Chapter 26

Interventions to Improve Antibiotic Prescribing in the Community

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Antimicrobial resistant bacterial pathogens have become an increasing threat to the world's population. Many common pathogens have become resistant to usual antimicrobial therapy leading to escalating use of combinations of powerful, broad-spectrum antibiotics. Worldwide, community-acquired infections with drug resistant *Salmonellae, Neisseria gonorrheae*, and *Mycobacterium tuberculosis* are quite prevalent. Given the ease of travel in the global community, these pathogens among others, threaten the ability to treat infections, even in areas with relatively effective public health and disease control programs. Antibiotic resistance in other community-acquired pathogens has become more frequent in the last years of the twentieth century and threatens our ability to treat common community-acquired infections in both the developing and developed world.

Streptococcus pneumoniae is the most common community-acquired pathogen causing meningitis, bacteremia, pneumonia, and otitis media in young children. Population-based surveillance for invasive pneumococcal disease by the US Centers for Disease Control in selected regions has revealed an overall incidence of 21–24 cases per 100,000 population (Centers for Disease Control and Prevention, 2001). Antimicrobial resistance, especially penicillin resistance, among isolates of *S. pneumoniae* has increased throughout the world (where the incidence is substantially greater) since the late 1980s and early 1990s and threatens the ability to treat pneumococcal infections. Over the course of 8 years, the prevalence of invasive penicillin-resistant (intermediate

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and fully resistant) isolates increased from 2.8% to 6.8% in 10 Canadian pediatric hospitals (Scheifele *et al*., 1996, 2000). Active surveillance by the US Centers for Disease Control for invasive *S. pneumoniae* infections has revealed an increase in the proportion of penicillin-resistant invasive isolates from 6.7% (Breiman *et al*., 1994) to 27.5% in 8 years across the country, with some regions (Tennessee) reporting 54% of isolates resistant to at least one antibiotic (Whitney *et al*., 2000). In Europe, 11.4% of invasive pneumococcal isolates from 1999 to 2001 were penicillin non-susceptible (EARSS, 2001). However, this was an average over all with penicillin non-susceptibility rates as high as 45% and 35% in France and Spain down to as low as 1–2% in the Netherlands.

Organisms other than *S. pneumoniae* causing infections in the community are also demonstrating clinically significant antibiotic resistance. While less of a problem in North America than Europe and Japan, macrolide resistant Group A streptococci have been isolated with increasing frequency (Cornaglia *et al*., 1996; Maruyama *et al*., 1979; Seppälä *et al*., 1992). In addition to concerns about increasing resistance in respiratory tract pathogens, researchers have also documented increasing rates of antibiotic-resistant *Escherichia coli* urinary isolates. Several studies from different regions of the world have documented resistance to trimethoprim-sulfamethoxazole among community urinary isolates varying from 18% to 28% (Brown *et al*., 2002; Ladhani and Gransden, 2003; Zhanel *et al*., 2000).

The risk factors associated with colonization or infection with antibiotic-resistant *S. pneumoniae* have been well characterized (Arason *et al*., 1996; Block *et al*., 1995; Boken *et al*., 1995; Duchin *et al*., 1995; Jackson *et al*., 1984; Nasrin *et al*., 2002; Nava *et al*., 1994; Pallares *et al*., 1987; Radetsky *et al*., 1981; Reichler *et al*., 1992; Tan *et al*., 1993; Zenni *et al*., 1995). There is evidence that antibiotic exposure is associated with carriage of resistant *S. pneumoniae* at the level of the individual (Brook and Gober, 1996; Dagan *et al*., 1998). Antibiotic use in the preceding 3–6 months has been associated with a 2–5-fold increase in the risk of nasopharyngeal colonization with antibiotic-resistant *S. pneumoniae* (Arason *et al*., 1996; Boken *et al*., 1995; Duchin *et al*., 1995; Nasrin *et al*., 2002; Radetsky *et al*., 1981; Reichler *et al*., 1992; Zenni *et al*., 1995). The risk of invasive disease with antibiotic-resistant pneumococci (compared with infection due to susceptible bacteria) is increased substantially following antibiotic exposure as well (Block *et al*., 1995; Jackson *et al*., 1984; Nava *et al*., 1994; Pallares *et al*., 1987; Tan *et al*., 1993). In a study of the dynamics of pneumococcal carriage during antibiotic treatment (Dagan *et al*., 1998), it was observed that 19/120 children had a new pneumococcal isolate colonizing the nasopharynx at 3–4 days into treatment, 16/19 of which were resistant to the antibiotic the child was taking.

The association between antibiotic use and resistance in bacteria has been demonstrated for many other important community-acquired pathogens.

Macrolide resistant Group A streptococcal infections in Europe and Japan have been linked to the popularity of azithromycin (Priest *et al*., 2001; Seppälä *et al*., 1995). Studies from Europe and Asia have documented substantial decreases in the rates of erythromycin resistance following decreases in use of macrolide agents (Fujita *et al*., 1994; Seppälä *et al*., 1997). In addition, antimicrobial resistance in urinary tract pathogens has also been associated with recent antibiotic use (Allen *et al*., 1999; Brown *et al*., 2002; Magee *et al*., 1999; Steinke *et al*., 2000; Zhanel *et al*., 2000).

Thus, there is compelling evidence that exposure of the community and the individual to antibiotics enhances the risk of an individual's harboring a resistant organism. For *S. pneumoniae* carriage, it appears that frequent repeated exposure to antibiotics in children (who are most likely to be carriers of the organism) reduces the pool of circulating strains that are susceptible to antibiotics, allowing resistant strains to multiply and spread easily among children.

There is a major body of literature documenting the substantial misuse of antibiotics throughout the world for viral infections and other diseases, such as asthma, for which antibiotics are of no known benefit (Cronk *et al*., 1954; Gordon *et al*., 1974; Hardy and Traisman, 1956; Kaiser *et al*., 1996; Lexomboon *et al*., 1971; Stott and West, 1976; Taylor *et al*., 1977; Townsend, 1960; Townsend and Radebaugh, 1962). Antibiotics were the second leading class of drugs prescribed in the United States according to the US National Ambulatory Medical Care Surveys (NAMCS) (McCaig and Hughes, 1995) between 1980 and 1992 with the majority of such prescriptions for respiratory tract infections. In another analysis of the 1992 NAMCS data (Nyquist *et al*., 1998), antibiotic prescription rates for colds, upper respiratory tract infections, and bronchitis in children were 44%, 46%, and 75% respectively, with similar rates of inappropriate prescribing for adults (Gonzales *et al*., 1997). In a pediatric practice in Memphis, Tennessee, 43% of children with a diagnosis of uncomplicated upper respiratory infection (URI) or asthma received a prescription for an antimicrobial (Arnold *et al*., 1996). In a Kentucky Medicaid study, 60% of patients received an antibiotic prescription for the common cold (Mainous *et al*., 1996).

In England and Scotland, the number of antibiotic prescriptions increased by 45.8% between 1980 and 1991. Rates of growth in antibiotic prescribing in Germany and France were 78% and 65%, respectively in the same period (Davey *et al*., 1996; Taboulet, 1990). In Canada, an analysis of Saskatchewan Health Databases demonstrated that 85% of outpatient antibiotic prescriptions for respiratory tract infections in children under the age of 5 years in that province were inappropriate (Wang *et al*., 1999).

In addition to using antibiotics for inappropriate indications, physicians are using more broad-spectrum antimicrobials, considered as second- or third-line agents to treat common infections. In the NAMCS survey of 1980–92, the authors noted an increase in the rates of use of amoxicillin and cephalosporins with a concomitant decrease in the use of penicillin (McCaig and Hughes, 1995). In another analysis of the NAMCS, the authors examined antibiotic treatment for sore throat in adults from 1989 to 1999 (Linder and Stafford, 2001). They not only found excessive antibiotic use (prescribed for 73% of visits for sore throat in a population expected to have a rate of streptococcal pharyngitis of 5–17%) but also that there was a significant decline in the use of recommended antibiotics (penicillin and erythromycin) and an overall rate of prescribing non-recommended antibiotics of 68%.

Changing physician behavior requires identifying and addressing barriers to change in practice. In a systematic review of interventions to improve physicians' practice and implement findings of medical research in practice, Oxman and colleagues found "no magic bullets" for improving the quality of healthcare (Oxman *et al.*, 1995). They found that simple interventions such as conferences or the mailing of unsolicited materials produced little or no change in behavior for a variety of areas of patient care. Complex (and expensive) interventions such as educational outreach visits or training of local opinion leaders were moderately effective in producing changes in physician behavior. Overall, conclusions could not be made regarding effectiveness of different types of interventions because the scope of identified practice deficiencies, types of physicians, and variations of interventions is too diverse. What these authors did recommend was the careful evaluation of focused interventions on specific practice areas after the elucidation of the root causes of suboptimal performance and the identification of barriers to change.

Research has enhanced the understanding of the underlying reasons for inappropriate antibiotic use for viral respiratory tract infections. The following factors appear to be significant determinants of antibiotic use in clinical situations where they are not indicated are: (1) physician–patient interaction; (2) physician characteristics; (3) physician time constraints; and (4) diagnostic uncertainty (Arnold *et al.*, 1999; Bauchner *et al.*, 1999; Hamm *et al.*, 1996; Hutchinson and Foley, 1999; Mainous *et al.*, 1997, 1998; McIsaac and Butler, 2000; Murray *et al.*, 2000; Palmer and Bauchner, 1997; Steinke *et al.*, 2000; Watson *et al.*, 1999).

