knowledge, taking elements from social learning theory to develop a group education programme (Cebatorenco & Bush, 2008). However, the second most effective programme (Croft et al., 2007) was based on a fairly simple information brochure for parents of children in a day-care facility. The three other interventions with small to moderate effects ( $d$ 's  $>0.30$ ), all involved delaying or refusing a prescription with or without giving additional information. Apparently, delaying or not giving a prescription can in itself change attitudes and appeared to be equally effective as providing patients with information. An explanation for this unexpected finding could be that when a physician delays or refuses antibiotics, a certain amount of information will be given to explain why antibiotics are not prescribed even when this may not have been part of the intervention protocol.

### *Effects on antibiotic use*

Twenty-one studies examined the effectiveness of patient-oriented interventions on antibiotic use: 12 studies based findings on prescription rates by the provider or pharmacy dispensation rates, and nine on self-reported use by patients with follow-up times ranging from one week up to five years. There was a clear country bias in how outcomes were reported. All studies in the USA based their results on prescription or dispensation rates. Nearly all studies outside the USA based their results on patient self-reports. Given the large variety in how changes in antibiotic use were reported, we chose to calculate effective sizes as the difference in proportions between the experimental and control group after the intervention. On this basis, the 21 studies (26 substudies) included 31 comparisons (see Table 3)

The overall effective size was significant but small ( $d = -0.21$ ,  $p < 0.001$ ), indicating that antibiotic use was slightly lower in the intervention groups than the control groups at post-intervention measurement. Effective sizes ranged from  $-0.86$  to  $0.19$ . Six comparisons showed moderate to large effective sizes ( $>0.50$ ). In each of these, an intervention involving no or delayed prescription was compared with a condition in which antibiotics were given immediately. Of the remaining 25 comparisons, three showed a small to moderate effective size ( $-0.30$  to  $-0.50$ ), three a small effective size ( $-0.20$  to  $-0.30$ ) and nine showed a negligible effective size of which four even showed a positive effect indicating that antibiotic use was higher in the intervention group than in the control group.

The  $Q$  score of 220.31 ( $df = 15$ ,  $p < 0.001$ ) revealed considerable heterogeneity between studies, indicating that the variance could not be explained by sampling

Table 3. Content and effectiveness of the interventions investigating effects on antibiotic use in terms of prescription rates, dispensation rates, or self-reported use.

Study	Control condition	Experimental condition	ES <i>d</i>
Altiner et al., 2007 (Germany)	Usual care	Poster and leaflet (+ physician receives communication training)	-0.24
Arroll et al., 2002 (New Zealand)	Immediate prescription	Delayed prescription (3 days)	-0.41
Belongia et al., 2001 (USA)	Usual care	Physician intervention + posters/pamphlets in community	-0.02
Belongia et al., 2005 (USA)	Usual care	Physician intervention plus written education for general public	-0.03
Cebatorenco and Bush, 2008 (Moldavia)	Usual care	Student (aged 12 – 13) taught group education.	-0.19
	Usual care	Adult group education, multiple materials	-0.36
Dowell, 2001 (UK)	Immediate prescription	Delayed prescription (7 days)	-0.55
Finkelstein et al., 2001 (USA)	Usual care	Parental brochure + physician intervention	-0.14
Finkelstein et al., 2008 (USA)	Usual care (child 3 – 24 months)	Combined physician and parent intervention using mailing, posters.	-0.01
	Usual care (child 24–48 months)	Combined physician and parent intervention using mailing, posters	-0.04
	Usual care (child 48–72 months)	Combined physician and parent intervention using mailing, posters	-0.07
Flottorp et al., 2002 (Norway)	Attention control (info on UTI)	Physician guidelines and patient information: focus sore throat	-0.06
	Attention control (info on sore throat)	Physician guidelines and patient information: focus UTI	0.03
Gonzales, Steiner, & Lum, 1999 (USA)	Usual care	Physician intervention and office and home based patient materials	-0.28
Gonzales, 2001	Usual care	Office-based materials	-0.01
	Office-based materials	Physician intervention and office and home-based patient materials	-0.21
Gonzales, 2005 (USA)	Usual care	Office- and home-based patient materials	0.07
	Usual care	Physician intervention and office and home-based patient materials	-0.09

Table 3 (Continued)

