Cochrane Library

Cochrane Database of Systematic Reviews

Interventions to improve antibiotic prescribing practices in ambulatory care (Review)

Arnold SR, Straus SE

Arnold SR, Straus SE.
Interventions to improve antibiotic prescribing practices in ambulatory care.
Cochrane Database of Systematic Reviews 2005, Issue 4. Art. No.: CD003539.
DOI: 10.1002/14651858.CD003539.pub2.

www.cochranelibrary.com

WILEY

TABLE OF CONTENTS

[Intervention Review]

Interventions to improve antibiotic prescribing practices in ambulatory care

Sandra R Arnold[1], Sharon E Straus[2]

[1]Pediatrics, University of Tennessee, Memphis, TN, USA. [2]Internal Medicine, University of Toronto, Toronto, Canada

Contact address: Sandra R Arnold, Pediatrics, University of Tennessee, Le Bonheur Children's Medical Center, 50 N Dunlap St., Memphis, TN, 38103, USA. sarnold@utmem.edu.

Editorial group: Cochrane Effective Practice and Organisation of Care Group
Publication status and date: Edited (no change to conclusions), published in Issue 1, 2009.

Citation: Arnold SR, Straus SE. Interventions to improve antibiotic prescribing practices in ambulatory care. *Cochrane Database of Systematic Reviews* 2005, Issue 4. Art. No.: CD003539. DOI: 10.1002/14651858.CD003539.pub2.

ABSTRACT

Background

The development of resistance to antibiotics by many important human pathogens has been linked to exposure to antibiotics over time. The misuse of antibiotics for viral infections (for which they are of no value) and the excessive use of broad spectrum antibiotics in place of narrower spectrum antibiotics have been well-documented throughout the world. Many studies have helped to elucidate the reasons physicians use antibiotics inappropriately.

Objectives

To systematically review the literature to estimate the effectiveness of professional interventions, alone or in combination, in improving the selection, dose and treatment duration of antibiotics prescribed by healthcare providers in the outpatient setting; and to evaluate the impact of these interventions on reducing the incidence of antimicrobial resistant pathogens.

Search methods

We searched the Cochrane Effective Practice and Organisation of Care Group (EPOC) specialized register for studies relating to antibiotic prescribing and ambulatory care. Additional studies were obtained from the bibliographies of retrieved articles, the Scientific Citation Index and personal files.

Selection criteria

We included all randomised and quasi-randomised controlled trials (RCT and QRCT), controlled before and after studies (CBA) and interrupted time series (ITS) studies of healthcare consumers or healthcare professionals who provide primary care in the outpatient setting. Interventions included any professional intervention, as defined by EPOC, or a patient-based intervention.

Data collection and analysis

Two review authors independently extracted data and assessed study quality.

Main results

Thirty-nine studies examined the effect of printed educational materials for physicians, audit and feedback, educational meetings, educational outreach visits, financial and healthcare system changes, physician reminders, patient-based interventions and multi-faceted interventions. These interventions addressed the overuse of antibiotics for viral infections, the choice of antibiotic for bacterial infections such as streptococcal pharyngitis and urinary tract infection, and the duration of use of antibiotics for conditions such as acute otitis media. Use of printed educational materials or audit and feedback alone resulted in no or only small changes in prescribing. The exception was a study documenting a sustained reduction in macrolide use in Finland following the publication of a warning against their use for group A streptococcal infections. Interactive educational meetings appeared to be more effective than didactic lectures. Educational outreach visits and physician reminders produced mixed results. Patient-based interventions, particularly the use of delayed prescriptions for infections for which antibiotics were not immediately indicated effectively reduced antibiotic use by patients and did not result in excess morbidity. Multi-faceted interventions combining physician, patient and public education in a variety of venues and formats were the most successful in reducing antibiotic prescribing for inappropriate indications. Only one of four studies demonstrated a sustained reduction in the incidence of antibiotic-resistant bacteria associated with the intervention.

Authors' conclusions

The effectiveness of an intervention on antibiotic prescribing depends to a large degree on the particular prescribing behaviour and the barriers to change in the particular community. No single intervention can be recommended for all behaviours in any setting. Multi-faceted interventions where educational interventions occur on many levels may be successfully applied to communities after addressing local barriers to change. These were the only interventions with effect sizes of sufficient magnitude to potentially reduce the incidence of antibiotic-resistant bacteria. Future research should focus on which elements of these interventions are the most effective. In addition, patient-based interventions and physician reminders show promise and innovative methods such as these deserve further study.

PLAIN LANGUAGE SUMMARY

Improving how antibiotics are prescribed by physicians working in the community.

Antibiotics are used to treat infections, such as pneumonia or ear infections, that are caused by bacteria. Over time however, many bacteria have become resistant to antibiotics. This means that even when antibiotics are taken they may fail to cure an infection if a resistant bacteria is present. Bacteria become resistant because antibiotics are used too often and incorrectly.

Research has shown that physicians in the community (in doctors' offices and clinics) can be partly to blame for resistant bacteria. Studies have shown that physicians inappropriately prescribe antibiotics for infections caused by viruses (such as the common cold). They also prescribe antibiotics that kill a wide variety of bacteria when an antibiotic that kills specific bacteria should be prescribed. Physicians may also prescribe the wrong dose for the wrong length of time. Inappropriate prescribing is due to many factors including patients who insist on antibiotics, physicians who do not have enough time to explain why antibiotics are not necessary and therefore simply prescribe them to save time, physicians who do not know when to prescribe antibiotics or how to recognise a serious bacterial infection, or physicians who are overly cautious.

To improve how physicians prescribe antibiotics in the community, methods have been studied. In this review, 39 studies were analysed to determine what works. Using printed materials to educate physicians about prescribing or to give them feedback about how they prescribed did not improve their prescribing or only improved it by a small amount. Meetings to educate physicians improved their prescribing but lectures did not. It was not clear whether personal visits to the physicians by educators worked or not or whether reminders to physicians worked or not . The use of delayed prescriptions decreased use of antibiotics without increasing the risk of serious illness. A delayed prescription means the physician gives a patient a prescription for an antibiotic a few days after the doctor visit; it is thought that if the infection is not serious it will clear up on its own over that time and the patient does not need the antibiotics. The studies also found that using many methods together, such as the ones above, worked better than using one method alone.

Since there are many reasons why physicians in the community prescribe antibiotics inappropriately, one method cannot be recommended. But using many methods to change prescribing may be successful.

BACKGROUND

Many common bacterial 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 gonorrhoeae 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 also 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 invasive infections and otitis media in young children (CDC 2001). Antimicrobial resistance, especially penicillin resistance, among isolates of *S. pneumoniae* has increased throughout the world since the late 1980s and early 1990s and threatens the ability to treat pneumococcal infections. Over the course of eight years the prevalence of invasive penicillin-resistant (intermediate and fully resistant) isolates increased from 2.8% to 6.8% in 10 Canadian pediatric hospitals (Scheifele 2000). Active surveillance by the US Centers for Disease Control for invasive *S. pneumoniae* infections revealed an increase in the proportion of penicillin-resistant invasive isolates from 6.7% to 27.5% in eight years across the country, with some regions (Tennessee) reporting 54% of isolates resistant to at least one antibiotic (Whitney 2000). In Europe, 11% of invasive pneumococcal isolates in the period from 1999 to 2001 were penicillin non-susceptible (EARSS 2002). However, this was an average and penicillin non-susceptibility rates were as high as 35% in Spain and as low as 1 to 2% in the Netherlands.

Other organisms causing infections in the community are demonstrating clinically significant antibiotic resistance. While less of a problem in North America than in Europe and Japan, macrolide resistant group A streptococci have been isolated with increasing frequency (Maruyama 1979; Seppala 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 2002; Ladhani 2003; Zhanel 2000).

The risk factors associated with colonization or infection with antibiotic-resistant *S. pneumoniae* at the population level have been well characterized (Arason 1996; Block 1995;Nasrin 2002; Nava 1994; Pallares 1987; Reichler 1992; Tan 1993). There is evidence that antibiotic exposure is associated with carriage of resistant *S. pneumoniae* at the level of the individual (Brook 1996; Dagan 1998). In a study of the dynamics of pneumococcal carriage during antibiotic treatment (Dagan 1998) it was observed that 19 of 120 children had a new pneumococcal isolate colonizing the nasopharynx at three to four days into treatment and in 16 of the 19 this isolate was resistant to the antibiotic the child was taking. The association between antibiotic use and resistance in bacteria has also been demonstrated for many other important community-acquired pathogens (Allen 1999; Brown 2002; Priest 2001; Seppala 1995; Zhanel 2000).

Thus, there is compelling evidence that exposure of the community and the individual to antibiotics enhances the risk of an individual harbouring 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.

There is a major body of literature documenting the substantial misuse of antibiotics for viral infections and other diseases, such as asthma, for which antibiotics are of no known benefit (Taylor 1977). Rates of prescribing antibiotics for viral upper respiratory infections in the United States have been reported to be between 40 and 75% (Gonzales 1997; Nyquist 1998). In England and Scotland, the number of antibiotic prescriptions increased by 45.8% between the years 1980 and 1991 (Davey 1996). In Canada, one analysis 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 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 (Linder 2001).

One approach to reducing the incidence of infections due to antibiotic-resistant organisms is to reduce the inappropriate use of antibiotics in both the hospital and community settings. Changing physician behaviour 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 health care (Oxman 1995). More recent reviews have confirmed that traditional forms of education such as conferences or printed educational materials produce little or no change in behaviour for a variety of areas of patient care (Freemantle 2004; O'Brien 2004c). More complex interventions such as educational outreach visits or training of local opinion leaders seem to be more effective in producing changes in physician behaviour (O'Brien 2004a; O'Brien 2004b). Definitive conclusions are difficult to make 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 has been recommended is methodologically sound evaluations 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. Aspects of the physician-patient interaction have been studied extensively and many physicians argue that they prescribe antibiotics for viral infections because they feel pressured to do so by patients or parents (Bauchner 1999; Palmer 1997; Watson 1999). Physicians who have been in practice for a longer duration of time or are not involved in medical teaching appear to misuse antibiotics more frequently (Mainous 1998; Steinke 2000). Physicians who see more patients and, presumably, spend less time with each patient prescribe more antibiotics than those who see fewer patients (Arnold 1999; Hutchinson 1999). In addition, difficulty in distinguishing a benign, self-limited viral infection from a more serious infection requiring antibiotic therapy has been shown to contribute to unnecessary antibiotic use in adults with pharyngitis (McIsaac 2000), sinusitis (Murray 2000) and bronchitis (Mainous 1997; Murray 2000). When there is uncertainty in any potentially infectious condition physicians tend to be cautious and prescribe an antibiotic if it could be at all beneficial.