Aspects of the physician–patient interaction have been studied extensively. Many physicians argue that they prescribe antibiotics for viral infections because they feel pressured to do so by patients or parents (Bauchner *et al.*, 1999; Palmer and Bauchner, 1997; Watson *et al.*, 1999); however, it appears that physicians frequently misjudge patients' or parents' intentions (Hamm *et al.*, 1996). Physicians with certain characteristics, such as longer duration of time in practice (Mainous *et al.*, 1998) or not being involved in medical teaching (Steinke *et al.*, 2000), appear to overuse antibiotics more frequently. Physicians who see more patients and presumably, spend less time with each patient (Arnold *et al.*, 1999; Hutchinson and Foley, 1999) prescribe more antibiotics than those who see fewer patients. The issue of diagnostic uncertainty (difficulty in distinguishing a benign, self-limited viral infection from a more serious infection requiring antibiotic therapy) has received less attention than these other areas in the medical literature and requires further study. It has been shown that physicians frequently overestimate the probability that a patient with a respiratory tract infection has a bacterial infection, particularly for pharyngitis (McIsaac and Butler, 2000), sinusitis (Murray *et al*., 2000), and bronchitis (Mainous *et al*., 1997; Murray *et al*., 2000). These studies have mainly been performed in adult populations. Diagnostic uncertainty regarding the presence of invasive bacterial infections in young children with high fever (Bass *et al*., 1993; Carroll *et al*., 1983; Jaffe *et al*., 1987; McGowan *et al*., 1973; Teele *et al*., 1975; Waskerwitz and Berkelhamer, 1981) is a distinct clinical problem in pediatrics which likely has an impact on the use of antibiotics in children with respiratory tract infection. When there is uncertainty in any potentially infectious condition, physicians tend to be cautious and prescribe an antibiotic if it could, at all, be beneficial.

Some of these identified barriers are amenable to change. However, given the multifactorial nature of the problem, it is unlikely that a single approach will work for all physicians in all regions. In addition, different patient populations and conditions may warrant a variety of interventions. This chapter will explore published studies of interventions to improve antibiotic prescribing in the ambulatory care setting. It will include reviews of studies targeting overall antibiotic use, use for specific conditions, and use of recommended and nonrecommended agents (usually defined locally). These studies predominantly address common infectious clinical syndromes seen in ambulatory care including urinary tract infections, respiratory tract infections (viral and bacterial), and infectious diarrhea in a large variety of ambulatory care settings around the world.

1. METHODS OF LITERATURE REVIEW

This review was initiated under the auspices of the Effective Practice and Organization of Care (EPOC) review group of the Cochrane Collaboration. The Cochrane Collaboration comprises a worldwide group of individuals dedicated to systematically reviewing the literature on topics relevant to modern health-care and maintaining an up-to-date database of these high-quality systematic reviews. The focus of the EPOC review group is on "reviews of interventions designed to improve professional practice and the delivery of effective health services" (www.epoc.uottawa.ca/scope.htm).

The research relevant to this particular review was obtained by searching the specialized register maintained by the EPOC review group. This register was created to identify studies relevant to the EPOC scope. A search strategy was designed and compared to a gold standard of studies obtained by hand searching the *BMJ* and *Medical Care* journals as well as electronic searching of OVID for all relevant articles from the *Annals of Internal Medicine, BMJ, JAMA*, and *Lancet*. Compared to this gold standard, the EPOC search strategy was found to have a sensitivity of 92.4% and a precision of 18.5%. The register includes studies obtained by searching MEDLINE back to 1966, HealthSTAR back to 1975, EMBASE back to 1980, and CINAHL back to 1982. Monthly updates are obtained automatically from OVID. The Cochrane Controlled Clinical Trials register is searched every 3 months and the contents of several key journals are scanned regularly. The EPOC search strategies are available on the EPOC website (www.epoc.uottawa.ca/register.htm) and the register can be accessed via the trials search coordinator.

For the purpose of this study, additional articles were obtained by searching the bibliographies of retrieved articles and personal files. From all of these sources a total of 148 titles and abstracts were obtained searching through the end of 2002. On the first pass, many studies were excluded based on review of the title and abstract. These early exclusions occurred for the following reasons: systematic review of literature (used references as a source of studies), hospital-based study, duplicate publication in another language, not an antibiotic prescribing intervention, or we were unable to obtain the full study after contacting the authors or publishers (predominantly studies produced and published by INRUD—International Network for the Rational Use of Drugs).

Several types of studies were considered for inclusion in this review. Any randomized controlled trials (RCT) as well as quasi-randomized controlled trials were reviewed. A quasi-randomized controlled trial is one in which participants (or groups of participants) are prospectively assigned to one or more intervention groups using a quasi-random allocation method, for example, alternation, date of birth, patient or physician identifier number. In addition, controlled before and after (CBA) studies, where subjects or groups of subject were assigned to study group by some nonrandom method, were included. Finally, studies designed to detect a trend in behavior of a single group without controls were included. These are called interrupted time series (ITS) studies.

Studies of qualified physicians or other trained medical workers (including nurse practitioners) of all ages and level of experience, who prescribe antibiotics and provide primary care in community or academic ambulatory settings, as well as healthcare consumers were included. Studies including medical trainees only were excluded. Studies examining the prescribing of multiple drug classes were included provided that specific data on antibiotic prescribing could be extracted.

Interventions addressing professional practice or education, or financial or structural changes to the method of delivery of care, alone or in combination, were included.

1. Distribution of educational materials: distribution of published or printed recommendations for clinical care, including clinical practice guidelines, audio–visual materials, and electronic publications. The materials may have been delivered personally or through mass mailings.
2. Educational meetings: healthcare providers who have participated in conferences, lectures, workshops, or traineeships.
3. Local consensus processes: inclusion of participating providers in discussion to ensure that they agreed that the chosen clinical problem was important and the approach to managing the problem was appropriate.
4. Educational outreach visits: use of a trained person who met with providers in their practice settings to give information with the intent of changing the provider's practice. The information given may have included feedback on the performance of the provider(s).
5. Local opinion leaders: use of providers nominated by their colleagues as "educationally influential." The investigators must have explicitly stated that their colleagues identified the opinion leaders.
6. Patient mediated interventions: new clinical information (not previously available) collected directly from patients and given to the provider, for example, depression scores from an instrument.
7. Audit and feedback: any summary of clinical performance of healthcare over a specified period of time. The summary may include recommendations for clinical action. The information may have been obtained from medical records, computerized databases, or observations from patients.
8. Reminders: patient or encounter-specific information, provided verbally, on paper or on a computer screen, which is designed or intended to prompt a health professional to recall information. This would usually be encountered through their general education; in the medical records or through interactions with peers and so remind them to perform or avoid some action to aid individual patient care. Computer aided decision support and drugs dosage are included.
9. Marketing: use of personal interviewing, group discussion ("focus groups"), or a survey of targeted providers to identify barriers to change and subsequent design of an intervention that addresses identified barriers.
10. Mass media: (1) varied use of communication that reached great numbers of people including television, radio, newspapers, posters, leaflets, and booklets, alone or in conjunction with other interventions; (2) targeted at the population level.
11. Financial interventions: method of physician remuneration, patient-oriented approaches such as user fees, formularies.

Outcomes that were considered relevant for improving the manner in which ambulatory care physicians prescribe antibiotics were any one or more of: the decision to prescribe an antibiotic or the prescribing of a recommended choice, dose or duration of antibiotic. In addition, secondary outcomes of interest were considered. These included the incidence of colonization with or infection due to antibiotic-resistant organisms prior to and following changes in prescribing behavior, other adverse drug-related events (rash, gastrointestinal disturbances, allergic reactions) and the incidence of adverse events associated with reduced use or duration of antibiotics or use of narrow-spectrum antibiotics.

A total of 116 articles were retrieved from the EPOC specialized register. In addition, 32 articles were retrieved from personal files and review of bibliographies of retrieved articles and review articles for a total of 148 articles to be reviewed. Three studies were excluded as they were duplicates of studies published in another language (two studies) or as an abstract (one study). Two additional papers were long-term follow-up publications from earlier studies. These were considered as single studies along with the original publication. Thirty-six studies retrieved from the EPOC search were excluded prior to full review based on the title and abstract as they were neither intervention studies nor studies of medical healthcare workers, or were hospital-based studies or systematic reviews.

Sixty-eight further studies that were excluded after more detailed review were excluded based on failure to meet minimum methodological criteria, the most common reasons for which were: an ITS study without enough data points, a nonrandomized controlled study without baseline prescribing data, and unavailability of specific data for prescribing antibiotics (or data incompletely reported or mixed with other prescribing data). If the published report did not report appropriate baseline data or contained inextricable antibiotic prescribing data, the authors of the study were contacted in an attempt to obtain the data prior to excluding the study from review.

2. PROBLEMS WITH INTERPRETATION OF PUBLISHED STUDIES

Among the 39 studies selected for review, there were 24 randomized (RCT) or quasi-randomized clinical trials (QRCT), 13 controlled before and after studies (CBA) and two interrupted time-series studies (ITS). The methodological quality of the included studies was highly variable. The most significant problem with the RCTs and the CBAs was the failure to account for clustering of patients within physicians or practices when the unit of randomization or assignment was physician, practice, or region. In many studies, groups of physicians (often in pre-existing practice groups or by geographic region) were assigned (randomly or not) to intervention and control groups to prevent contamination of subjects. Using such a cluster design requires larger sample sizes since the physicians within these groups cannot be considered completely independent as there will be similarities in the way that these physicians practice medicine and in the characteristics of the patients attending their practices (Diwan *et al.*, 1992). Most of these cluster randomized studies did not report sample size calculations. This is of concern as it is possible that many of these studies are underpowered to detect significant differences in prescribing between study groups.