Study	Control condition	Experimental condition	ES <i>d</i>
Little et al., 1997 (UK)	Immediate prescription + advice	No prescription + advice pack	-0.86
	Immediate prescription + advice	Delayed prescription (3 days) + advice package	-0.68
Little et al., 2001 (UK)	Immediate prescription + oral advice	Delayed prescription (3 days) + oral advice physician	-0.75
	Immediate prescription	No prescription	-0.80
Little et al., 2005 (UK)	Immediate prescription	Delayed prescription (3 days)	-0.76
	No leaflet (prescript varied)	Leaflet	-0.02
Macfarlane et al., 2002 (UK)	Delayed prescription (verbal reassurance)	Delayed prescription + reassurance + info brochure	-0.15
Perz et al., 2002 (USA)	Usual care	Physician intervention plus community intervention	-0.11
Pshetizky et al., 2003 (Israel)	Delayed prescription	Delayed prescription (48 hrs) + oral advice	-0.46
Rubin et al., 2005 (USA)	Usual care	Physician intervention + office- and community-based information	-0.05
Samore et al., 2005 (USA)	Usual care	Physician intervention + community	0.16
	Usual care	Community intervention	0.19
Welschen et al., 2006 (The Netherlands)	Usual care	Physician intervention + written educational material	-0.14

error alone. For this reason, we chose a mixed random effects model to examine potential predictors of variance. We first included quality descriptors including the aforementioned variables of study year, country and randomisation. This model was found to explain a significant proportion of the variance ( $R^2 = 0.46$ ,  $p < 0.001$ ), showing that the heterogeneity between studies was completely explained by the country in which the study took place ( $Q$  score 26.8,  $p < 0.001$ ;  $Q$  score residual 32.0,  $p = 0.27$ ). A subsequent ANOVA comparing studies conducted in versus outside the USA indicated that the US studies were significantly less effective ( $d_{(US)} = -0.05$ ,  $p = 0.32$  versus  $d_{(not\ US)} = -0.37$ ,  $p < 0.001$ ). A homogeneity analysis revealed that studies conducted in the USA were homogenous ( $Q = 5.7$ ,  $p = 0.97$ ), indicating that the variance between US studies is the result of sampling error and not potential differences between studies. In contrast, studies conducted outside the USA were relatively heterogeneous ( $Q = 40.6$ ,  $p < 0.001$ ). For this reason, we focused on studies which took place outside the USA to examine potential explanations for variance between studies. Given the small number of

studies taking place outside the USA ( $n=16$ ), we conducted a series of mixed model ANOVAs to examine the effects of potential moderators. A regression analysis in which all variables were included simultaneously was not possible given the fact that not all variables were reported in each study. As such, these analyses must be considered explorative at best, giving a first indication of which ingredients are effective in reducing antibiotic use.

#### *Prescription style*

Studies, which manipulated prescription style ( $n=9$ ) were compared with studies which did not ( $n=7$ ), showed larger effective sizes in the former ( $d=-0.62$ ,  $p<0.001$ ) compared to the latter ( $d=-0.14$ ,  $p<0.01$ ).

#### *Intervention type*

The effects of intervention type were examined by categorising interventions into no information component ( $n=4$ ), information provision only ( $n=8$ ), or information provision guided by theoretical considerations about what information should be provided to patients in order to change their behaviour ( $n=4$ ). The subsequent ANOVA was significant ( $F=13.1$ ,  $p<0.001$ ). Notably, interventions with no information component had the highest effective size ( $d=-0.64$ ), followed by those with information provision alone ( $d=-0.41$ ). Theory driven interventions did not show a significant effect ( $d=-0.14$ ,  $p=0.13$ ). It must be noted however that the information component was associated with prescription style as the interventions without information provision also comprised the manipulation of prescription style whereas none of the theory driven interventions did.

#### *Inclusion of a physician component*

Studies were categorised based on the presence ( $n=4$ ) or absence ( $n=12$ ) of an additional intervention focussing on the physician. The subsequent ANOVA was significant ( $F=13.1$ ,  $p<0.001$ ). Notably, interventions without a physician component were more effective than interventions including such a component ( $d=-0.50$ ,  $p<0.001$  vs.  $d=-0.10$ ,  $p=0.28$ ). Again, there was an association of interventions with a physician component with prescription style as the majority of interventions without a physician component manipulated prescription styles whereas none of the other studies did.

#### *Summary*

Overall, patient-oriented interventions appeared to be successful in achieving a small but significant decreases in antibiotic use, although there was considerable variation between studies. The sole most important predictor of effectiveness was whether or not the intervention took place in the USA, with interventions outside the USA being more effective than those in the USA. One potential explanation for the differential effectiveness across countries could be the way in which antibiotic use was assessed with studies in the USA reporting findings on prescription or dispensation rates and other studies generally relying on self-report measures.