Some of these identified barriers are amenable to change. However, given the multi-factorial 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 review will explore studies of interventions to improve antibiotic prescribing in the ambulatory care setting.

OBJECTIVES

The main objective of this study was to systematically review the literature to find trials to enable an estimate of the effectiveness of interventions targeting professionals, when given alone or in combination, in improving antibiotic prescribing by healthcare providers; in the outpatient setting with both adults and children. Prescribing behaviours included:
(a) the decision to prescribe an antibiotic for a specific condition;
(b) the type of antibiotic prescribed;
(c) the dose and duration of antibiotic therapy.

The secondary objective of this systematic review was to estimate the effect of any of the interventions on patient outcomes that were related to antibiotic use, including:
(a) colonization or infection with antibiotic-resistant organisms
(b) adverse drug reactions (allergic and non-allergic) and antibiotic associated diarrhoea
(c) adverse events related to non-use of antibiotics, use of narrower spectrum antibiotics or a reduced duration of antibiotic therapy.

METHODS

Criteria for considering studies for this review

Types of studies

All randomised and quasi-randomised controlled trials (RCT/QRCT), controlled before and after studies (CBA) and interrupted time series (ITS) studies were included. Studies examining prescribing of multiple drug classes were included provided that specific data on antibiotic prescribing could be extracted.

Types of participants

Studies of healthcare consumers, qualified physicians of all ages and level of experience and physician extenders who prescribe antibiotics and provide primary care in community or academic ambulatory settings were included. Studies including only medical trainees were excluded.

A primary care setting was considered one in which the patient was first seen for the problem of interest. A healthcare setting was considered ambulatory care if patients were not admitted to the hospital (including the emergency department) at the time they were assessed. This would include outpatient clinics in hospitals or hospital-affiliated clinics, government-run clinics, private doctors' offices and walk-in clinics.

Types of interventions

Professional interventions in the Effective Practice and Organisation of Care Group (EPOC) scope included the following:

(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 participating in conferences, lectures, workshops or traineeships.
(3) Local consensus processes: inclusion of participating providers in discussion to ensure that they agree that the chosen clinical problem is important and the approach to managing the problem is appropriate.
(4) Educational outreach visits: use of a trained person who meets with providers in their practice settings to give information with the intent of changing the providers' practices. 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.
(7) Audit and feedback: any summary of clinical performance of health care over a specified period of time. The summary may also have included recommendations for clinical action. The information may have been obtained from medical records, computerised 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 drug 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 subsequently lead to the design of an intervention that addresses identified barriers.
(10) Mass media: (i) varied use of communication that reaches great numbers of people, including television, radio, newspapers, posters, leaflets, and booklets, alone or in conjunction with other interventions; (ii) targeted at the population level.
(11) Financial interventions: methods of physician remuneration, patient-oriented approaches such as user fees and formularies.

Types of outcome measures

The primary outcome measure was the rate of appropriate antibiotic prescribing. This included, depending on the specific condition, the decision to prescribe an antibiotic, or not; or the rate of prescribing a recommended choice, dose or duration of use of antibiotic.
Secondary outcome measures were:
(a) the incidence of colonization with, or infection due to, antibiotic-resistant organisms and other adverse events associated with antibiotic use;

(b) the incidence of adverse events associated with reduced use or duration of treatment with antibiotics or use of narrow-spectrum antibiotics.

Search methods for identification of studies

The initial search was carried out using OVID based upon the EPOC search strategies for MEDLINE and EMBASE. Terms were added to the EPOC search strategies in order to limit retrieved studies to those involving antibiotics in an ambulatory care setting.

MEDLINE (1966 to May 2000) was searched with the following terms:

(exp anti-infective agents/ OR antibiotic$.tw.) AND (ambulatory care/ OR ambulatory care facilities/ OR office visits/ OR outpatient?.tw. OR outpatient clinics, hospital/)

1. exp anti-infective agents/
2. antibiotic$.tw.
3. 1 or 2
4. ambulatory care/
5. ambulatory care facilities/
6. office visits/
7. outpatient?.tw.
8. or/4-8
9. 3 and 8
10. AND EPOC search strategy

These groups of terms were combined using "AND" with the full EPOC search strategy for MEDLINE (see the specialized register in the EPOC Module on The Cochrane Library for a description of the search strategies).

EMBASE (1980 to May 2000) was searched with the following terms:

(exp anti-infective agents/ OR antibiotic$.tw.) AND (ambulatory care/ OR ambulatory adj1 care.tw./ OR outpatient care/ OR outpatient?.tw. OR outpatient department/ OR primary medical care/)

These groups of terms were combined using "AND" with the full EPOC search strategy for MEDLINE (see the specialized register in the EPOC Group Module on The Cochrane Library for a description of the search strategies).
These two groups of terms were combined with the EPOC search terms which specify the behaviours and interventions of interest and the types of studies.
The EPOC specialized register was searched for studies relating to antibiotic prescribing and ambulatory care (to the end of 2002). See the specialized register in the Group Module on The Cochrane Library for a description of the search strategies. The strategy was developed using relevant terms from the EPOC classification system and keywords (antibiotic* or antimicrob* or antibacteria* or infect* or sore throat or otitis media or tonsillitis or bronchitis or pneumonia or uti) and (behaviour=prescribing). Additional studies were sought from the bibliographies of retrieved articles and personal files. There were no language limitations.

Data collection and analysis

Citations and abstracts retrieved in the search were reviewed for potential inclusion by the primary author. The methodological quality of eligible studies was assessed by both authors according to the criteria described by the EPOC group (EPOC Resources). Assessments for inclusion were done independently by two review authors without blinding to study author or location. Disagreements were resolved by discussion and consensus.

Data abstraction was performed by the two review authors using a template from the EPOC Group (EPOC Resources) including information on: study design, type of intervention, presence of controls, type of targeted behaviour, participants, setting, methods (unit of allocation, unit of analysis, study power, methodological quality, consumer involvement), outcomes and results.

Data from RCTs and CBAs was presented using the format suggested by EPOC (EPOC Resources). Data was reported in natural units in the results table. Where baseline results were available from RCT/QRCTs and CBAs, pre-intervention and postintervention means or proportions were reported for both study and control groups and the difference in absolute change from baseline was calculated (change in study group values minus change in control group values) along with 95% confidence intervals or P values, if available. When baseline data were not available, results were expressed as the relative percentage change (the difference between postintervention values in the study and control groups expressed as a percentage of postintervention values in the control group). Where trials compared more than one intervention or a combination of interventions, comparisons of each intervention to the control group were handled separately. When several outcomes were reported in one trial we extracted results only for the primary outcome. If a primary outcome was not specified, we calculated the mean effect size for the multiple outcomes reported in the trial.

It has been found that many ITS studies do not include an appropriate analysis of time-series data (Grilli 1997). For ITS studies, re-analysis of the data was undertaken, where the original paper did not include such an analysis, using the recommended EPOC methods (WEBSITE).

The retrieved studies were very heterogenous with respect to the reported outcomes (for example reducing duration of therapy, increasing use of first-line agents or reducing use of antibiotics for a particular condition) and the units of measure (for example absolute number of prescriptions, number of prescriptions per unit of population, defined daily doses, proportion of patients receiving a prescription). This made quantitative analysis difficult. Thus, studies were reviewed qualitatively. In addition, unit of analysis errors were reported when present but reanalysis of the data in studies with these errors was not undertaken as there would be no quantitative analysis. These errors were noted in the Characteristics of Included Studies table.

R E S U L T S

Description of studies

One hundred and eighteen references were retrieved from a search of the EPOC specialized register through to the end of 2002. In addition, 33 articles were retrieved from both personal files and a review of bibliographies of retrieved articles and systematic reviews, giving a total of 151 articles. Three studies were excluded as they were duplicates of studies published in another language. Two additional papers were long-term follow-up publications from earlier studies. These were considered as single studies along with the original publication. Fifty-one studies were excluded prior to full review, based on the title and abstract, as they were not intervention studies, not studies of medical healthcare workers, were hospital-based studies or systematic reviews. Fifty-two further studies were excluded after more detailed review on the basis of failure to meet minimum methodological criteria set out by the EPOC Group (see the Characteristics of Excluded Studies table) or antibiotic data could not be extracted or obtained from authors (Leach 1999, Ornstein 1997, Putnam 1985).

Studies from eight of the 11 categories of interventions were reviewed. Several studies included more than one intervention and, thus, were discussed in two different comparisons. The comparisons examined in this review were as follows.
Comparison 1: printed educational materials compared to another intervention or controls (four studies).
Comparison 2: audit and feedback (with or without printed educational materials) compared to another intervention or controls (four studies).
Comparison 3: group educational meetings (with or without audit and feedback and printed educational materials) compared to another intervention or controls (ten studies).
Comparison 4: educational outreach visits (academic detailing) compared to another intervention or controls (eight studies).
Comparison 5: financial or healthcare delivery changes compared to another intervention or controls (two studies).
Comparison 6: physician reminders compared to another intervention or controls (three studies).
Comparison 7: patient-based interventions compared to another intervention or controls (five studies).
Comparison 8: multi-faceted interventions (combinations of multiple interventions to physicians, patients and the general public) compared to another intervention or controls (seven studies).

The interventions targeted a variety of prescribing behaviours. There were 13 studies aimed at reducing antibiotic prescribing for particular conditions: diarrhoea (two); and respiratory tract infections including non-specific viral upper respiratory infections (URI), sore throat, pharyngitis, tonsillitis, acute otitis media and acute bronchitis (11). In nine studies the target of the intervention was to reduce oral (or intramuscular in one study) antibiotic use for any condition. Authors of five studies sought to reduce the use of particular antibiotics considered to be contraindicated for routine use, such as tetracyclines, chloramphenicol, cephalexin (three studies); or to be overused (macrolides for group A streptococcal infections, ciprofloxacin) (two studies). There were studies where the goal was to increase use of recommended first-line antibiotics (and reduce use of second- or third-line agents) for a variety of conditions (eight studies: urinary tract infection, acute otitis media, tonsillitis); and to reduce the duration of prescribed therapy for certain conditions (five studies: urinary tract infection, acute otitis media). There were two studies examining the effect of reducing antibiotic use on patient illness resolution and four examining the effect on antibiotic-resistant bacteria in study communities. The largest number of studies came from the United States or Canada (16). The remaining studies came from Great Britain (five), Australia and New Zealand (five), Norway (three), Spain (two), and one study each from Sri Lanka, Zambia, Sweden, South Africa, Mexico, Indonesia, Finland and the Netherlands.