In addition to issues regarding sample size, assignment to study group in clusters requires that the data be analyzed in a manner that adjusts for these clusters. Unit of analysis errors are considered to have occurred if the provider or groups of providers have been assigned to intervention groups but the outcomes are measured at the level of the individual patient or prescription. This is a significant problem as it ignores the correlation in the physician's prescribing behavior among all the patients. That is, a physician's decision to prescribe an antibiotic each time he or she sees a patient is not a completely independent event as the physician will tend to behave in a similar fashion from one patient to the next. In addition, physicians not only tend to manage patients with similar problems in similar ways but also tend to attract patients who have similar characteristics and treatment expectations. For this reason, data from physician intervention studies should be analyzed with methods adjusting for the clustering of patients under physicians and if necessary, the clustering of physicians in practices or other groups. Using simple statistical techniques such as paired *t*-tests, chi-square tests, or even simple least squares regression analysis ignores the effects of these correlations. This leads to inflated results, where the point estimates for the effect size are accurate but the standard errors are too small leading to erroneously small confidence intervals and *p*-values. This has the effect of making the intervention appear more effective than it is.

The choice of appropriate analysis depends upon the research design (Austin *et al.*, 2001; Moerbeek *et al.*, 2003). One may use regression with fixed effects which includes terms for the cluster (physician or physician group) and an interaction term between the cluster and the intervention. One may also use a summary measures method where the cluster is the unit of analysis and the outcome at the patient level is considered a repeated measure. The generalized estimating equation (GEE) has also been used which takes into account the correlation of the repeated measures within subjects (physicians' repeated decisions to prescribe or not to prescribe). Finally, multilevel or hierarchical regression is considered by many methodologists to be the most appropriate analytic method as it accounts for the multiple levels of data and leads to results that do not appear to overestimate the intervention effect. Multilevel regression is, however, complicated to perform and understand and thus the simpler methods described previously may be acceptable as long as the limitations are recognized. The studies for which appropriate statistical considerations of this problem were undertaken, generally utilized the GEE or multilevel regression in their cluster analyses, both in sample size calculations and in statistical analysis of the results.

In addition to problems with analysis there were other methodological issues with many of the studies to bear in mind while reviewing the summary of the results. In many of the randomized clinical trials the method of randomization was not reported and thus it is difficult to judge if the study is truly randomized. In addition, in the control groups in some of these studies, physicians, knew what the intervention was and might have altered their behavior during the period of the study blunting the apparent effect of the intervention. In order to prevent such contamination, many researchers utilized a cluster design so that physicians practicing in the same group or geographic region were all assigned to the same group. Another method used in a few studies was the application of the intervention to change performance in two different areas, with each group acting as a control for the other, to control for the Hawthorne effect (positive effect of being in a study).

In most of the studies, the methods reported for measuring the prescribing rates was objective, using pharmacy or insurance databases. However, there were a few studies where less objective measures were used. In these, the prescribing rates were frequently determined using chart review or interview of the patient. The reliability of measures was frequently not reported making it difficult to interpret the results of the studies. Studies using chart review or interview methods of data collection were performed primarily in developing countries.

Interrupted time-series studies were included if they reported enough data points for appropriate statistical inference. Only two ITS studies were included as the remainder did not report enough data points or could not define a point in time when the intervention occurred. There were significant problems with the statistical analysis of the two included ITS studies. Neither reported all available data points and neither used appropriate statistical methods to appropriately test for trends in the data over time. The data from these studies was, thus, reanalyzed using appropriate time-series methods.

A summary of the results from the reviewed studies follows. Studies are grouped according to intervention type. There are no studies from all the categories of potential interventions listed previously. In addition, results of some studies are reported more than once if the study compared two or more interventions that fall into different categories.

3. DISCUSSION OF INCLUDED STUDIES

3.1. Distribution of educational materials

There were four studies (Angunawela *et al*., 1991; Avorn and Soumerai, 1983; Ray *et al*., 1985; Schaffner *et al*., 1983; Seppälä *et al*., 1997) in which physicians received printed educational materials regarding appropriate antibiotic prescribing (see Table 1). One study (Ray *et al*., 1985) reports long

Table 1. Distribution of educational materials

Study citation	Design	Analysis	Outcome measure	Results as reported in the study
Seppälä *et al*. (1997)	ITS	No time series analysis reported	Reduction in use of macrolide antibiotics	2.40 DDD per 1,000 popln in 1991 to 1.38 in 1992 ($p = 0.007$)
Avorn *et al*. (1983)	Cluster RCT	No cluster analysis	Reduction in use of cephalexin	Change in mean number of units prescribed − 100 (p = NS)
Angunawela *et al*. (1991)	Cluster RCT	No cluster analysis	Reduction in use of antibiotics for viral infections	Mean difference in proportion of patients receiving prescription of −7.4%
Schaffner *et al*. (1983)	CBA	No cluster analysis	Reduction in use of contraindicated antibiotics and cephalosporins	No difference (numbers not given)

term follow up data from a preceding study (Schaffner *et al*., 1983). These materials consisted of information regarding treatment of specific infectious conditions and/or recommendations regarding the use of certain medications (including at least one antibiotic). No materials referring to the specific physician's practice (i.e., audit of practice pattern with feedback) were sent. These educational materials were unsolicited and sent by mail (Avorn *et al*., 1983; Schaffner *et al*., 1983; Anunawela *et al*., 1991) or published in a national medical journal (Seppala *et al*., 1997).

There were two RCTs (one cluster RCT in which groups of healthcare workers rather than individuals are randomized), one CBA, and one ITS involving distribution of educational materials. One study aimed to reduce use of the oral cephalosporin, cephalexin (among other non-antibiotic medications) in general practice and compared printed educational materials alone or combined with audit and feedback (see Section 3.2) to a no intervention control group (Avorn and Soumerai, 1983). The second study compared the effect of printed educational materials with or without group educational seminars to controls (three study groups) on reducing inappropriate use of antibiotics for acute viral respiratory tract infections (Angunawela *et al*., 1991). In a CBA study from Tennessee, researchers compared a mailed educational brochure to an outreach visit by a pharmacist or physician (2 groups) and to controls to reduce the use of certain antibiotics (oral cephalosporins, clindamycin, tetracycline, and chloramphenicol) (Ray *et al*., 1985; Schaffner *et al*., 1983). Finally, Finnish medical authorities sought to reduce the use of erythromycin for Group A streptococcal infections with a published recommendation against their routine use (Seppälä *et al*., 1997).

None of the first three studies showed any effect of printed educational materials alone, in changing prescribing behavior. This was despite the fact that the lack of adjustment for clustering likely resulted in an overestimation of the intervention effect in these studies. The Finnish study demonstrated a significant reduction in macrolide antibiotic use following publication of the recommendation which seemed to decay (not statistically significant) somewhat over time (by time-series analysis not presented in the published paper). Thus, written educational materials alone appear to have a limited impact overall with three of four studies demonstrating no change in prescribing behavior. The specific circumstances of the Finnish study, that is, there being an increase in resistance to macrolides in Group A streptococci may have substantially contributed to the effectiveness of the published recommendations in that particular study. Interventions tailored to circumstances may, therefore, be more likely to be effective.

3.2. Audit and feedback with or without other educational materials

The process of audit and feedback refers to the collection and analysis of individual or group prescribing data followed by distribution of these materials back to prescribing physicians. Additional materials distributed accompanying the feedback material may include any one or more of the following: an explanation of the prescribing data, comparative data for other physicians or groups of physicians, and educational materials promoting more optimal prescribing practices. Audit and provision of feedback data may also be a part of the information provided at individual or group educational meetings or seminars. In this section, only those studies involving distribution of written audit material with or without accompanying comparative data and/or printed educational materials are considered. This type of intervention has been popular as it is relatively simple and inexpensive to perform. This means that even modest reductions in inappropriate prescribing may result in substantial cost savings for insurers although the impact on antibiotic resistance may be less impressive.

There were four studies, three RCTs (Hux *et al*., 1999; Mainous *et al*., 2000) (one cluster RCT [O'Connell *et al*., 1999]) and one CBA trial (Rokstad *et al*., 1995), in this category (Table 2). In the first RCT (Mainous *et al*., 2000), authors examined the effect of audit and feedback alone and audit and feedback with patient educational materials compared with a no intervention control group in an intervention designed to reduce antibiotic prescribing for viral pediatric respiratory tract infection. The second study (Hux *et al*., 1999), compared the effect of audit and feedback to controls on the prescribing of recommended first-line antibiotics for community-acquired infections to senior

Table 2. Audit and feedback

Study citation	Design	Analysis	Outcome measure	Results as reported in the study
Mainous *et al*. (2000)	Cluster RCT	No cluster analysis	Reduction in antibiotic use for viral URI	Overall increase in proportion of patients with colds having prescriptions, gain scores compared with controls significantly lower by Dunnett's T ($p < 0.05$)
Hux *et al*. (1999)	RCT	No cluster analysis	Increase in prescribing of first-line agents	Change of 2.5% in intervention compared with −1.7% in controls ($p < 0.01$)
O'Connell *et al*. (1999)	Cluster RCT	Acknowledged intracluster correlations for sample size calculations but did not use in analysis	Reduction in overall antibiotic use	No change in median prescribing rates per 100 medicare services
Rokstad *et al*. (1995)	CBA	No cluster analysis	Increase prescribing of first-line agents for UTI	Increase in mean number of prescriptions for trimethoprim of 32.5 (3.5–61.7) in intervention group and reduction in control group −31.8 (−54.7 to −3.5)

citizens. In the cluster RCT (O'Connell *et al*., 1999), physicians were randomized by postal code regions to receive audit and feedback on the prescribing of oral antibiotics (and four other classes of medication) or no intervention. Finally, in the CBA study (Rokstad *et al*., 1995), Norwegian general practitioners received audit and feedback material along with clinical practice guidelines for the management of urinary tract infection (UTI) in women (diagnostic, first-line antibiotics, duration of therapy), with a control group receiving similar information on the management of insomnia.