Self-reported use of antibiotics could be substantially lower as a result of not picking up prescriptions or not taking antibiotics. Another potential explanation could be that studies within the USA often used a similar intervention with materials derived from the Centre of Disease Control. These brochures have been implemented previously across the country, and indeed, in nearly all studies, slight decreases in antibiotic use could be also witnessed in populations serving as controls. The most apparent difference between studies within and outside the USA, however, is that none of the US interventions manipulated prescriptions, while nine (out of 16) interventions outside the USA did. Examining Table 2, it is readily apparent that delaying or refusing prescriptions is the most effective way to reduce antibiotic use as eight out of the ten most effective interventions manipulated prescriptions. This finding was supported by our exploratory analysis of potential moderators of variance in effectiveness. Interventions involving the manipulation of prescriptions had an effective size of  $-0.62$  compared to  $-0.14$  for interventions which did not. We also examined the predictive value of other variables, but these were most likely confounded by the variation in prescription styles. For example, one would expect interventions including a GP component to be more effective than other interventions, but in fact we found the exact opposite. This is primarily because the latter nearly all involved interventions manipulating prescription style. In fact, of the 22 interventions not manipulating prescription style, only four had an effective size above  $-0.20$  ( $d$ 's varying from  $-0.21$  to  $-0.36$ ); the remainder showed marginal decreases or even increases in antibiotic use.

### *Effects on satisfaction*

Eight studies (11 comparisons) investigated patient satisfaction with the consult following a patient-oriented intervention to reduce antibiotic use. In all cases, these involved the manipulation of prescriptions. One could expect patients to be less satisfied when they received a delayed prescription or were refused a prescription. However, the overall effectiveness was not significant ( $d = -0.019$ ,  $p = 0.44$ ), indicating that patients receiving no or delayed prescription were not less satisfied than patients receiving a prescription immediately. Follow up of patients ranged from one day to four weeks, but this had no effect on satisfaction. There was also little variation between studies ( $d$ 's ranging from  $-0.14$  to  $0.17$ ), and a homogeneity analysis of the model controlling for prescription style indicated a homogeneous model ( $Q = 1.1$ ,  $p = 0.57$ ). Overall then, regardless of whether or not they received a prescription for antibiotics, most patients were very satisfied with their consult.

### **Discussion**

This study systematically reviewed the literature to examine the content and effectiveness of patient-oriented interventions aimed at reducing antibiotic use. Based on a meta-analysis of 28 studies, we found that these interventions significantly improved the knowledge and attitudes about antibiotics in both patients and potential patients in the community and also significantly reduced antibiotic use, although effects were overall small. We could not find any evidence for a decrease in patient satisfaction with their treatment when their physician delayed the prescription of antibiotics or did not prescribe these drugs at all. Based on these

findings we must conclude that overall patient-oriented interventions do not appear to be very successful in engendering change with regard to (knowledge and attitudes about) antibiotic use, although there are no negative side effects in terms of patient satisfaction either.

The finding that patient-oriented interventions are only moderately successful appears somewhat in contrast to a previous meta-analysis by Arnold and Strauss (2005) who found that patient-based interventions could be effective, particularly in the form of multifaceted interventions combining physician, patient and public education. Their study focused on interventions for educating medical professionals, however, and included only a few interventions that were specifically geared to patients. Given the larger number of studies on patient-oriented interventions in our study we were able to perform a meta-analysis and explore specific characteristics of the interventions which could explain their differential effects on knowledge and attitudes about antibiotics and antibiotic use. Based on this detailed examination of characteristics, we may conclude that the majority of patient-oriented interventions that aim to educate the public about antibiotics do not achieve significant results regardless of their specific features. In fact, rather the simple procedure of delaying or refusing prescriptions seems to be the most effective strategy, which is in line with the findings of the meta-analysis by Arnold and Strauss (2005). The manipulation of prescription styles dramatically decreased antibiotic use and was associated with a large effect ( $d = -0.62$ ). This finding may seem obvious at first glance but needs to be stated nonetheless. Many interventions that are directly aimed at patients (e.g., through brochures or leaflets) appear to implicitly assume that these interventions are equally effective in reducing the use of antibiotics, perhaps based on the idea that physicians' prescriptions are guided by patient expectations. This study shows that they are, in fact, not as effective. Furthermore, interventions refusing or delaying antibiotics were, in themselves, also associated with significant positive changes in patients' attitudes and knowledge without reducing their overall satisfaction with the consult. When prescription style was controlled for, other interventions were no longer successful in reducing antibiotic use. We were not able to identify other elements of interventions which could moderate their effectiveness.

The search for additional effective elements was difficult due to serious limitations in the design and reporting of intervention studies included in the analysis. The studies used a wide range of methods and often failed to report relevant information about participants (e.g., socioeconomic characteristics) and procedures (e.g., non-response and accrual rates). Ideally, a study examining intervention effectiveness would consist of a pre- and post-test measurement in both the control and intervention group. This was rarely the case, and when a study included both measurements, these were often taken in different patient populations. For example, a common design in primary care interventions was that a measurement was taken within the practice at baseline based on patients coming for a specific illness, an intervention was subsequently implemented in the practice and (other) patients subsequently visiting the practice for similar complaints were then tested. Whether or not there was overlap between the pre- and post-test populations was never reported. We ultimately had to base the meta-analysis on post-intervention measures in the intervention and control group as this was by far the most common design.