Risk of bias in included studies

The methodological characteristics of the studies are in the Characteristics of Included Studies table. There were 25 randomised controlled trials (RCTs), one quasi-randomised control trial (QRCT), 11 controlled before and after studies (CBA) and two interrupted time series (ITS) studies. Most of these studies had methodological limitations as assessed by the quality criteria of the EPOC study group. Five of the 20 RCT/QRCTs and one of 11 CBA studies that included providers or groups of providers as the unit of allocation completed appropriate statistical analyses. The remaining six studies were either randomised at the patient level (five studies) or at the physician level, with only one patient per physician analysed (one study). Five RCTs reported methods of randomisation resulting in adequate concealment of allocation to the study groups. Sample size or power calculations were reported in 13 RCTs and no CBA studies. Only four CBA studies reported baseline measurements that were similar between intervention and control groups.

The two ITS studies also had significant methodological issues. In neither study was it stated that the intervention occurred independently of other changes that might affect prescribing of the particular antibiotic. In addition, neither study undertook appropriate statistical analysis for time series data. The data was re-analysed using time-series regression techniques. The original results and the results from the time-series regression analysis were reported.

Effects of interventions

Comparison 1: printed educational materials versus other intervention or controls

See Table 1. There were four studies in which physicians received unsolicited, printed educational materials regarding appropriate antibiotic prescribing either by mail (Angunawela 1991; Avorn 1983; Schaffner 1983) or by publication in a national medical journal (Seppala 1997). No materials referring to the specific physician's practice (that it is an audit of prescribing practices with feedback) were used in these studies. None of the studies using mailed materials demonstrated a statistically significant change in prescribing behaviour despite unit of analysis errors. The ITS study (Seppala 1997) demonstrated a significant reduction in macrolide antibiotic use across Finland following publication of a recommendation to avoid macrolides as first-line agents for group A streptococcal throat and soft tissue infections. The pre- to postintervention change reported in the study was -1.02 defined daily doses (DDD) per 1000 inhabitants (P value 0.007). By time-series regression analysis (not performed by study authors) there was a change of -1.59 DDD per 1000 inhabitants following the intervention. Pre-intervention, the slope of the curve of macrolide prescribing over time was 0.12 DDD per year, a significant increase in the yearly rate of macrolide prescribing. As there was no significant change in the slope of the prescribing curve following the intervention, this indicates that the intervention effect was maintained over the period of time studied post intervention.

Comparison 2: audit and feedback with or without other educational materials versus other intervention or control

See Table 2. In the studies of audit and feedback additional materials distributed along with the feedback material included any one or more of the following: an explanation of the prescribing data, anonymous comparative data for other physicians or groups of physicians, or educational materials promoting more optimal prescribing practices. Interventions using audit and feedback as a component of educational meetings or academic detailing were discussed in comparisons 3 and 4 respectively.

There were four studies in this comparison, three randomised controlled trials (Hux 1999; Mainous 2000; O'Connell 1999) and one controlled before and after trial (Rokstad 1995), all of which had unit of analysis errors. Two studies failed to demonstrate a significant change in prescribing indicators of overall antibiotic use in rural Australia (O'Connell 1999) or use of first-line antibiotics for UTI in Norway (Rokstad 1995). In the latter study, however, there was a reduction in the duration of therapy for intervention group compared with controls (-7.7 DDD). In a study from Canada (Hux 1999) there was an absolute increase in prescribing of first-line antibiotics from baseline compared to controls, of 5.1% (P value <0.01), with a median cost saving of $3.32 per physician (P value <0.002). In a US study (Mainous 2000) comparing audit and feedback, patient educational materials or a combination of the two to controls, the proportion of patients prescribed antibiotics for colds increased in all study groups after the intervention. However, this increase was significantly lower for audit and feedback plus patient educational materials (-7.3%) compared to controls.

Comparison 3: educational meetings versus other interventions or control

See Table 3. Educational meetings included one or more of the following: audiovisual review of recommendations for appropriate prescribing practices for particular conditions or particular antibiotics, review of a clinical practice guideline or other published recommendations, a combination of the two, and provision of audit and feedback. It excluded educational outreach visits (academic detailing: see comparison 4), which are one-on-one meetings between the prescribing physician and another individual (physician, pharmacist or drug detailer).

There were seven RCTs (Angunawela 1991; Bexell 1996; Lagerlov 2000; Lundborg 1999a; Meyer 2001; Santoso 1996; Veninga 2000), one quasi-RCT (Harris 1984) and two CBA studies (McNulty 2000, Perez-Cuevas 1996) reviewed in this section. Three RCTs, from Sweden (Lundborg 1999a), the Netherlands (Veninga 2000) and Norway (Lagerlov 2000) used group educational meetings with audit and feedback to promote prescribing of first-line antibiotics for urinary tract infection. Controls in these studies received a similar intervention targeting asthma management. All three studies were without unit of analysis errors. The change in the proportion of patients prescribed a first-line antibiotic compared to controls ranged from 1.0% (Veninga 2000) to 17% (P value <0.001) (Lundborg 1999a). Two studies (Lagerlov 2000; Veninga 2000) were able to demonstrate changes in the duration of therapy with antibiotics for UTI. In Lagerlov 2000 a relative increase of 13.1% of patients received short-course therapy, P value <0.0001; and in Veninga 2000 there was a change in defined daily doses of antibiotics of -1.89 (P value 0.05).

Four RCTs examined the effect of educational meetings on reducing overall antibiotic use in the developing countries South Africa (Meyer 2001), Zambia (Bexell 1996), Sri Lanka (Angunawela 1991) and Indonesia (Santoso 1996). All of these studies had unit of analysis errors. The content of the interventions in the first three studies was based on rational prescribing guidelines produced by the World Health Organization, focusing on reducing antibiotic use for viral respiratory tract infection and acute diarrhoea (De Vries 1994). Similarly a study from Indonesia (Santoso 1996), in which health centres were randomised to small or large group educational meetings or no intervention, aimed to reduce inappropriate antibiotic use for acute diarrhoea. The changes in the proportion of patients receiving an antibiotic compared with controls in these studies were -21.6% (Meyer 2001), -8.1% (Bexell 1996), -6.9% (Angunawela 1991) and -6.7% for formal large group seminars and -13.7% for small, interactive discussion groups (Santoso 1996).

Two studies from Great Britain, one using multiple small group meetings compared to controls (Harris 1984) and one using small group interactive prescribing workshops compared to large, formal microbiology tutorials (McNulty 2000) demonstrated no significant reduction in the overall use of antibiotics. Modest reductions in the proportion of patients with viral URI who were prescribed an antibiotic were seen following group meetings targeting this behaviour in Mexico (-7.4% in one clinic type, -32.9% in the second clinic type) (Perez-Cuevas 1996). All of these studies had unit of analysis errors.

Comparison 4: educational outreach visits versus other intervention or control

See Table 4. The eight studies in this section use similar methods of educational outreach to those used by pharmaceutical representatives (Avorn 1983; Dolovich 1999; Schaffner 1983). All eight studies had unit of analysis errors. The detailers in these studies were clinical or research pharmacists except for the study by Schaffner (Schaffner 1983) where they compared the effectiveness of physician and pharmacist detailers. Four studies, three RCTs (Avorn 1983; Font 1991; McConnell 1982) and one CBA (Schaffner 1983), examined the effect of academic detailing on prescribing of certain antibiotics considered contraindicated or overused by community physicians. McConnell et al (McConnell 1982) in the US were able to reduce the mean number of prescriptions for tetracycline (-6.4 prescriptions, P value <0.05). Avorn and Soumerai were able to reduce the mean number of units of cephalexin prescribed in four US regions (-382, P value 0.0006) using pharmacist detailers and printed educational materials. In Spain (Font 1991), pharmacist detailers were unable to significantly reduce the prescribing of various oral and injectable antibiotics after three meetings (mean of several antibiotics: -1.31 containers per doctor per month). In the Schaffner study (Schaffner 1983) the mean change in prescribing (combining data for contraindicated antibiotics and oral cephalosporins) was not improved by physician detailing (change in number of prescriptions per physician compared to controls: 13.0) but was somewhat improved by pharmacist detailers (change in number of prescriptions per physician compared to controls: -10.4). Follow up of physicians one year later (Ray 1985) indicated that these changes were maintained in the second year after the intervention (physician detailers compared to controls: 6.5; pharmacist detailers compared to controls: -9.0).

Three studies from Australia examined the effect of academic detailing on increasing the prescribing of first-line antibiotics: two were RCTs (De Santis 1984; Ilett 2000) and one a CBA (Peterson 1997). Peterson et al (Peterson 1997) were able to increase the proportion of defined daily doses for first-line antibiotics for UTI by 9.5% compared to controls (P value <0.0001). Using a similar procedure, Ilett (Ilett 2000) increased the number of prescriptions for first-line antibiotics for respiratory tract infection and UTI by 152.6 compared to controls. DeSantis (De Santis 1984) was, however, unable to demonstrate an improvement in the prescribing of first-line antibiotics for tonsillitis (-3.3% for the median proportion of prescriptions for first-line agents).

The other RCT (Dolovich 1999) used pharmaceutical industry detailers in an attempt to increase prescribing of amoxicillin for acute otitis media in Canada. The market share of amoxicillin increased by 1.35% in the intervention regions compared with control regions receiving routine detailing; however, after adjusting for various factors this was not a statistically significant change.