In these studies, audit and feedback with or without written educational materials or prescribing guidelines had little or no impact on antibiotic prescribing in general terms. Two studies demonstrated no significant change in prescribing behavior in response to the intervention (Mainous *et al*., 2000; O'Connell *et al*., 1999). The remaining two studies (Hux *et al*., 1999; Rokstad *et al*., 1995) showed a small but statistically significant increase in the prescribing of recommended first-line antibiotics. In none of these studies was appropriate statistical analysis to account for clustering of patients within physicians undertaken and thus, the results of the latter two studies might be rendered nonsignificant on reanalysis. The results from these studies indicate that there may be certain prescribing situations that are more amenable to interventions such as those studies seeking to increase prescribing of certain selected "first-line" agents. In contrast, interventions aimed at reducing antibiotic overuse (for viral infections, for example) may require more complex interventions.

3.3. Educational group meetings or seminars

This category of study includes those in which the intervention consists of one or more group educational sessions. It excludes educational outreach visits which are generally one-on-one meetings between the prescribing physician and another individual (physician, pharmacist, drug detailer). Information reviewed at the meetings generally includes an oral and audiovisual review of recommendations for appropriate prescribing practices for particular conditions or particular antibiotics and/or review of a clinical practice guideline or other published recommendations. Some educational meetings include a review of practice audit material for the group.

There were seven cluster RCTs (Augunawela *et al.*, 1991; Bexell *et al.*, 1996; Lagerlov *et al.*, 2000; Lundborg *et al.*, 1999; Meyer *et al.*, 2001; Santoso, 1996; Veninga *et al.*, 2000), one cluster QRCT (Harris *et al.*, 1984), and two CBA studies (McNulty *et al.*, 2000; Perez-Cuevas *et al.*, 1996) reviewed in this section, Table 3. Three cluster RCTs, from Sweden (Lundborg *et al.*, 1999), the Netherlands (Veninga *et al.*, 2000), and Norway (Meyer *et al.*, 2001), used group educational meetings to promote prescribing of first-line agents for UTI. Controls in these studies received a similar intervention targeting asthma management. Three cluster RCTs, two from Africa (Bexell *et al.*, 1996; Meyer *et al.*, 2001) and one from Sri Lanka (Angunawela *et al.*, 1991) examined the effect of group educational sessions on reducing overall antibiotic use in community health clinics compared with controls receiving no education. The content of these interventions was based on rational prescribing guidelines promoted by the World Health Organization focusing on reducing antibiotic use for viral respiratory tract infection and acute diarrhea (De Vries *et al.*, 1994). Similarly, a study from Indonesia (Santoso, 1996), in which health centers were randomized to small or large group educational meetings or to no intervention, aimed to reduce inappropriate antibiotic use for acute diarrhea.

In the European UTI prescribing studies, there was a moderate increase in the use of recommended first-line agents in one study (Lundborg *et al.*, 1999). The other two studies showed modest reductions in the use of long courses of therapy but showed no significant change in the prescribing of first-line agents (Lagerlov *et al.*, 2000; Veninga *et al.*, 2000). The two African

Table 3. Educational meetings

Study citation	Design	Analysis	Outcome measure	Results as reported in the study
Angunawela *et al*. (1991)	Cluster RCT	No cluster analysis	Reduction in use of antibiotics for viral infections	Mean difference in proportion of patients receiving prescription of − 7.3%.
Lundborg *et al*. (1999)	Cluster RCT	Multilevel regression used for cluster analysis	Increase use of first-line agents and reduce duration of treatment for UTI, reduce use of antibiotics for asthma	Increase in proportion of UTI episodes with a first-line agent 18% in intervention, 1% in control ($p < 0.001$). Reduction in duration of antibiotics in both groups (7.51 to 7.41 days and 7.60 to 7.44 days). Increase in number of courses of antibiotics per asthma patient (0.26 to 0.32 and 0.27 to 0.26).
Veninga *et al*. (2000)	Cluster RCT	Use multilevel regression for cluster analysis	Increase use of first-line agents and reduce duration of treatment for UTI	No significant change in the proportion of patients receiving first-line agents (0.12, SE 0.12; relative effect size, 1%). Reduction in the number of DDD of antibiotics (−0.37 DDD, SE 0.02; relative effect size, 31%).
Harris *et al*. (1984)	QRCT	No cluster analysis	Reduction in the use of penicillins (among many other drugs)	No change in intervention group (16.5 prescriptions per 1,000 to 16.7/1,000) vs increase in control group (16.0/1,000 to 18.9/1,000).
Meyer *et al*. (2001)	Cluster RCT	No cluster analysis	Reduction in prescribing of antibiotics for URI and diarrhea	Reduction in proportion of patients with URI with antibiotic prescription 66.3 to 29.41 ($p < 0.05$) compared with 53.99 to 45.64 (p = NS) in controls. For diarrhea change from 66.41 to 44.03 ($p < 0.05$) compared with 11.15 to 5.86 (p = NS) in controls.
Santoso (1996)	Cluster RCT	No cluster analysis	Reduction in prescribing antibiotics for diarrhea	Reduction in proportion of patients receiving antibiotics for diarrhea in small groups (77.4 to 60.4, $p < 0.001$) and large groups (82.3 to 72.3, $p < 0.001$) but not for controls (82.6 to 79.3, p = NS).
Lagerlov *et al*. (2000)	Cluster RCT	Use multilevel regression for cluster analysis	Increase in the number of UTIs treated with short course antibiotics (4 days)	Relative increase in proportion of UTIs treated with short course therapy, 13.1% ($p < 0.0001$) and relative reduction in long course therapy, 9.6% ($p = 0.0004$)
Bexell *et al*. (1996)	Cluster RCT	No cluster analysis	Reduction in overall antibiotic use	Proportion of patients prescribed antibiotics changed from 41.2% to 34.2% in intervention compared with 41.0% to 42.1 % in controls.

Table 3. *Continued*

Study citation	Design	Analysis	Outcome measure	Results as reported in the study
McNulty *et al*. (2000)	CBA	No cluster analysis	Reduction in overall antibiotic use; increase in use of narrow-spectrum and reduction in use of broad-spectrum antibiotics	Reduction of 2,458 antibiotic prescriptions for intervention compared with reduction of 1,209 for control ($p = 0.09$); change in narrow-spectrum agent use of −139 for intervention compared with −1,248 in controls ($p = 0.003$); change in broad-spectrum use −1612 for intervention compared with +561 for controls ($p = 0.002$).
Perez-Cuevas *et al*. (1996)	CBA	No cluster analysis	Reduction in antibiotic use for rhinopharyngitis	Proportion of patients prescribed antibiotics reduced by 17.7% in intervention compared with 10.6% in controls ($p < 0.05$).

studies (Bexell *et al*., 1996; Meyer *et al*., 2001) produced a moderate reduction in overall antibiotic use at the intervention clinics while the study from Sri Lanka did not (Angunawela *et al*., 1991). In the Indonesian study (Santoso, 1996), small group meetings resulted in a larger reduction in antibiotic prescribing for diarrhea than large group meetings; however, both type of meetings were only modestly effective.

The quasi-randomized cluster trial from Britain showed a minimal reduction in the use of penicillin with repeated small group meetings that included the use of audit material (Harris *et al*., 1984). Antibiotic prescribing workshops in Northern England (McNulty *et al*., 2000) were more successful in reducing the use of broad-spectrum antibiotics than in reducing overall antibiotic use for viral respiratory tract infections. Modest reductions in antibiotic use for viral URI were seen following group meetings targeting this behavior in Mexico (Perez-Cuevas *et al*., 1996).

Overall, the results from studies of group educational meetings are modest. Greater effect sizes are seen when the recommendations of the study are for the use of certain proscribed “first-line” antibiotics and are much less impressive for those studies whose goal is to reduce overall inappropriate antibiotic use for viral respiratory tract infection or diarrhea. Only two studies appropriately adjusted for the clustering of patients within physicians and physicians within larger groups (Lagerlov *et al*., 2000; Veninga *et al*., 2000). Both of these studies demonstrated a significant reduction in the duration of antibiotic therapy for uncomplicated UTI.

3.4. Educational outreach/academic detailing

Face-to-face detailing has been used by the pharmaceutical industry for many years to market its products to physicians. The studies in this section use similar methods of detailing physicians regarding appropriate prescribing. The detailers in these studies were either clinical or research pharmacists or medical doctors. In some studies the effectiveness of different types of detailers are compared. This method is attractive for appropriate prescribing education as it has been used very successfully by the pharmaceutical industry, possibly because of the one-on-one attention paid to the prescriber. Materials discussed in the sessions include the review of audit material from the physician's own practice.