Another problem related to methodology was the operationalisation and measurement of outcomes. Knowledge and attitudes were assessed using a variety

of instruments, none of which included any psychometric information on reliability or validity. Antibiotic use was also measured in a variety of forms, including prescription rates, dispensation rates, and self-reports of antibiotic use. Differences in prescription, retrieval and use of antibiotics by individual patients have been duly noted and could potentially confound the results. This heterogeneity of measures is probably one of the main causes of the heterogeneity found in the effective sizes of the main outcomes of this meta-analysis. The large differences in intervention effects between studies taking place in and outside the USA could in part be explained by the measurement of antibiotic use, with all US studies based on prescriptions or dispensation rates and all studies outside the USA based on self-reported antibiotic use. A more likely explanation, however, remains the large effects found in studies manipulating prescription styles, all of which took place outside the USA.

Another major limitation in the selected studies is the lack of information on the content and theoretical background of the interventions. The majority of interventions primarily focussed on educating the patient and changing their attitudes, often addressing attitudes and beliefs such as illness vulnerability, treatment effectiveness, risk perceptions and social norms, elements which are also part of leading social cognitive theories on health behaviour and health promotion. However, explicit consideration of such theories was absent in the majority of studies where choices involving the type of information and the way it should be communicated to (potential) patients appeared to be based on common sense rather than on theory – which is actually different from intervention methods that have been adopted in other areas of health behaviour change (cf. Abraham & Graham-Rowe, 2009; Dombrowski et al., 2010). In fact, only four of the 28 studies alluded to specific theories (in particular, social learning theory; e.g., Cebatorenco & Bush, 2008) and even then it was not fully explained how these were employed in the intervention. An easy comment would be to argue that these interventions are not successful in reducing antibiotic use because they do not incorporate psychological theories of behaviour change. However, it must also be recognised that antibiotic use is a unique form of health behaviour which is not easily grasped by existing theories. Mostly behaviour change theories implicitly assume that patients have a choice in whether or not to engage in a specific healthbehaviour. With antibiotics, however, patients have very little choice as they have to rely on the physician who decides about the appropriate treatment. The fact that simply refusing or delaying prescriptions is so effective is a prime example of the important role which physicians play in reducing the inappropriate use of antibiotics. When the physician advises against the use of antibiotics either by refusing or delaying a prescription, patients reduce their antibiotic use accordingly. That said, there is considerable room for improvement of interventions by incorporating concepts from theories such as shared decision making or social learning theory, which may guide a more sophisticated design of what kind of information should be given to patients and in what way to encourage behavioural change (Finch et al., 2004). In a similar vein, more research on the reasons patients may have for whether or not wanting antibiotics could illuminate the relevant determinants that can subsequently be targeted in newly developed interventions.

Importantly, refusing or delaying antibiotics generally did not undermine patient satisfaction with treatment. Based on these findings, we would argue that interventions to help physicians reduce their prescriptions would be a suitable target

for reducing antibiotic use in primary care. According to the principles of intervention mapping (Green & Kreuter, 2005) that specifies the core ingredients of an intervention, we would argue that (potential) patients may not be the primary target of interventions that aim to reduce the use of antibiotics when it is not considered appropriate. Patients may have a relatively poor understanding of antibiotics but most studies find that patients, despite this poor understanding, do not expect or want antibiotics in the consult and are quite satisfied with not receiving antibiotics as long as they are taken seriously and it is explained why. This stresses the importance of a patient-centred approach to help patients in adopting a more active role in shared decision making about antibiotics. Interventions that motivate physicians to reduce their prescriptions of antibiotics and teaching them the communication skills to convey this to the patient could be an important contribution in this regard. Are patient-oriented interventions obsolete then? We would argue that in countries with relatively low prescription rates such costly interventions would have little or no effect. In countries with high prescription rates, community interventions could help to support physicians to make the step to reduce their prescribing rates. Unfortunately, this meta-analysis included no studies from high prescribing countries, and this therefore remains a hypothesis to be addressed in future research.

### Acknowledgements

Bart Thoolen and Denise de Ridder were supported by a grant from the European Community FP6 Research Programme (grant number SP5A-CT-2007-044317 to the CHAMP consortium: Changing behaviour of health care professionals and the general public towards a more prudent use of antimicrobial agents). The authors acknowledge input and comment from the Champ consortium

### Note

1. The higher number of eligible studies identified in MEDLINE as compared to EMBASE and PSYCINFO probably relates to the fact that studies on antibiotics use are mostly performed in the medical setting by researchers who are employed at medical faculties and consider medical journals as their primary outlet.

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