Comparison 5: financial and healthcare system changes versus other intervention or control

See Table 5. Researchers in Nova Scotia, Canada, studied the effect of a change in the provincial drug formulary limiting the use of fluoroquinolones (FQ) to certain specific conditions in the elderly (MacCara 2001), using time-series methods. They reported the absolute change in the average monthly number of FQ prescriptions between the month immediately prior to and the month immediately following the formulary change to be -1441.5 prescriptions. Reanalysis of the data using time-series regression analysis detected the same significant drop in the level of prescribing between pre- and post-formulary changes (-1532.34, P value <0.001). Neither the pre- nor postintervention slopes for the rate of change in monthly FQ prescribing were statistically significant (pre-intervention slope 3.95 prescriptions per month, p=0.29; post-slope 10.74 prescriptions per month, P value 0.33), there was a trend toward an increased postintervention slope, which may indicate a decay in the intervention effect over time. The total number of antibiotic prescriptions to seniors in this time period did not change, with a compensatory increase in the prescribing of macrolide antibiotics.

In a controlled before and after study from Spain (Juncosa 1997), researchers examined the effect of primary care reform on antibiotic prescribing in one county, using regions that had not yet undergone reform as the controls. The primary care reform consisted, mainly, of changes in staffing, reimbursement and the organization of services. They demonstrated a change in the reform regions compared with controls of -454 monthly packages of antibiotics. This study suffered from unit of analysis errors.

Comparison 6: reminders versus other intervention or controls

See Table 6. Physician reminders at the point of care have been assessed in three RCTs attempting to reduce antibiotic prescribing for two clinical syndromes, acute otitis media (Christakis 2001) and sore throat (McIsaac 1998; McIsaac 2002). In the otitis study (Christakis 2001), an online prescription writer at a primary care pediatric clinic in Seattle, Washington, was used to present computer-based point-of-care evidence on the optimal duration of antibiotics for acute otitis media in children. Postintervention, there was a 44.43% relative increase in proportion of short course prescriptions in the intervention group compared with 10.48% in the control group (P value < 0.01). No adjustments for clustering of patients with physicians were made.

In two studies, researchers in Ontario, Canada, examined the effects of a paper-based decision support tool for diagnosis and management of sore throat. The tool consisted of a scoring system to help determine the likelihood that a patient was suffering from streptococcal pharyngitis utilizing common signs and symptoms followed by management recommendations. The first study (McIsaac 1998) compared the provision of a score card and a patient-encounter form to a patient-encounter form that required the physician to calculate a sore throat score. Since each physician contributed only one sore throat encounter there was no unit of analysis error. In a multiple logistic regression model (controlling for patient characteristics) the odds ratio for prescribing in the intervention group compared with controls was 0.44 (95% CI 0.21 to 0.92). The second study (McIsaac 2002) was designed to determine if repeated prompts to use the same checklist and score would reduce prescribing for sore throat further. 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 (as repeated prompts to use the score). The absolute difference in the proportion of patient receiving antibiotics in the intervention compared with the control groups was -0.2%; and there was no reduction in the odds of prescribing associated with the intervention (odds ratio 0.57, 95% CI 0.27 to 1.17).

Comparison 7: patient-based interventions versus other intervention or control

See Table 7. There were five studies examining the effects of a variety of patient-based interventions alone. These studies evaluated the effect of patient educational materials with or without physician audit and feedback (Mainous 2000), a patient information leaflet regarding antibiotics for acute bronchitis (Macfarlane 2002) and the use of delayed prescriptions for infections where patients desired antibiotics but physicians did not feel antibiotics were necessary (Arroll 2002; Dowell 2001; Little 2001). These studies were all RCTs with patients as the unit of randomization for the last three studies.

In the study by Mainous (Mainous 2000), despite an increase in prescribing across all study groups, the proportions of children receiving antibiotics for viral URI in the groups receiving patient educational materials (with or without audit and feedback) were reduced significantly compared with controls (-9.9% for patient materials alone; -7.2% for patient materials plus physician audit and feedback); although there was unit of analysis error in this study. Macfarlane (Macfarlane 2002) randomised patients who were thought to desire but not need antibiotics, as assessed by the physician, to receive either a leaflet explaining why antibiotics were unnecessary or a blank leaflet. This intervention resulted in an absolute difference in the proportion of patients taking antibiotics of -15.2%.

Three additional studies utilizing a similar concept for the common cold (Arroll 2002; Dowell 2001) or acute otitis media (Little 2001) randomised patients to receive and fill a prescription immediately or to delay filling the perscription for three to seven days. In all three studies, patients in the delayed arm were significantly less likely to obtain their antibiotic prescriptions. The absolute differences in the proportion of patients obtaining prescription between intervention and control groups were -45% (Arroll 2002), -55% (Dowell 2001) and -74.5% (Little 2001).

Comparison 8: multi-faceted interventions versus other intervention or control

See Table 8. Seven of the most recent studies in this review have capitalized on the modest success of the previously-described interventions and have created complex, multi-faceted interventions to reduce antibiotic misuse (Belongia 2001; Finkelstein 2001; Flottorp 2002; Gonzales 1999; Hennessy 2002; Perz 2002; Stewart 2000). These interventions generally employed physician education in a variety of forums as well as education of the patient or parent and the general public on 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 out of the seven studies in this category (Belongia 2001; Finkelstein 2001; Hennessy 2002; Perz 2002). Three were CBAs (Belongia 2001; Hennessy 2002; Perz 2002) and one an RCT (Finkelstein 2001). Three of the studies did not have unit of analysis errors(Finkelstein 2001; Flottorp 2002; Gonzales 1999). Three studies examined the effect of multi-faceted interventions on the rate of penicillin-resistant *S. pneumoniae* infections (Perz 2002) or colonization (Belongia 2001; Hennessy 2002) reviewed in comparison 9.

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. Health-care provider education was undertaken in the form of small group sessions, traditional CME lectures, hospital and clinic staff meetings and grand rounds. The content of the educational message was based upon the Principles of Judicious Antimicrobial. Use for pediatric upper respiratory infections (Dowell 1998) drafted by the CDC, the American Academy of Pediatrics and the American Academy of Family Physicians. 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 centres 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. All of these studies were successful in significantly reducing the inappropriate use of antibiotics for viral respiratory tract infections. In the one RCT (Finkelstein 2001) the difference in the absolute change from baseline between intervention and controls was -0.07 antibiotic courses per person year for children aged between 3 to less than 36 months and -0.05 antibiotic courses per person year for children aged 36 to 72 months. When the effect of clustering and patient covariates were taken into account, the relative intervention effects were a reduction of 16% (5% to 23%) and 12% (2% to 21%) for these two age groups respectively. Belongia (Belongia 2001) showed a change in the median number of prescriptions per clinician (reported here as the mean of liquid and solid preparations but reported separately in the study) of -17.5 between intervention and control regions. Perz et al (Perz 2002) showed a reduction in the antibiotic prescription rate per 100 person-years by 20 in intervention regions compared with controls. Finally, Hennessy et al (Hennessy 2002) were able to reduce prescribing by 0.33 antibiotic courses per person in intervention villages compared to control villages. This intervention effect was maintained in the second year of the study.

In a CBA study, Gonzales and colleagues (Gonzales 1999) applied a full intervention (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 (-3.0%). The remaining two studies demonstrated minimal (Stewart 2000; Flottorp 2002) changes in prescribing despite extensive interventions. Stewart et al (Stewart 2000) launched a community-wide intervention in a town in Canada to improve antibiotic prescribing but were able to demonstrate only a small reduction in the prescribing of second-line antibiotics compared with the remainder of the province; the odds ratio for prescribing in the pre- versus postintervention periods was 1.41 (95% CI 1.23 to 1.62). The Norwegian study (Flottorp 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 only demonstrate a minimal reduction in the use of antibiotics for sore throat (-3.0% compared with controls, P value 0.03).

Comparison 9: effect of any intervention versus control on bacterial resistance

See Table 9. Among the 39 studies reviewed, only four studies simultaneously assessed the effect of the interventions on antimicrobial resistance in the study communities (Belongia 2001; Hennessy 2002; Perz 2002; Seppala 1997). Seppala et al (Seppala 1997) examined the effect of a reduction in consumption of macrolides on the rate of isolation of macrolide-resistant group A streptococci. 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 to 0.5). This held true when the data were analysed by region. This data could not be subjected to time series analysis as there were an insufficient number of pre-intervention points.

The other three studies examined the effect of reducing overall antibiotic use in the study communities on the rate of isolation of penicillin-resistant *S. pneumoniae* from individuals in the community. In two studies (Belongia 2001; Hennessy 2002) researchers measured the effect of the intervention on the rate of penicillin resistance (either intermediate or full resistance) in pneumococcal isolates from nasopharyngeal specimens. In a multivariate logistic regression model controlling for clustering of children within childcare centres, Belongia et al (Belongia 2001) were unable to show a significant reduction in the odds of harbouring a penicillin-resistant pneumococcus for those living in an intervention community (odds ratio 0.46, 0.18 to 1.18). In Alaska, the proportion of pneumococcal isolates that were penicillin non-susceptible (with intermediate or full resistance) decreased from 41% to 29% in region A (intervention region) but did not significantly change in the control regions B and C (24% to 22%). In the second year of the study the intervention continued in region A and was expanded to regions B and C. 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%).

In the community intervention study in Tennessee (Perz 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. Despite a reduction in antibiotic use the proportion of isolates resistant to penicillin did not change over the three years of the study (60% year 1, 74% year 2 and 71% year 3).

Comparison 10: effect of delayed antibiotics versus immediate antibiotics on resolution of patient symptoms

See Table 10. 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 (Arroll 2002; Little 2001). In the study of delayed antibiotics for the common cold (Arroll 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). It was found that patient temperatures and symptom scores (based on cough, nasal discharge, throat pain, headache etc, maximum possible score 15) for the two groups were essentially the same at various time points throughout the ten-day follow up.

In the otitis media study (Little 2001), parents were requested to complete a daily diary regarding the 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 children 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.

DISCUSSION

Given the broad array of targeted behaviours, the variation in interventions 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 all community settings. However, several general observations may be cautiously made. The simple, single-intervention studies (printed educational materials, audit and feedback) generally resulted in small (and some statistically significant) changes in prescribing behaviour. Previous systematic reviews have demonstrated that passive methods of physician education such as didactic lectures or distribution or publication of printed educational materials without discussion have very limited impact (Freemantle 2004; Jamtvedt 2004; O'Brien 2004c; Oxman 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 behaviour (audit and feedback) or recommending an alternate behaviour (educational materials), or both, may not provide the physician with the tools to change a behaviour that is likely to be quite ingrained and multifactorial in origin. It bears mentioning that these low-cost interventions may result in cost savings to insurers even if the results are marginal given the high cost of prescription medications; however, only one study performed an economic analysis reporting a cost saving from unsolicited mailed audit and feedback (Hux 1999). Small changes in prescribing are unlikely, however, to reduce the incidence of antibiotic-resistant bacteria in a community.