In this section, there were eight studies (Avorn and Soumerai, 1983; De Santis *et al.*, 1994; Dolovich *et al.*, 1999; Font *et al.*, 1991; Ilett *et al.*, 2000; McConnell *et al.*, 1982; Peterson *et al.*, 1997; Ray *et al.*, 1985; long term follow-up data for Schaffner *et al.*, 1983) (see Table 4). The two cluster RCTs,

Table 4. Educational outreach visits

Study citation	Design	Analysis	Outcome measure	Results as reported in the study
Dolovich *et al.* (1999)	Cluster RCT	Controlled for location of prescriber in multivariable analysis	Increased prescribing of first-line agents (amoxicillin) for acute otitis media	Mean percent change in market share for amoxicillin in intervention region 0.63 compared with −0.72 in controls ($p = 0.15$).
De Santis *et al.* (1994)	Cluster RCT	No cluster analysis	Increase prescribing of penicillin and erythromycin for tonsillitis	Increase in proportion of prescriptions that are pencillin or erythromycin from pre to post intervention in both groups—60.5% to 8 7.7% in intervention, 52.9% to 71.7% in controls.
Avorn and Soumerai (1983)	Cluster RCT	No cluster analysis	Reduction in use of cephalexin	Mean difference from controls between pre and post intervention periods −382 (mean number of units prescribed) ($p = 0.0006$).
Ilett *et al.* (2000)	RCT	No cluster analysis	Increase prescribing of first-line agents for UTI, bacterial tonsillitis, otitis media, bacterial bronchitis, mild pneumonia	Significant increase in prescribing of amoxicillin from median 293 prescriptions per physician to 594 ($p < 0.05$) and doxycycline from median 235 prescriptions per physician to 865 ($p < 0.05$) (within group comparison only). Both recommended first-line agents for otitis media and pneumonia, respectively.

Table 4. *Continued*

Study citation	Design	Analysis	Outcome measure	Results as reported in the study
McConnell *et al*. (1982)	RCT	No cluster analysis	Reduction in prescribing of tetracycline	Average number of tetracycline prescriptions per provider dropped from 12.6 to 1.8 ($p < 0.001$) in intervention group and 7.6 to 3.2 ($p < 0.001$) in controls.
Font *et al*. (1991)	RCT	No cluster analysis	Reduction in prescribing of antibiotics combined with symptomatic drugs, injectable cephalosporins and injectable penicillin/ streptomycin combination, increase in oral cephalosporins	Median number of prescriptions per month for combination agents fell from 86.53 to 75.89 ($p < 0.001$) for intervention group, 98.55 to 91.96 for controls ($p < 0.001$) between group comparison significantly different ($p < 0.01$); for oral cephalosporins 4.97 to 5.36 ($p < 0.05$), 6.43 to 5.98 (NS), between group comparison ($p < 0.01$); injectable cephalosporins no reduction; penicillin/streptomycin between group comparison NS.
Peterson *et al*. (1997)	CBA	No cluster analysis	Increase prescribing of first-line agents for UTI (amoxicillin clavulanic acid, cephalexin, trimethoprim)	Relative prescribing of first-line agents for UTI higher in intervention than control region compared with baseline ($p < 0.0001$)—ratio of recommended to non recommended antibiotics increased from 2.77 to 5.43 in intervention region and 4.29 to 4.92 in control region.
Schaffner *et al*. (1983)	CBA	No cluster analysis	Reduction in use of contraindicated antibiotics and cephalosporins	Relative reduction in number of prescriptions for contraindicated antibiotics of 67%, 85%, and 41% in pharmacist detailer, physician detailer, and control groups, respectively; for oral cephalosporins, corresponding changes were 35%, 50%, and 33% reduction.

randomized by geographic region, examined changes in the prescribing of first-line agents for acute otitis media (Dolovich *et al*., 1999) and tonsillitis (De Santis *et al*., 1994) in response to academic detailing by a pharmacist. Three of the physician randomized RCTs examined the effectiveness of academic detailing on reducing the use of particular antibiotics, oral cephalosporins (Avorn and Soumerai, 1983), tetracycline (McConnell *et al*., 1982), and antibiotics combined with symptomatic medications, oral and injectable cephalosporins, and an injectable combination of penicillin and streptomycin (Font *et al.*, 1991). Another RCT used academic detailing to promote the use of certain first-line agents for a variety of community-acquired bacterial infections (UTI, bacterial tonsillitis, otitis media, bacterial bronchitis, and mild pneumonia) (Ilett *et al.*, 2000).

The two cluster RCTs combined mailed educational materials with academic detailing by a pharmacist (De Santis *et al.*, 1994) or a traditional pharmaceutical industry detailer (Dolovich *et al.*, 1999) which focused on the content of the previously mailed materials. One of these studies demonstrated a small but significant benefit from academic detailing (De Santis *et al.*, 1994) while the other study showed not benefit (Dolovich *et al.*, 1999). Among the physician randomized studies, two demonstrated a reduction in the use of specific classes of antibiotics (cephalexin [Avorn and Soumerai, 1983] and tetracyclines [McConnell *et al.*, 1982]) compared with controls and printed educational materials alone (Avorn and Soumerai, 1983). In the third study (Ilett *et al.*, 2000), very small changes in the prescribing of recommended first-line agents were achieved; however, the large number of outcomes measured (many antibiotics examined) raises concerns regarding multiple comparisons and the possibility that small, significant results may be due to chance alone.

In the three CBA studies, academic detailing was successful in reducing inappropriate antibiotic use as defined by the individual studies. One group successfully increased the number of prescriptions for first-line agents in UTIs (Peterson *et al.*, 1997). The remaining two studies aimed to reduce the use of certain antimicrobials considered to be contraindicated for use in general practice. Physicians prescribed fewer antibiotics in combination with symptomatic medication and fewer courses of injectable cephalosporins in Barcelona following academic detailing by a pharmacist (Font *et al.*, 1991). The Tennessee statewide intervention mentioned previously used pharmacist or physician detailers and reduced the use of certain agents considered to be contraindicated with a greater reduction seen with physician detailers than pharmacists (Schaffner *et al.*, 1983). This reduction was sustained after two years (Ray *et al.*, 1985).

The effect of academic detailing on improving antibiotic prescribing appears to be moderate in the best cases. Most of the studies utilized pharmacist detailers and thus, it is difficult to generalize about the differences between pharmacist and physician detailers. In the one study comparing the two types of detailing, physician detailing clearly had a more substantial effect on changing prescribing behavior (Ray *et al.*, 1985; Schaffner *et al.*, 1983). The one study utilizing traditional pharmaceutical representatives (Dolovich *et al.*, 1999) to provide education did not demonstrate a significant impact. The overall success of these studies may, in part, be due to the fact that the primary goal in most of these studies was to reduce prescribing of certain agents and/or promote prescribing of recommended first-line agents. None of these studies sought to reduce overall use of antibiotics for inappropriate indications which appears to be a much more difficult task.

3.5. Financial/healthcare system changes

There are a variety of interventions which fall under the umbrella of financial interventions and/or changes in the healthcare system. These range from changes in formularies or benefits to the institution of user fees, or coinsurance for physician visits or medications. These are aimed at reducing utilization of specific drugs or physician services. Reforms to the local healthcare system usually involve changes in the manner in which healthcare delivery occurs such as the use of non-physician providers or changes in the organizational structure of health clinics or regions. It is inappropriate to compare interventions in this category head-to-head as they may involve disparate methods that defy comparison.

There are only two studies that fall into this category (MacCara *et al*., 2001; Juncosa and Porta, 1997) (Table 5). One examines the effect of a formulary change (MacCara *et al*., 2001) and the other the effect of primary care reform in a region of Spain (Junosa and Porta, 1997) Researchers in Nova Scotia, Canada, studied the effect of a change in the provincial drug formulary limiting the use of fluoroquinolones in the elderly to certain specific conditions (MacCara *et al*., 2001). Using ITS data they reported a significant drop in the mean number of fluoroquinolone prescriptions between the two time periods; however, they did not use appropriate time-series analysis which compares rates of prescribing over time before and after the intervention. Time-series analysis detected the same significant drop in the level of prescribing between pre- and post-formulary changes; the slope for fluoroquinolone prescribing, however, increased between pre- and post-formulary change periods. Thus while there was an immediate and dramatic impact of the formulary change, time trends suggest that the level of prescribing over time might be expected to return to pre-formulary change levels.

In a CBA study from Spain, researchers examined the effect of nationwide primary care reform on drug prescribing in one county, using areas that had not yet undergone reform as controls (Juncosa and Porta, 1997). The primary care reform consisted, mainly, of changes in staffing (all working full time as opposed to part time) and reimbursement (per capita payment changed to fixed salary) as well as changes in the organization of services and integration of preventive medicine services into the traditional curative model. Overall, there was a greater reduction in all antibiotic prescriptions in the reform primary care network compared with the non-reformed network.

The study from Nova Scotia demonstrates the substantial initial impact that formulary changes may have on prescribing of particular medications

Table 5. Financial/healthcare system changes

Study citation	Design	Analysis	Outcome measure	Results as reported in the study
MacCara *et al.* (2001)	ITS (formulary change)	No time-series analysis reported	Number of prescriptions for fluoroquinolones	Fluoroquinolone use dropped by 80.2% following intervention
Juncosa and Porta (1997)	CBA (primary care reform)	No cluster analysis	Overall number of antibiotic prescriptions	56.6% relative reduction in prescribing in reform network compared with 32.5% relative reduction in non-reform network

(MacCara *et al.*, 2001). However, overall antibiotic use did not change significantly with substitution of macrolide antibiotics for fluoroquinolones. This likely represents a substantial cost saving to the drug plan but does little to control overall antibiotic use. This study also demonstrates the pitfalls in not using appropriate analytic techniques for time-series data which, when performed, indicated that levels of fluoroquinolone use were increasing after the change and could eventually reach pre-intervention levels. The Spanish study demonstrates that structural changes in the way in which healthcare is delivered can have an impact on physicians' practice without applying specific educational interventions (Juncosa and Porta, 1997). It would be interesting to see if the reduction in antibiotic use were maintained over time or simply represents the early enthusiasm for the restructured system.