One exceptional result 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 in favour of the use of penicillin. This result is unexpected given the limited effect of published guidelines on physician behaviour. The impetus for the publication of the guideline was concern about potential treatment failures for serious group A streptococcal infections due to the high rate of macrolide resistance in Finland. This emphasis on patient safety may account for the impressive impact of the written recommendations compared with other studies of this type of intervention. In addition, a recommendation promoting the use of particular first-line antibiotics over other agents may be more easily adopted by physicians than recommendations to cease prescribing antibiotics for inappropriate indications.

Large didactic lectures, like those attended at conferences, and unsolicited audit and feedback are similar in their passive nature to printed educational materials. It has been suggested in other systematic reviews that interactive educational meetings as opposed to didactic lectures (O'Brien 2004c) or more complex audit and feedback delivery (coupled with local guideline development or peer comparison feedback) (Jamtvedt 2004) might produce greater changes in physician behaviour; but definitive data is lacking. In this review, all of the studies examining the effect of educational meetings utilizing interactive workshops produced modest but statistically significant results. The two studies directly comparing large, didactic lectures to smaller interactive workshops reported greater improvement in prescribing for the participants of the interactive workshops (McNulty 2000; Santoso 1996).

Physician reminders have been successful in improving prescribing behaviour in a number of settings (Bennett 2003). Information provided at the time of prescribing using an online prescription writer significantly reduced the number of patients receiving long courses of antibiotics for otitis media but did not reduce the number receiving antibiotics at all (although this was a secondary outcome) (Christakis 2001). Prompts to calculate a score to predict the likelihood of streptococcal pharyngitis in sore throat patients showed promise in a preliminary study but application in a setting where repeated use was required was not successful (McIsaac 1998; McIsaac 2002). Thus, the effects of physician reminders in studies reported here were mixed and the number of studies too small to draw any concrete conclusions.

Patient-based interventions appeared to be effective in some settings. Patient educational materials, along with limited physician education, produced small changes in the rate of prescribing antibiotics for viral respiratory tract infections (Gonzales 1999; Mainous 2000). Multi-faceted interventions involving physicians, patient and community education consistently produced moderate changes in prescribing behaviours. There was one study in this group that documented a sustained reduction in prescribing in the year following the intervention (Hennessy 2002). It is of interest that one of the best-designed studies in this review, from Norway (Flottorp 2002), where researchers designed the intervention to specifically address previously identified barriers to change reported in no significant change in antibiotic use for sore throat. The authors hypothesized that this may have been due to the passive nature of the interventions or inadequate duration of follow up.

Several studies used a novel concept of providing a delayed antibiotic prescription to allow time for the natural resolution of an infection, in cases where this was likely to occur. Thus, antibiotics were reserved for those situations where the infection failed to resolve in a timely fashion (three to seven days). The rationale was that patients who desired but did not require antibiotics would be satisfied to know they could have antibiotics in several days if they were not feeling better, but most would not need to retrieve or fill the prescription. For future illnesses, these patients would know that the natural history of these infections is spontaneous resolution and they would not demand antibiotics or even attend the clinic for the same problem. All of these studies demonstrated that when patients were asked to delay obtaining or filling an antibiotic prescription, they were much less likely to fill it than those offered an immediate prescription (Arroll 2002; Dowell 2001; Macfarlane 2002). Not surprisingly, significant patient morbidity was not observed as antibiotics will have no impact on the resolution of viral infections. 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 thought to be bacterial by many practitioners. The demonstration that there is no benefit with 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. The study by Little (Little 2001) demonstrated that waiting a few days to use an antibiotic among children diagnosed with otitis media did not increase morbidity from this disease either. 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 of the cases of acute otitis media diagnosed in the primary care setting most likely because this condition is over diagnosed. 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. One important caveat in the interpretation of these studies is that these interventions appear to be very successful because all patients in the control arms were given prescriptions to fill immediately, making the antibiotic use rate in these groups close to 100%; which is very different from the antibiotic-use rates in control groups from other types of studies.

There were five studies performed in the following non-industrialised nations: Sri Lanka, Zambia, South Africa, Mexico and Indonesia. The World Health Organisation has, under the auspices of the Essential Drugs Program, produced a book called the Guide to Good Prescribing. The intervention in two of five of these studies (Bexell 1996; Meyer 2001) was based upon this guide. These five studies were unique in that they involved predominantly non-physician prescribers. One study examined physicians only (Mexico); one used physicians and non-physician prescribers (Sri Lanka); and three had non-physician prescribers, for example clinical officers and nurses (Zambia, South Africa, Indonesia). Two of these studies based prescribing recommendations on prescribing guidelines produced through international development agencies: World Health Organisation Guide (Meyer 2001), Swedish International Development Authority (Bexell 1996). In all these studies, educational meetings with or without additional interventions (for example audit and feedback) were compared with no-intervention control groups. The changes in prescribing ranged from minimal (Angunawela 1991; Bexell 1996; Santoso 1996) to moderate (Meyer 2001; Perez-Cuevas 1996). Despite the greater difficulties in controlling prescribing in non-industrialized settings, these results appeared to be slightly better than results from studies examining the efficacy of educational meetings in industrialized countries. This may be due to the use of non-physician prescribers who may have fewer barriers to changing behaviour than physicians. What is certain is that these differences confirm the need to address interventions to specific healthcare settings and barriers to change as identified in these settings in order for them to be effective.

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 easy 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 difficult behavioural 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 individual patients, which often means a broad-spectrum agent to protect against potentially resistant organisms, regardless of the ecological consequences.

None of the trials addressed changes in the rates of adverse drug reactions as a result of improved prescribing of oral antibiotics. Several of the trials addressed other patient-based outcomes such as changes in antibiotic-resistance patterns as a result of altered antibiotic use (Belongia 2001; Hennessy 2002; Perz 2002; Seppala 1997) and illness outcomes following the withholding of antibiotics for certain conditions (Arroll 2002; Little 2001). Over the intervention periods (usually between one and three years) no substantial or persistent reductions in the incidence of resistant bacteria (either colonizing or as a cause of infection) were observed in any of the studies except for the Finnish macrolide study (Seppala 1997) where a reduction was observed in macrolide resistance rates after approximately two years and was sustained over three years. This sustained reduction was unlikely to be due to natural variation in resistance rates. In contrast, no sustained reduction in penicillin resistance was observed with overall reductions in antibiotic use in several communities (Belongia 2001; Hennessy 2002; Perz 2002). The initial reduction in the carrier rate of penicillin-resistant pneumococci in Alaska (Hennessy 2002) was most likely due to natural variation in resistance rates as this change did not persist in the second year of the study despite sustained reductions in prescribing. The reason for this lack of effect on antibiotic resistant rates has been suggested by mathematical modelling of the rates of change of antibiotic-resistance among bacteria (Stewart 1998). The conclusions from the model suggest that the time to observation of reductions in the incidence of antibiotic-resistant organisms is substantially longer than the preceding time to reach high levels of resistance. 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. This is well demonstrated in the Finnish macrolide study where changes in antibiotic consumption preceded changes in macrolide resistance rates by approximately three years. 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 the use of conjugate pneumococcal vaccines.

Finally, it is important to determine if the intervention effect wanes over time. This would not be unexpected as it has been demonstrated that the degree to which physicians adhere to recommended management of certain conditions (hypertension, viral respiratory tract infection) is associated with the time since graduation from medical school; thus by extension, the further out from the intervention the more likely the physician may be to slip back into old patterns of behaviour. The durability of the effect of an intervention on physician prescribing behaviour was evaluated in only three studies (Hennessy 2002; Ray 1985; Seppala 1997). Reassuringly, all three studies demonstrated that the intervention effect on prescribing behaviour was maintained over an additional year following the end of the intervention (for Ray and Hennessy). Only the ITS study (Seppala 1997) demonstrated a prolonged effect from the intervention, reporting data for fours years following the publication of prescribing recommendations.

AUTHORS' CONCLUSIONS

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 behaviour the ultimate goal of the intervention must be defined and local barriers to change identified and addressed. Small changes in prescribing, which may be cost-effective, may be achieved using simple interventions such as guideline publication and distribution, didactic educational meetings and audit and feedback. However, these interventions are unlikely to lead to a reduction in the incidence of antibiotic-resistant bacteria causing community-acquired infection. The one exception to this was the Finnish study which resulted in a major, sustained reduction in prescribing of macrolides for group A streptococcal infection but this cannot be expected to occur in most settings following guideline publication.

Higher complexity interventions appear to be more effective in changing antibiotic-prescribing behaviours. Interactive workshops, educational outreach, physician reminders and multi-faceted interventions which provide education to healthcare providers, patients and the general public in a variety of formats may produce moderate changes and, in an environment of highly-motivated prescribers, could have a large impact on antibiotic prescribing. However, very few of these studies provided information on the durability of the effect of the intervention. In addition, the cost-effectiveness of such interventions has not been established.

If one is attempting to reduce the use of antibiotics for certain conditions (viral respiratory tract infections, as an example), using a delayed prescription may be the most effective intervention with low cost and great appeal to physicians who feel they are frequently pressured for antibiotics. These prescriptions appear to satisfy patients, however, most do not fill the prescription as they are able, by delaying, to see that the illness is self-limited. Other studies have shown that patients who do not take antibiotics for viral illnesses are less likely to attend clinic for a similar problem in the future.

Implications for research

Multi-faceted interventions appear to play an important role in reducing the inappropriate use of antibiotics in the community setting as these interventions reach a large number of physicians and healthcare consumers. Evaluation of the cost-effectiveness of such interventions is required to determine their applicability outside the research setting. In addition, studies to determine which aspects of these interventions provide the greatest benefit might aid in reducing the complexity in their implementation, which might improve uptake of these interventions. Devising innovative, simple interventions such as delayed antibiotic prescriptions or reminders is another important focus for ongoing research in this area.

Long-term follow up of physicians in regions where successful interventions have been undertaken would provide needed information regarding the durability of the effect. In addition, surveillance for antibiotic-resistant pathogens in these regions over a span of several years (five to ten) would provide desired information concerning the effect of sustained reductions in antibiotic use on these pathogens. The best study design for new evaluations with long-term follow up would be interrupted time series as this lends itself well to a longer duration of evaluation. It would help to minimize the effects of normal fluctuations in resistance rates that may be observed over shorter periods of time, as seen in the CDC Alaskan village study (Hennessy 2002). Further, it would obviate the need to withhold an effective intervention from a control region simply to obtain follow-up data.

REFERENCES

References to studies included in this review

Angunawela 1991 *{published data only}*

Angunawela II, Diwan VK, Tomson G. Experimental evaluation of the effects of drug information on antibiotic prescribing: a study in outpatient care in an area of Sri Lanka. *International Journal of Epidemiology* 1991;**20**:558-64.

Arroll 2002 *{published data only}*

Arroll B, Kenealy T, Kerse N. Do delayed prescriptions reduce the use of antibiotics for the common cold?: a single-blind controlled trial. *Journal of Family Practice* 2002;**51**:324-8.

Avorn 1983 *{published data only}*

Avorn J, Soumerai SB. Improving drug-therapy decisions through educational outreach: a randomized controlled trial of academically based "detailing". *New England Journal of Medicine* 1983;**308**:1457-63.

Belongia 2001 *{published data only}*

Belongia EA, Sullivan BJ, Chyou PH, Madagame E, Reed KD, Schwartz B. A community intervention trial to promote judicious antibiotic use and reduce penicillin-resistant Streptococcus pneumoniae carriage in children. *Pediatrics* 2001;**108**:575-83.

Bexell 1996 *{published data only}*

Bexell A, Lwando E, von Hofsten B, Tembo W, Eriksson B, Diwan VK. Improving drug use through continuing education: a randomized controlled trial in Zambia. *Journal of Clinical Epidemiology* 1996;**49**:355-7.

Christakis 2001 *{published data only}*

Christakis DA, Zimmerman FJ, Wright JA, Garrison MM, Rivara FP, Davis RL. A randomized controlled trial of point-of-care evidence to improve the antibiotic prescribing practices for acute otitis media in children. *Pediatrics* 2001;**107**:e15.

De Santis 1984 *{published data only}*

De Santis G, Harvey KJ, Howard D, Mashford ML, Moulds RFW. Improving the quality of antibiotic prescription patterns in general practice: the role of education intervention. *Medical Journal of Australia* 1994;**160**:502-5.

Dolovich 1999 *{published data only}*

Dolovich L, Levine M, Tarajos R, Duku E. Promoting optimal antibiotic therapy for otitis media using commercially sponsored evidence-based detailing: a prospective controlled trial. *Drug Information Journal* 1999;**33**:1067-77.

Dowell 2001 *{published data only}*

Dowell J, Pitkethly M, Bain J, Martin S. A randomised controlled trial of delayed antibiotic prescribing as a strategy for managing uncomplicated respiratory tract infection in primary care. *British Journal of General Practice* 2001;**51**:200-5.

Finkelstein 2001 *{published data only}*

Finkelstein JA, Davis RL, Dowell SF, Metlay JP, Soumerai SB, Rifas-Shiman SL, et al. Reducing antibiotic use in children: a randomized trial in 12 practices. *Pediatrics* 2001;**108**:1-7.

Flottorp 2002 *{published data only}*

Flottorp S, Oxman AD, Havelsrud K, Treweek S, Herrin J. Cluster randomized controlled trial of tailored interventions to improve the management of urinary tract infections in women and sore throat. *BMJ* 2002;**325**:367-72.

Font 1991 *{published data only}*

Font M, Madridejos R, Catalan A, Jimenez J, Argimon JM, Huguet YM. To improve drug prescription in primary care: a controlled randomized study of an educational method [Mejorar la prescripcion de farmacos en atencion primaria: un estudio controlado y aleatorio sobre un metodo educativo]. *Medicina Clinica* 1991;**96**:201-5.

Gonzales 1999 *{published data only}*

Gonzales R, Steiner JF, Lum A, Barrett PH Jr. Decreasing antibiotic use in ambulatory practice: impact of a multi-dimensional intervention on the treatment of uncomplicated acute bronchitis in adults. *JAMA* 1999;**281**:1512-9.

Harris 1984 *{published data only}*

Harris CM, Jarman B, Woodman E, White P, Fry JS. Prescribing - a suitable case for treatment. *Journal of the Royal College of General Practitioners - Occasional Paper* 1984;**24**:1-39.

Hennessy 2002 *{published data only}*

Hennessy TW, Petersen KM, Bruden D, Parkinson AJ, Hurlburt D, Getty M, et al. Changes in antibiotic prescribing practices and carriage of penicillin-resistant Streptococcus pneumoniae: a controlled intervention trial in rural Alaska. *Clinical Infectious Diseases* 2002;**34**:1543-50.

Hux 1999 *{published data only}*

Hux JE, Melady MP, DeBoer D. Confidential prescriber feedback and education to improve antibiotic use in primary care: a controlled trial. *CMAJ* 1999;**161**:388-92.

Ilett 2000 *{published data only}*

Ilett KF, Johnson S, Greenhill G, Mullen L, Brockis J, Colledge CL, et al. Modification of general practitioner prescribing of antibiotics by use of a therapeutics adviser (academic detailer). *British Journal of Clinical Pharmacology* 2000;**49**:168-73.

Juncosa 1997 *{published data only}*

Juncosa S, Porta M. Effects of primary health care reform on the prescription of antibiotics: a longitudinal study in a Spanish county. *European Journal of Public Health* 1997;**7**:54-60.

Lagerlov 2000 *{published data only}*

Lagerlov P, Loeb M, Andrew M, Hjortdahl P. Improving doctors' prescribing behaviour through reflection on guidelines and prescription feedback: a randomised controlled study. *Quality in Health Care* 2000;**9**:159-65.

Little 2001 *{published data only}*

Little P, Gould C, Williamson I, Moore M, Warner G, Dunleavy J. Pragmatic randomised controlled trial of two prescribing strategies for childhood acute otitis media. *BMJ* 2001;**322**:336-42.

Lundborg 1999a *{published data only}*

Lundborg CS, Wahlstom R, Oke T, Tomson G, Diwan VK. Influencing prescibing for urinary tract infection and asthma in primary care in Sweden: a randomized controlled trial of an interactive educational intervention. *Journal of Clinical Epidemiology* 1999;**52**:801-12.

MacCara 2001 *{published data only}*

MacCara ME, Sketris IS, Comeau DG, Weerasinghe SDS. Impact of a limited fluoroquinolone reimbursement policy on antimicrobial prescription claims. *Annals of Pharmacotherapy* 2001;**35**:852-8.

Macfarlane 2002 *{published data only}*

Macfarlane J, Holmes W, Gard P, Thornhill D, Macfarlane R, Hubbard R. Reducing antibiotic use for acute bronchitis in primary care: blinded, randomised controlled trial of patient information leaflet. *BMJ* 2002;**324**:1-6.

Mainous 2000 *{published data only}*

Mainous AG III, Hueston WJ, Love MM, Evans ME, Finger R. An evaluation of statewide strategies to reduce antibiotic overuse. *Family Medicine* 2000;**32**:22-9.

McConnell 1982 *{published data only}*

McConnell TS, Cushing AH, Bankhurst AD, Healy JL, McIlvenna PA, Skipper BJ. Physician behavior modification using claims data: tetracycline for upper respiratory infection. *Western Journal of Medicine* 1982;**137**:448-50.

McIsaac 1998 *{published data only}*

McIsaac WJ, Goel V. Effect of an explicit decision-support tool on decisions to prescribe antibiotics for sore throat. *Medical Decision Making* 1998;**18**:220-8.

McIsaac 2002 *{published data only}*

McIsaac WJ, Goel V, To T, Permaul JA, Low DE. Effect on antibiotic prescribing of repeated clinical prompts to use a sore throat score: lessons from a failed community intervention study. *Journal of Family Practice* 2002;**51**:339-44.

McNulty 2000 *{published data only}*

McNulty CAM, Kane A, Joy CJW, Sykes J, Saunders P, Cartwright KAV. Primary care workshops can reduce and rationalize antibiotic prescribing. *Journal of Antimicrobial Chemotherapy* 2000;**46**:493-9.

Meyer 2001 *{published data only}*

Meyer JC, Summers RS, Moller H. Randomized, controlled trial of prescribing training in a South African province. *Medical Education* 2001;**35**:833-40.

O'Connell 1999 *{published data only}*

O'Connell DL, Henry D, Tomlins R. Randomised controlled trial of effect of feedback on general practitioners' prescribing in Australia. *BMJ* 1999;**318**:507-11.

Perez-Cuevas 1996 *{published data only}*

Perez-Cuevas R, Guiscafre H, Munoz O, Reyes H, Tome P, Libreros V, et al. Improving physician prescribing patterns to treat rhinopharyngitis: intervention strategies in two health systems of Mexico. *Social Science & Medicine* 1996;**42**:1185-94.

Perz 2002 *{published data only}*

Perz JF, Craig AS, Coffey CS, Jorgensen DM, Mitchel E, Hall S, et al. Changes in antibiotic prescribing children after a community-wide campaign. *JAMA* 2002;**287**:3103-9.

Peterson 1997 *{published data only}*

Peterson GM, Stanton LA, Bergin JK, Chapman GA. Improving the prescribing of antibiotics for urinary tract infection. *Journal of Clinical Pharmacy and Therapeutics* 1997;**22**:147-53.

Ray 1985 *{published data only}*

Ray WA, Schaffner W, Federspiel CF. Persistence of improvement in antibiotic prescribing in office practice. *JAMA* 1985;**253**:1774-6.

Rokstad 1995 *{published data only}*

Rokstad K, Straand J, Fugelli P. Can drug treatment be improved by feedback on prescribing profiles combined with therapeutic recommendations? A prospective, controlled trial in general practice. *Journal of Clinical Epidemiology* 1995;**48**:1061-8.

Santoso 1996 *{published data only}*

Santoso B. Small group intervention vs formal seminar for improving appropriate drug use. *Social Science & Medicine* 1996;**42**:1163-8.

Schaffner 1983 *{published data only}*

Schaffner W, Ray WA, Federspiel CF, Miller WO. Improving antibiotic prescribing in office practice: a controlled trial of three educational methods. *JAMA* 1983;**250**:1728-32.