3.6. Reminders

Physician reminders, at the point of care, have been assessed by three physician randomized RCTs attempting to reduce antibiotic prescribing for two clinical syndromes, acute otitis media (Christakis *et al.*, 2001) and sore throat (two studies of a similar intervention) (McIsaac and Goel, 1998; McIsaac *et al.*, 2002) (Table 6). The principle behind this type of intervention is that if physicians are provided with information about specific treatments, at the time they are making prescribing decisions, inappropriate antibiotic use may be reduced.

In one study, an online prescription writer was used to present computer-based point-of-care evidence on the optimal duration of antibiotics for acute otitis media in children in an effort to reduce the duration of prescribing for this condition (Christakis *et al.*, 2001). The results indicated a significant increase in the proportion of prescriptions for otitis media that were of less than 10 days duration for intervention physicians compared with controls.

Table 6. Reminders

Study citation	Design	Analysis	Outcome measure	Results as reported in the study
Christakis *et al*. (2001)	RCT	No cluster analysis	Reduction in duration of therapy for acute otitis media to <10 days	Change in mean number of patients receiving <10 days of antibiotics 44.43% vs 10.48 % in controls ($p = 0.000$)
McIsaac *et al*. (1998)	RCT	No cluster analysis needed (only one patient per provider)	Reduction in antibiotic prescriptions for sore throat	Proportion of patients receiving prescription for sore throat 27.8% in intervention group, 35.7% in control group; odds ratio for an antibiotic prescription associated with intervention 0.44 (0.21–0.92)
McIsaac *et al*. (2002)	RCT	Cluster analysis performed	Reduction in antibiotic prescriptions for sore throat	Proportion of patients receiving antibiotics for sore throat 28.1% in intervention group, 27.9% for controls; odds ratio for antibiotic prescribing associated with intervention 0.57 (0.27–1.17)

In the two studies of reminders for sore throats (McIsaac and Goel, 1998; McIsaac *et al*., 2002) (both by the same authors), a paper-based decision support tool for diagnosis and management of sore throat was developed in an effort to reduce inappropriate antibiotic use for this condition. This decision support tool consisted of a scoring system for signs and symptoms of sore throat to help determine the likelihood that a particular patient suffers from streptococcal pharyngitis. Management recommendations were then based upon scores. In the first study, family physicians received a package containing information on the study, a score card for diagnosing streptococcal sore throat and a form to complete for one sore throat patient encounter. Physicians in the study group received a form that required them to calculate a score based on four items. The control form was identical except that the score items were listed and physicians were not asked to calculate a score. Since each physician contributed only one sore throat encounter, there was no need to adjust the analysis for clustering. The authors were able to demonstrate a reduction in the odds of prescribing an antibiotic for sore throat in the intervention group compared with controls.

In the second study (McIsaac *et al*., 2002), by the same authors, the same checklist and score were used. All physicians received a pocket card summarizing the score, eight patient encounter and consent forms and a one page survey of practice characteristics. Physicians in the intervention group received stickers to place on the patient encounter forms with the score items and a place to calculate the score. This resulted in the intervention physicians' receiving repeated prompts regarding the score and management recommendations. The control physicians completed similar encounter forms without stickers. In this study there was no reduction in the odds for prescribing an antibiotic associated with the repeated prompts compared with controls.

From this limited dataset, physician reminders appear to have some effect on altering prescribing behavior. In the otitis media study, intervention physicians prescribed fewer long courses of antibiotics. In addition, however, physicians had an opportunity to view information on the overall need for antibiotics in otitis media. There was no reduction in overall prescribing for otitis associated with this part of the intervention. While the sore throat score seemed to modestly reduce antibiotic use for this condition when used for a single patient, repeated prompts in the clinical setting did not have a beneficial effect, limiting the usefulness of this intervention. This may have been due to the effect of the control physicians' receiving the score (without using the repeated prompts) in the control group, leading to reduced prescribing overall. It may also be that physicians stopped interacting with the score after using it several times either out of fatigue or the sense that they could judge the probability of streptococcal infection well enough after using the score a few times.

3.7. Patient-based interventions

In several studies, patient-based interventions were evaluated in conjunction with other interventions. There were, however, five studies that examined the effect of a variety of patient-based interventions alone (Table 7). These studies evaluated the effect of patient educational materials (Mainous *et al*., 2000), a patient information leaflet regarding antibiotics for acute bronchitis (Macfarlane *et al*., 2002) and the use of delayed prescriptions for infections where patients desired antibiotics but physicians did not feel antibiotics were necessary (Arroll *et al*., 2002; Dowell *et al*., 2001; Little *et al*., 2001).

In the one study examining the effect of patient educational materials alone (Mainous *et al*., 2000), there was a modest effect seen in the group with this intervention compared with the control group. This effect was similar to that seen in the other intervention groups (audit and feedback alone, or combined with patient educational materials). In a study of prescribing for acute bronchitis in adults (Macfarlane *et al*., 2002), patients who were not felt to need antibiotics by the physician but appeared to desire a prescription received a prescription along with either a flyer explaining why antibiotics were unnecessary for this condition or a blank leaflet. Patients in the intervention group were less likely to fill their prescriptions than those in the control group.

Three additional studies, utilizing the same concept, randomized patients to receive and fill a prescription immediately or to fill the prescription later

Table 7. Patient-mediated interventions

Study citation	Design	Analysis measure	Outcome	Results as reported in the study
MacFarlane *et al*. (2002)	RCT—patient randomized	No cluster analysis required	Reduction in number of patients filling prescription for antibiotic for acute bronchitis	Proportion of patients filling prescription 47% in intervention vs 62% in control; hazard ratio for taking antibiotic for intervention compared with control 0.66 (0.46–0.96)
Mainous *et al*. (2000)	RCT	No cluster analysis	Reduction in number of prescriptions for URI	Overall increase in proportion of patients with colds with prescriptions—gain score compared with controls significantly lower by Dunnett's T ($p < 0.05$)
Arroll *et al*. (2002)	RCT—patient randomized	No cluster analysis required	Reduction in the number of patients filling prescriptions for URI	48% of patients in delayed prescription group filled prescription vs 89% in controls; odds ratio for filling prescription for delayed prescription 0.12 (0.05–0.29)
Dowell *et al*. (2001)	RCT—patient randomized	No cluster analysis required	Reduction in the number of patients filling prescriptions for URI	45% of patients in delayed prescription group received a prescription vs 82% in the control group (information obtained from authors)
Little *et al*. (2001)	RCT—patient randomized	No cluster analysis required	Reduction in the number of patients filling prescriptions for otitis media	24% of patients in delayed prescription group filled a prescription vs 98% in the control group

(3–7 days depending on the study) if symptoms did not improve. In the two studies of adult patients with the common cold, patients were much less likely to fill the prescription in the delayed group (Arroll *et al*., 2002; Dowell *et al*., 2001). A similar effect of delayed prescriptions was seen in the study of prescribing for otitis media in children (Little *et al*., 2001).

The attractiveness of this type of intervention is that physicians advise against the need for an antibiotic for viral infections while still feeling that they have satisfied perceived patient demands. Indeed, some of the physicians in these studies felt that they would continue to use this intervention with demanding patients. Ultimately, the goal is that the patient will not fill the prescription and recover from the illness with the knowledge that an antibiotic was not necessary. He or she may then be less inclined to request a prescription during the next illness or possibly even forgo a visit to the physician for this problem as he or she now knows that it is benign and self-limited. One could argue, however, that giving a patient a prescription when it is not necessary sends a mixed message and places the onus of the decision on the patient. Simply taking the time to explain why an antibiotic is not necessary may accomplish the same goal.

3.8. Multifaceted interventions

Many of the older studies presented in the preceding sections have indicated that it is very difficult to produce anything but modest changes in physicians' antibiotic prescribing practices especially if one is attempting to reduce overall use for viral infections as opposed to promoting use of first-line agents. As a result, seven of the most recent studies examined the effect of complex, multifaceted interventions on reducing antibiotic misuse (see Table 8). (Belongia *et al*., 2001; Finkelstein *et al*., 2001; Flottorp *et al*., 2002; Gonzales *et al*., 1999; Hennessy *et al*., 2002; Perz *et al*., 2002; Stewart *et al*., 2000). These interventions include physician education in a variety of forums as well as education of the patient/parent and the general public as to the appropriate use of antibiotics. The public education message in these studies has focused on the individual and public health hazards of antibiotic overuse. The US Centers for Disease Control (CDC) was involved in the design and implementation of four (Belongia *et al*., 2001; Finkelstein *et al*., 2001; Hennessy *et al*., 2002; Perz *et al*., 2002) out of seven studies in this category.

In the four CDC sponsored studies, the interventions involved a combination of healthcare provider and consumer education aimed at reducing inappropriate antibiotic use for viral respiratory tract infections. Healthcare provider education was undertaken in the form of small group sessions, traditional CME lectures, hospital and clinic staff meetings and grand rounds, the exact combination depending on the particular study. The content of the educational message was based upon the Principles of Judicious Antimicrobial use for pediatric upper respiratory infections (Dowell *et al*., 1998) drafted by the CDC, the American Academy of Pediatrics (AAP), and the American Academy of Family Physicians (AAFP). Patient and community education was primarily undertaken using printed educational materials produced by the CDC which were distributed at hospitals, during doctor visits, and at community centers and schools. Samples of this material can be found at http://www.cdc.gov/drugresistance/community/tools.htm. In addition, some studies used community meetings and local media to promote the judicious use of antibiotics.