Seppala 1997 *{published data only}*

Seppala H, Klaukka T, Vuopio-Varkila J, Muotiala A, Helenius H, Lager K, et al. The effect of changes in the consumption of macrolide antiibotics on erythromycin resistance in Group A Streptococci in Finland. *New England Journal of Medicine* 1997;**337**:441-6.

Stewart 2000 *{published data only}*

Stewart J, Pilla J, Dunn L. Pilot study for appropriate anti-infective community therapy: effect of a guideline-based strategy to optimize use of antibiotics. *Canadian Family Physician* 2000;**46**:851-9.

Veninga 2000 *{published data only}*

Veninga CCM, Denig P, Zwaagstra R, Haaijer-Ruskamp FM. Improving drug treatment in general practice. *Journal of Clinical Epidemiology* 2000;**53**:762-72.

References to studies excluded from this review

Armstrong 1999 *{published data only}*

Armstrong EP, Langley PC. Treatment of pneumonias in a managed-care organisation: the impact of a treatment guideline promotion on physician prescribing behaviour. *Disease Management and Health Outcomes* 1999;**6**:159-73.

Armstrong 2001 *{published data only}*

Armstrong 2001. Clinical and economic outcomes of an ambulatory urinary tract infection disease management program. *American Journal of Managed Care* 2001;**7**:269-80.

Barwitz 1999 *{published data only}*

Barwitz HJK. Sore throat consultation - what is the value of a treatment guideline? [Beratungsunlass Halsschmerzen - was nutzt eine handlungsleitlinie? Studie zur rationalisierung des vorgehens in einer allgemeinpraxis]. *Fortschritte der Medizin* 1999;**141**:750-4.

Braybrook 1996 *{published data only}*

Braybrook S, Walker R. Influencing prescribing in primary care: a comparison of two different presciribing feedback methods. *Journal of Clinical Pharmacy and Therapeutics* 1996;**21**:247-54.

Bryars 1991 *{published data only}*

Bryars CH III, deGruy FV, Dickinson LC, Waller AM. The effects of the rapid strep test on physician management of streptococcal pharyngitis. *Journal of the American Board of Family Practice* 1991;**4**:139-43.

Bush 1979 *{published data only}*

Bush PJ, Rabin DL, Spector KK. Evaluation of a drug therapy protocol in an HMO. *Medical Care* 1979;**17**:566-77.

Cates 1999 *{published data only}*

Cates C. An evidence based approach to reducing antibiotic use in children with acute otitis media: controlled before and after study. *BMJ* 1999;**318**:715-6.

Chalker 2001 *{published data only}*

Chalker J. Improving antibiotic prescribing in Hai Phong Province, Viet Nam: the "antibiotic-dose" indicator. *Bulletin of the World Health Organization* 2001;**79**:313-20.

Cohen 2000 *{published data only}*

Cohen R, Allaert FA, Callens A, Menn S, Urbinelli R, Roden A. Medico-economic evaluation of an educational intervention to optimize children uncomplicated nasopharyngitis treatment in ambulatory care [Evaluation medico-economique d'une interventin educative pour l'optimisation du traitment des rhinopharyngites aigues non compliquees de l'enfant en pratique de ville]. *Medicine et Maladies Infectieuses* 2000;**30**:691-8.

Damsgaard 2001 *{published data only}*

Damsgaard JJ, Schaefer K, Michelsen JW, Frimodt-Moller N, Munck AP, Vach K, Kragstrup J. Antibiotic treatment of infections in general practice - effect of audit [Antibiotikabehandling af infektioner i almen praksis: effekten af audit bedomt ved ordinationsdata fra Sygesikringens register og loegernes selvregistrering]. *Ugeskrift for Laeger* 2001;**163**:165-8.

Deiderichsen 2000 *{published data only}*

Diederichsen HZ, Skamling M, Diederichsen A, Grinsted P, Antonsen S, Petersen PH, et al. Randomised controlled trial of CRP rapid test as a guide to treatment of respiratory infection in general practice. *Scandinavian Journal of Primary Health Care* 2000;**18**:39-43.

Ekedahl 1995 *{published data only}*

Ekedahl A, Andersson SI, Hovelius B, Molstad S, Liedholm H, Melander A. Drug prescription attitudes and behaviour of general practitioners: effects of a problem-oriented educational programme. *European Journal of Clinical Pharmacology* 1995;**47**:381-7.

Erramouspe 1989 *{published data only}*

Erramouspe J. Impact of education by clinical pharmacists on physician ambulatory care prescribing of generic verus brand-name drugs. *DICP, The Annals of Pharmacotherapy* 1989;**23**:770-3.

Fagan 2001 *{published data only}*

Fagan MS. Can the use of antibiotic in the treatment of acute bronchitis be reduced? [Kan bruk av antibiotika ved akutt bronkitt reduseres?]. *Tidsskrift for den Norske Laegeforening* 2001;**121**:455-8.

Farris 1996 *{published data only}*

Farris KB, Kirking DM, Shimp LA, Opdycke RAC. Design and results of a group counter-detailing DUR educational program. *Pharmaceutical Research* 1996;**13**:1445-52.

Faryna 1987 *{published data only}*

Faryna A, Wergowske GL, Goldenberg K. Impact of therapeutic guidelines on antibiotic use by residents in primary care clinics. *Journal of General Internal Medicine* 1987;**2**:102-7.

Friis 1989 *{published data only}*

Friis H, Bro F, Mabeck CE, Vejlsgaard R. An information campaign - an important measure in controlling the use of antibiotics. *Journal of Antimicrobial Chemotherapy* 1989;**24**:993-9.

Friis 1993 *{published data only}*

Friis H, Bro F, Eriksen NR, Mabeck CE Vejlsgaard R. The effect of reimburement on the use of antibiotics. *Scandinavian Journal of Primary Health Care* 1993;**11**:247-51.

Garica Lirola 1999 *{published data only}*

Garcia Lirola MA, Cabeza Barrera J, Lirola Garcia E. Intervention to improve the quality of antibacterial drug prescribing practies in primary care [Intervencion para mejorar la calidad de la prescripcion de antibacterianos en atencion primaria]. *Farmacia Hospitalaria* 1999;**23**:42-7.

Goode 2000 *{published data only}*

Goode CJ, Tanaka DJ, Krugman M, O'Connor PA, Bailey C, Deutchman M, et al. Outcomes from use of an evidence-based practice guideline. *Nursing Economics* 2000;**18**:202-7.

Guiscafre 1988 *{published data only}*

Guiscafre H, Munoz O, Padilla G, Reyes RM, Gonzalez E, Bronfman M, Gutierrez G. Evaluation of the strategy designed to promote changes in the prescription pattern of oral hydration, antibiotic and restricitive diets by family physicians [Evaluacion de una estrategia dirigida a los medicos familiares, para incrementar el uso do la hidratacion oral y disminuir el de antimicrobianos y dietas restrictivas]. *Archivos de Investigacion Medica (Mex)* 1988;**19**:395-406.

Guiscafre 1995 *{published data only}*

* Guiscafre H, Martinez H, Reyes H, Perez-Cuevas R, Castro R, Munoz O, Gutierrez G. From research to public health interventions. I. Impact of an educational strategy for physicians to improve treatment practices of common diseases. *Archives of Medical Research* 1995;**26 (Suppl)**:31-9.

Gutierrez 1994 *{published data only}*

Gutierrez G, Guiscafre H, Bronfman M, Walsh J, Martinez H, Munoz O. Changing physician prescribing patterns: evaluation of an educational strategy for acute diarrhea in Mexico City. *Medical Care* 1994;**32**:436-46.

Hueston 1997 *{published data only}*

Hueston WJ, Mainous AG III, Brauer N, Mercuri J. Evaluation and treatment of respiratory infections: does managed care make a difference?. *Journal of Family Practice* 1997;**44**:572-7.

Ibrahim 1997 *{published data only}*

Ibrahim S, Isani Z. Evaluation of doctors trained at diarrhoea training unit of National Institute of Child Health, Karachi. *Journal of the Pakistani Medical Association* 1997;**47**:7-11.

Ives 1987 *{published data only}*

Ives TJ, Frey JJ, Furr SJ, Bentz EJ. Effect of an educational intervention on oral cephalosporin use in primary care. *Archives of Internal Medicine* 1987;**147**:44-7.

Kafle 1995 *{published data only}*

Kafle KK, INRUD. Intervention test of training and supervision on prescribing practices. Report to the National Pharmaceutical Management Project, Kathmandu, Nepal 1995.

Klein 1981 *{published data only}*

Klein LE, Charache P, Johannes RS. Effect of physician tutorials on prescribing patterns of graduate physicians. *Journal of Medical Education* 1981;**56**:504-11.

Leach 1999 *{published data only}*

Leach RH, Wakeman A. An evaluation of the effectiveness of community pharmacists working with GPs to increase the cost-effectiveness of prescribing. *Pharmaceutical Journal* 1999;**263**:206-9.

Lohr 1980 *{published data only}*

* Lohr KN, Brook RH, Kaufman MA. Quality of care in the New Mexico Medicaid program 1971-1975: the effect of the New Mexico experimental medical care review organization on the use of antibiotics for common infectious diseases. *Medical Care* 1980;**18 (Suppl i-vi)**:1-129.

Lundborg 1999b *{published data only}*

Lundborg CS, Wahlstrom R, Diwan VK, Oke T, Martenson D, Tomson G. Combining feedback from simulated cases and prescribing: design and implementation of an educational intervention in primary care in Sweden. *International Journal of Technology Assessment in Health Care* 1999;**15**:458-73.

Mallet 2001 *{published data only}*

Mallet HP, Njikam A, Scouflaire SM. Evaluation of prescription practices and the rational use of medicines in Niger [Evaluation des habitudes de prescription et de l'usage rationnel des medicaments au Niger: enquetes successives dans 19 centres de sante integres de la region de Tahoua]. *Sante* 2001;**11**:185-93.

Margolis 1992 *{published data only}*

Margolis CZ, Warshawsky SS, Goldman L, Dagan O, Wirtschafter D, Pliskin JS. Computerized algorithms and pediatricians' management of common problems in a community clinic. *Academic Medicine* 1992;**67**:282-4.

Melander 1999 *{published data only}*

Melander E, Bjorgell A, Bjorgell P, Ovhed I, Molstad S. Medical audit changes physicians' prescribing of antibiotics for respiratory tract infections. *Scandinavian Journal of Primary Health Care* 1999;**17**:180-4.