Three of the CDC-sponsored studies in this category examined the effect of the intervention on rates of penicillin-resistant *S. pneumoniae* in the communities

Table 8. Multifaceted interventions

Study citation	Design	Analysis	Outcome measure	Results as reported in the study
Belongia *et al.* (2001)	CBA	No cluster analysis	Reduction in antibiotic use in children	11% reduction in intervention region vs 12% increase in control region ($p = 0.019$) for liquid antibiotics; 19% reduction in intervention region vs 8% reduction in control ($p = 0.042$) for solid antibiotics.
Finkelstein *et al.* (2001)	Cluster RCT	Used generalized estimating equation for cluster analysis	Reduction in antibiotic use in children	0.23 (0.08–0.39, $p < 0.01$) fewer antibiotic courses per person 3 to < 36 mos per year; 0.13 (0–0.27, $p = 0.06$) fewer antibiotic courses per person 36 to <72 mos per year
Hennessey *et al.* (2002)	CBA	No cluster analysis	Reduction in overall antibiotic use	First year: reduction from 1.24 to 0.81 antibiotic courses per person ($p < 0.01$) in intervention region vs 0.63 to 0.57 ($p =$ NS) Second year: initial intervention region constant 0.85 to 0.81 antibiotic courses per person, 0.55 to 0.4, 0.55 to 0.41 ($p < 0.01$) in expanded intervention region (control from first year)
Perz *et al.* (2002)	CBA	Used binomial regression controlling for region	Reduction in antibiotic use in children	19% reduction in antibiotic prescriptions per 100 person years in intervention vs 8% reduction in controls (intervention attributable effect 11% (8–14%) reduction ($p < 0.001$)
Gonzales *et al.* (1999)	CBA	Cluster analysis performed using study site as a fixed effect in regression analysis	Reduction in antibiotic prescribing for acute bronchitis in adults	Proportion of cases with antibiotics prescribed reduced from 74% to 48% in full intervention site vs 82% to 77% in limited intervention site ($p = 0.02$ between site)
Stewart *et al.* (2000)	CBC	No cluster analysis	Increase prescribing of first-line agents	No change in prescribing first-line agents compared with control (adjusted odds

Table 8. *Continued*

Study citation	Design	Analysis	Outcome measure	Results as reported in the study
				ratio 1.02 [0.99–1.06]); increase in prescribing second-line agents in control region vs intervention region (odds ratio 1.40 [1.32–1.49])
Flottorp *et al*. (2002)	RCT	Multilevel regression use for cluster analysis	Reduction in prescribing antibiotics for sore throat	Proportion of cases of sore throat with antibiotics reduced from 48.1% to 43.8% in intervention vs 50.8% to 49.5% in control region ($p = 0.032$)

being studied (Belongia *et al*., 2001; Hennessy *et al*., 2002; Perz *et al*., 2002). This very important secondary endpoint will be discussed in detail in the section entitled "Effect of interventions on antibiotic resistance."

Among the CDC-sponsored studies, there was one cluster randomized trial (Finkelstein *et al*., 2001) and three CBA studies (Belongia *et al*., 2001; Hennessy *et al*., 2002; Perz *et al*., 2002). All of these studies were successful in significantly reducing the inappropriate use of antibiotics for viral respiratory tract infections. Effect sizes ranged from moderate (12–16% relative reduction in antibiotic use) (Finkelstein *et al*., 2001) to a more substantial relative reduction in antibiotic use of 31% (Hennessy *et al*., 2002).

In a CBA study, Gonzales and colleagues (Gonzales *et al*., 1999) applied a full intervention (consisting of physician education and patient materials in the office and sent to homes) to one site and compared the effect to an intervention limited to patient education materials at another site and two (no intervention) control sites. This study demonstrated a substantial absolute reduction in prescribing from baseline for the full intervention site compared with controls (24%) while the patient intervention alone had no significant effect. The remaining two studies demonstrated little (Stewart *et al*., 2000) or no change (Flottorp *et al*., 2002) in prescribing despite extensive interventions. The Norwegian study (Flottorp *et al*., 2002) purported to use interventions that were tailored to locally identified barriers to change and included changes to the fee schedule for phone calls with patients in order to reduce the number of visits to physicians for sore throat and UTI. Despite this study's excellent design and execution, the authors could not demonstrate a reduction in the use of antibiotics for sore throat.

Overall the methodology of these studies was better than for studies in other categories. In addition, these combined interventions appeared to be more effective in reducing inappropriate antibiotic use than single interventions.

4. EFFECT OF INTERVENTIONS ON ANTIBIOTIC RESISTANCE

Among the 39 studies reviewed, only 4 studies simultaneously assessed the effect of the interventions on bacterial antimicrobial resistance in the study communities (Belongia *et al*., 2001; Hennessy *et al*., 2002; Perz *et al*., 2002; Seppälä *et al*., 1997). Seppälä *et al*. (1997) examined the effect of a reduction in consumption of macrolides on the rate of isolation of macrolide-resistant Group A streptococci from throat swabs and pus specimens. The reduction in macrolide use in Finland was observed following a published recommendation against use of macrolides as first-line agents for Group A streptococcal infections. For the analysis of the trend in macrolide resistance, they used data from 1992 as the recommendations were issued in late 1991 and early 1992. This data could not be subjected to time-series analysis as there were an insufficient number of pre-intervention data points with which to perform such an analysis. Using logistic regression, it was determined that the odds of an isolate being erythromycin resistant in 1996 were half the odds of it being resistant in 1992 indicating a significant reduction in the rate of resistance (odds ratio 0.5 [95% CI 0.4–0.5]). This held true when the data were analyzed by region. Thus, these researchers were able to demonstrate that a reduction in consumption of one class of antibiotics could result in a reduction in resistance to that antibiotic class in the population. Of course, the reduction in macrolide consumption was accompanied by an increase in use of other antibiotics for Group A streptococcal infections; however, Group A streptococcal resistance to penicillin has never been documented in Finland and thus penicillin represents an effective alternative that, at least currently, is safe from the problems of antibiotic resistance.

The other three studies addressing the effect of interventions on antimicrobial resistance are three of the four studies sponsored by the CDC. In all three of these studies, the researchers examined the effect of multifaceted interventions on reducing overall antibiotic use in the study communities and on the rates of isolation of penicillin-resistant *S. pneumoniae* from individuals in the community. In the CBA community study from Wisconsin (Belongia *et al*., 2001), the effect of the intervention on the rate of penicillin resistance (either intermediate or full resistance as defined by NCCLS criteria) in pneumococcal isolates was determined by performing nasopharyngeal swabs and cultures for pneumococcal carriage on children attending child care facilities in the study communities. The intervention resulted in a moderate reduction in antibiotic consumption following the intervention compared with the control regions. In a multivariate logistic regression model controlling for clustering of children within child care centers, nasopharyngeal carriage of a resistant pneumococcus was not associated with living in a particular community (odds ratio 0.46 [0.18–1.18]).

This indicates that over the period of the study (2 years) there was no significant reduction in the odds of harboring a penicillin-resistant pneumococcus due to the intervention.

In the multifaceted, community intervention trial in Alaska (Hennessy *et al*., 2002), nasopharyngeal swabbing was performed on any community member (adult or child) who consented to the procedure. After the initial education intervention in region A, the proportion of pneumococcal isolates that were penicillin non-susceptible (intermediate or full resistance) decreased from 41% to 29% in region A but did not significantly change in the control regions B and C (24% to 22%). The intervention continued in region A and was expanded to regions B and C in the second year of the study. In the second year, the reduction in the rate of resistance observed in region A was not sustained and the proportion of pneumococci that were penicillin non-susceptible increased from 29% to 43%. In the expanded intervention regions, the proportion of pneumococci that were penicillin non-susceptible did not change following the intervention (22% vs 26%). Thus, the initial reduction in region A cannot be attributed to the reduction in antibiotic consumption observed following the intervention.

In the community intervention study in Tennessee (Perz *et al*., 2002), the effect of the intervention on the rate of pneumococcal resistance was assessed by examining the rate of isolation of resistant (intermediate or full resistance) pneumococci from sterile site isolates (blood, cerebrospinal fluid, other usually sterile body fluids) from children under 15 years of age. While the intervention resulted in an overall reduction in antibiotic use, the proportion of invasive, sterile site isolates resistant to penicillin did not change over the 3 years of the study (60% year 1, 74% year 2, and 71% year 3).

The results of these three multifaceted community intervention studies indicate that despite the moderate success of the interventions in reducing overall antibiotic used in the relative short term (1–2 years), a similar effect on antibiotic resistance rates has not been demonstrated in the same time period.

5. EFFECT OF INTERVENTIONS ON PATIENT OUTCOMES

Two studies examining the effect of patient-based interventions on antibiotic use also examined the effect of withholding antibiotics on the clinical outcomes of enrolled patients. Both of these studies examined the effect of delaying antibiotic prescriptions, one for acute otitis media in children and one for the common cold in adults. Both studies documented reduced antibiotic use by those patients randomized to the delayed antibiotics groups of the respective studies.

In the study of delayed antibiotics in the common cold by Arroll and colleagues (Arroll *et al.*, 2002), patients completed daily symptom checklists until the tenth day after the initial medical visit. These checklists were collected and symptom scores were tabulated for the two groups (immediate and delayed prescription groups). Using the general linear model for repeated measures, it was found that patient temperatures did not differ between the two groups over the course of the study. In addition, the symptom scores (based on cough, nasal discharge, throat pain, headache, etc.—maximum score 15) for the two groups were essentially the same at time points throughout the 10 day follow-up.

In the otitis media study (Little *et al.*, 2001), parents were requested to complete a daily diary regarding presence of symptoms (earache, unwellness, sleep disturbance), perceived severity of pain, number of episodes of distress, use of paracetamol, and temperature measurements. Overall, parents of patients in the immediate antibiotic group reported fewer days of crying and sleep disturbance as well as less paracetamol use; however, there was no difference in mean pain scores, episodes of distress or absence from school.

It is not surprising that delaying (and ultimately preventing) antibiotic use in the common cold had no effect on resolution of symptoms given the viral etiology. In addition, the recruiting physicians could choose not to enroll anyone they felt required an antibiotic (presumably for bacterial rhinosinusitis, ear infection, or pneumonia detected clinically). The otitis study confirms that, in many cases, patients diagnosed with otitis media will improve spontaneously, despite the bacterial origin of their disease. There has been a great deal of controversy about this as it may be that acute otitis media is so loosely defined in many studies, including this one, that many of the children may not truly have bacterial infection but red painful ears due to viral infection. In that case, spontaneous resolution, would be the rule. The authors of this study describe it as pragmatic, however, pointing out that in the real world, many of these children are diagnosed with acute otitis media and treated with antibiotics. Delaying the collection of a prescription in this setting reduces antibiotic use and will not result in excess morbidity. One might, however, also argue that teaching appropriate diagnostic technique for acute otitis media, with antibiotics prescribed only to those children who meet strict diagnostic criteria, would have a similar effect.

6. DISCUSSION OF RESULTS AND IMPLICATIONS FOR PRACTICE

Given the broad array of targeted behaviors, the variation in interventions (even within categories) and the differences in the clinical settings, it is difficult to generalize the results from these individual studies and arrive at broadly applicable recommendations for improving antibiotic prescribing in any community. However, several general observations may be cautiously made.

The simple, single intervention studies (mailed or published educational materials, audit and feedback) generally resulted in no or little change in prescribing behavior. Previous systematic reviews have concluded that passive methods of physician education such as traditional conferences and lectures as well as publication of guidelines have very limited impact (O'Brein *et al.*, 2003a–d; Oxman *et al.*, 1995). The most plausible explanation for this is that these interventions often fail to address the root causes of inappropriate prescribing. Simply drawing the physician's attention to the behavior (audit and feedback) or recommending an alternate behavior (educational materials) may not provide the physician with the tools to change a behavior that likely is quite ingrained and multifactorial in its origins. It bears mentioning that these low cost interventions may result in cost savings to governments and other insurers even if the results are marginal given the high cost of prescription medications. Small changes in prescribing are unlikely, however, to reduce the incidence of antibiotic resistant bacteria in a community.

The one exception to this lack of effect of simple interventions was the impressive change in macrolide use in Finland following publication of a guideline recommending against the use of this class of antibiotics for Group A streptococcal infection. This result is unexpected given the limited effect of published guidelines on physician behavior. The basis of the recommendation was patient safety as there were concerns regarding treatment failures due to the increasing rate of macrolide resistance. This emphasis on patient safety may account for the impressive impact of the written recommendations compared with other reports of this intervention. However, as time-series analysis demonstrated, the effect of this single intervention (occurring at one point in time, i.e., single publication) appeared to wane somewhat over time as indicated by the positive slope of the post-intervention prescribing rates. Thus, over the long term, the effect of this recommendation may wane as memory of the publication fades.

The more complex the intervention, the more likely it was to produce important changes in antibiotic prescribing behavior. Educational meetings produced modest improvements in prescribing. The study examining patient education materials alone or in combination with another intervention demonstrated the benefit of including patient-based education in the intervention (Mainous *et al.*, 2000). This observation provided the rationale and impetus for the community-based, multifaceted interventions undertaken by the CDC and other groups of researchers. Combinations of interventions in most instances, produced moderately large reductions in antibiotic use which was sustained in those studies with follow-up data, depending on the specific intervention and targeted behavior (Belongia *et al.*, 2001; Finkelstein *et al.*, 2001; Flottorp *et al*., 2002; Gonzales *et al*., 1999; Hennessy *et al*., 2002; Perz *et al*., 2002; Stewart *et al*., 2000). One notable exception was the Norwegian study (Flottorp *et al*., 2002) where researchers designed the intervention to specifically address previously identified barriers to change. There was no change in antibiotic use for sore throat in this study, despite the tailored interventions possibly due to the passive nature of the interventions or an inadequate duration of follow-up. This strengthens the impression that one cannot derive broad-based recommendations from these studies to apply to any clinical situation in any community.

It appears that interventions aimed at increasing the prescribing of certain recommended first-line antibiotics for specific infections are more likely to produce substantial changes in prescribing than those interventions targeting overall inappropriate antibiotic use. As discussed in the introduction, the root causes of antibiotic misuse in the community outpatient setting are manifold and may include physicians' succumbing to pressure from patients, lack of understanding by the physician as to the necessity for antibiotics in certain clinical conditions, diagnostic uncertainty as to the true nature of the patient's illness, and constraints on the physician's time to explain the nature of the illness and the reasons an antibiotic is not indicated. Convincing a physician or patient that a particular antibiotic (usually the most narrow spectrum agent for the condition) should be his or her first choice should be relatively simple as long as appropriate justification for the recommendation is made. It stands to reason, however, that completely eliminating prescribing for a particular indication, such as a viral URI, in a clinical situation in which the physician would usually prescribe an unnecessary antibiotic would be a more difficult behavioral change. While this generally holds true for most of the reviewed studies, promoting the prescribing of first-line agents was not as straightforward a task as might be predicted. One potential explanation for this is that physicians may consider these prescribing recommendations a limitation to their clinical freedom. In addition, physicians want to prescribe what they think are the best medications for the individual patient which often means a broad-spectrum agent to protect against potentially resistant organisms regardless of the ecological consequences.

Several of the trials addressed patient-based outcomes such as changes in antibiotic resistance patterns as a result of altered antibiotic use (Belongia *et al*., 2001; Hennessy *et al*., 2002; Perz *et al*., 2002; Seppälä *et al*., 1997) and illness outcomes following the withholding of antibiotics for certain conditions (Arroll *et al*., 2002; Little *et al*., 2001). Over the intervention periods (usually between 1 and 3 years) no substantial or persistent reductions in incidence of isolating resistant bacteria were observed in any of the studies except for the Finnish macrolide study (Seppälä *et al*., 1997), where changes were observed in macrolide resistance rates after approximately 2 years. In contrast, no sustained reduction in penicillin resistance was observed with overall reductions in antibiotic use in several communities (Belongia *et al*., 2001; Hennessy *et al*., 2002; Perz *et al*., 2002). The reason for this has been suggested by a mathematical model of rates of change of antibiotic resistance among bacteria (Stewart *et al*., 1998). The conclusions from the model suggest that the period time to observe reductions in the incidence of antibiotic-resistant organisms will be longer than the preceding increases. Thus, it may be many years before sustained reductions in antibiotic use produce reductions in penicillin-resistant pneumococci. In addition, larger reductions in antibiotic use may be necessary to produce more rapid changes in resistance patterns. Assessing the full effect of reductions in community-wide antibiotic use may be made complicated by the already observed reductions in invasive pneumococcal infections in immunized children and their contacts due to conjugate pneumococcal vaccines.

In the studies of the use of delayed antibiotic prescriptions for URIs and otitis media, significant patient morbidity was not observed (Arroll *et al*., 2002; Dowell *et al*., 2001; Little *et al*., 2001). As the outcome of viral respiratory tract infections is not altered by antibiotics, these are not unexpected results for the studies of URIs. It is important, however, to have data that demonstrates this lack of morbidity for illnesses such as acute bronchitis and purulent rhinitis where the etiologic agent, while usually viral, is often thought to be bacterial by many practitioners. The demonstration that there is no benefit to immediate use of antibiotics may serve to convince many physicians and patients that antibiotics are not needed for these conditions. Delayed prescriptions for acute otitis media in children are frequently used in many European countries but have not gained popularity in North America. This pragmatic study (Little *et al*., 2001) demonstrates that waiting a few days to use an antibiotic among children diagnosed with otitis media does not increase morbidity from this disease. It has been argued that studies like this do not validly assess the effect of antibiotics on acute otitis media as the diagnostic criteria are not strict enough, leading to the inclusion of many patients who did not truly have bacterial otitis media; however, this argument only serves to strengthen the conclusions from this study that antibiotics are not required for most cases of acute otitis media diagnosed in the primary care setting most likely because this condition is overdiagnosed. Withholding immediate antibiotic helps to weed out those children with URIs and red tympanic membranes from those with true bacterial middle ear disease, leading to more appropriate antibiotic use.

6.1. Implications for practice

The selection of the most effective intervention to improve the prescribing of antibiotics appears to be condition and situation specific. In designing an intervention to change a particular prescribing behavior, the ultimate goal of the intervention must be defined and barriers to change identified and addressed by the intervention.

Small changes in the prescribing of narrow-spectrum, first-line agents may be achieved to varying degrees with the use of simple, single interventions such as guideline publication and distribution, educational meetings, and audit and feedback. These incremental changes may result in substantial cost savings as these interventions are relatively inexpensive. These interventions are unlikely to lead to a reduction in the incidence of antibiotic-resistant bacteria causing community-acquired infection.

It appears that more complex interventions produce more substantial reductions in antibiotic prescribing. These interventions are also very expensive and may not be cost-effective. Multifaceted interventions, however, are more likely to result in the sort of changes in prescribing that may eventually lead to reductions in the incidence of antibiotic-resistant bacteria. That this was not observed in the studies measuring this outcome is most likely a function of time. Long-term follow-up of the intervention communities may reveal changes in the antibiotic susceptibilities of community-acquired bacterial infections.

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