Molstad 1989 *{published data only}*

Molstad S, Hovelius B. Reduction in antibiotic usage following an educational programme. *Family Practice* 1989;**6**:33-7.

Molstad 1994 *{published data only}*

Molstad S, Ekedahl A, Hovelius B, Thimansson H. Antibiotics prescription in primary care: a 5-year follow-up of an educational programme. *Family Practice* 1994;**11**:282-6.

Molstad 1999 *{published data only}*

Molstad S, Cars O. Major change in the use of antibiotic following a national programme for the rational use of antimicrobial agents and surveillance of resistance (STRAMA). *Scandinavian Journal of Infectious Diseases* 1999;**31**:191-5.

Motheral 1999 *{published data only}*

Motheral BR, Henderson R. The effect of a closed formulary on prescription drug use and costs. *Inquiry* 1999/2000;**36**:481-90.

Munck 1998 *{published data only}*

Munck AP, Gahm-Hansen B, Sogaard P, Sogaard J. Long-lasting improvement in general practitioers' prescribing of antibiotics by means of medical audit. *Scandinavian Journal of Primary Health Care* 1999;**17**:185-90.

Needham 1988 *{published data only}*

Needham A, Brown M, Freeborn S. Introduction and audit of a general practice antibiotic formulary. *Journal of the Royal College of General Practitioners* 1988;**38**:166-7.

North England 1992 *{published data only}*

Russell IT, Addington-Hall JM, Avery PJ, Bamford CH, Barton AG, Donaldson C, et al. Medical audit in general practice. I:

Effects on doctors' clinical behaviour for common childhood conditions. *BMJ* 1992;**304**:1480-4.

O'Connor 1996 *{published data only}*

O'Connor PJ, Solberg LI, Christianson J, Amundson G, Mosser G. Mechanism of action and impact of a cystitis clinical practice guideline on outcomes and costs of care in an HMO. *Journal on Quality Improvement* 1996;**22**:673-82.

Ochoa 1996 *{published data only}*

Gonzalez Ochoa E, Armas Perez L, Bravo Gonzalez JR, Cabrales Escobar J, Rosales Corrales R, Abreu Suarez G. Prescription of antibiotics for mild acute respiratory infections in children. *Bulletin of PAHO* 1996;**30**:106-17.

Ornstein 1997 *{published data only}*

Ornstein SM, Jenkins RG, Lee FW, Sack JL, LaKier EI, Roskin SD, Wulfman JS, Wriston GA. The computer-based patient record as a CQI tool in a family medicine center. *Journal on Quality Improvement* 1997;**23**(7):347-361.

Perez Rodriguez 1994 *{published data only}*

Perez Rodriguez MT, Catalan Ramos A, Parellada Esquius N. Criteria for elaborating a formulary for medicines in a health district and its influence on prescription [Criterios de elaboracion de un formulario de medicamentos en un area basica de salud e impacto sobre la prescripcion]. *Atencion Primaria* 1994;**14**:1128-34.

Poses 1995 *{published data only}*

Poses RM, Cebul RD, Wigton RS. You can lead a horse to water - improving physicians' knowledge of probablilities may not affect their decisions. *Medical Decision Making* 1995;**15**:65-75.

Putnam 1985 *{published data only}*

Putnam RW, Curry L. Impact of patient care appraisal on physician behaviour in the practice setting. *Canadian Medical Association Journal* 1985;**132**:1025-9.

Raz 1995 *{published data only}*

Raz R, Porat V, Ephros M. Can an educational program improve the diagnosis and treatment of pharyngotonsillitis in the ambulatory care setting?. *Israel Journal of Medical Sciences* 1995;**31**:432-5.

Saint 1999 *{published data only}*

Saint S, Scholes D, Fihn SD, Farrell RG, Stamm WE. The effectiveness of a clinical practice guideline for the management of presumed uncomplicated urinary tract infection in women. *American Journal of Medicine* 1999;**106**:636-41.

Stuart 1997 *{published data only}*

Stuart ME, Macuiba J, Heidrich F, Farrell RG, Braddick M, Etchison S. Successful implementation of an evidence-based clinical practice guideline: acute dysuria/urgency in adult women. *HMO Practice* 1997;**11**:150-7.

Suchyta 2001 *{published data only}*

Suchyta MR, Dean NC, Narus S, Hadlock CJ. Effects of a practice guideline for community-acquired pneumonia in an outpatient setting. *American Journal of Medicine* 2001;**110**:306-9.

Temte 1999 *{published data only}*

Temte JL, Shult PA, Kirk CJ, Amspaugh J. Effects of viral respiratory disease education and surveillance on antibiotic prescribing. *Educational Research and Methods* 1999;**31**:101-6.

Vedsted 1997 *{published data only}*

Vedsted P, Nielsen JN, Olesen F. Does a computerized price comparison module reduce prescribing costs in general practice?. *Family Practice* 1997;**14**:199-203.

Walley 2000 *{published data only}*

Walley T, Murphey M, Codd M, Johnston Z, Quirke T. Effects of a monetary incentive on primary care prescribing in Ireland: changes in prescribing patterns in one health board 1990-1995. *Pharmacoepidemiology and Drug Safety* 2000;**9**:591-8.

Wood 1997 *{published data only}*

Wood KM, Mucklow JC, Boath EH. Influencing prescribing in primary care: a collaboration between clinical pharmacology and clinical pharmacy. *International Journal of Pharmacy Practice* 1997;**5**:1-5.

Wyatt 1992 *{published data only}*

Wyatt TD, Reilly PM, Morrow NC, Passmore CM. Short-lived effects of a formulary on anti-infective prescribing - the need for continuing peer review. *Family Practice* 1992;**9**:461-5.

Zuriguel 1993 *{published data only}*

Zuriguel IC. Intervention in a health area, in order to improve the way in which antibiotics are prescribed [Intervencion para mejorar la calidad de prescripcion de antibioticos en una area basica de saludq]. *Atencion Primaria* 1993;**11**:37-9.

Zwar 1995 *{published data only}*

Zwar NA, Gordon JJ, Sanson-Fisher RW. Evaluation of an educational program in rational prescribing for GP trainees. *Australian Family Physician* 1995;**24**:833-8.

Zwar 1999 *{published data only}*

Zwar N, Wolk J, Gordon J, Sanson-Fisher R, Kehoe L. Influencing antibiotic prescribing in general practice: a trial of prescribing feedback and management guidelines. *Family Practice* 1999;**16**:495-500.

Zwar 2002 *{published data only}*

Zwar N, Henderson J, Britt H, McGeechan K, Yeo G. Influencing antibiotic prescribing by prescriber feedback and management guidelines: a 5-year follow-up. *Family Practice* 2002;**19**:12-7.

References to studies awaiting assessment

Chalker 2005 *{published data only}*

Chalker J, Ratanawijitrasin S, Chuc NTK, Petzold M, Tomson G. Effectiveness of a multi-component intervention on dispensing practices at private pharmacies in Vietnam and Thailand

- a randomized controlled trial. *Social Science in Medicine* 2005;**60**:131-41.

Coenen 2004 *{published data only}*

Coenen S, Van Royen P, Michiels B, Denekens J. Optimizing antibiotic prescribing for acute cough in general practice: a cluster randomized controlled trial. *Journal of Antimicrobial Chemotherapy* 2004;**54**:661-72.

Dormuth 2004 *{published data only}*

Dormuth CR, Maclure M, Bassett K, Jauca C, Whiteside C, Wright JM. Effect of periodic letters on evidence-based drug therapy on prescribing behaviour: a randomized trial. *CMAJ* 2004;**26**:1057-61.

Doyne 2004 *{published data only}*

Doyne EO, Alfaro MP, Siegel RM, Atherton HD, Schoettker PJ, Bernier J. A randomized controlled trial to change antibiotic prescribing patterns in a community. *Archives of Pediatrics and Adolescent Medicine* 2004;**158**:577-83.

Gonzales 2004 *{published data only}*

Gonzales R, Sauaia A, Corbett KK, Maselli JH, Erbacher K, Leeman-Castillo BA, et al. Antibiotic treatment of acute respiratory tract infections in the elderly: effect of a multidimensional education intervention. *Journal of the American Geriatric Society* 2004;**52**:39-45.

Gonzales 2005 *{published data only}*

Gonzales R, Corbett KK, Leeman-Castillo BA, Glazner J, Erbacher K, Darr CA, et al. The "Minimizing Antibiotic Resistance in Colorado" project: impact of patient education in improving antibiotic use in private office practices. *Health Services Research* 2005;**40**:101-16.

Greene 2004 *{published data only}*

Greene RA, Beckman H, Chamberlain J, Partridge G, Miller M, Burden D, et al. Increasing adherence to a community-based guideline for acute sinusitis through education, physician profiling, and financial incentives. *American Journal of Managed Care* 2004;**10**:670-8.

Harris 2003 *{published data only}*

Harris RH, MacKenzie TD, Leeman-Castillo B, Corbett KK, Batal HA, Maselli JH, et al. Optimizing antibiotic prescribing for acute respiratory tract infections in an urban urgent care clinic. *Journal of General Internal Medicine* 2003;**18**:326-34.

Hickman 2003 *{published data only}*

Hickman D, Stebbins MR, Hanak JR, Guglielmo BJ. Pharmacy-based intervention to reduce antibiotic use for acute bronchitis. *Annals of Pharmacotherapy* 2003;**37**:187-91.

Madridejos-Mora 2004 *{published data only}*

Madridejos-Mora R, Amado-Guirado E, Perez-Rodriguez MT. Effectiveness of the combination of feedback and educational recommendations for improving drug prescription in general practice. *Medical Care* 2004;**42**:643-8.

Newby 2003 *{published data only}*

Newby DA, Fryer JL, Henry DA. Effect of computerised prescribing on use of antibiotics. *Medical Journal of Austrailia* 2003;**178**:210-3.

Smabrekke 2002 *{published data only}*

Smabrekke L, Verild D, Giaever A, Myrbakk T, Fuskevag A, Ericson JU, et al. Educational intervention for parents and healthcare providers leads to reduced antibiotic use in acute otitis media. *Scandinavian Journal of Infectious Diseases* 2002;**34**:657-9.

Sondergaard 2003 *{published data only}*

Sondergaard J, Andersen M, Stovring H, Kragstrup J. Mailed prescriber feedback in addition to a clinical guideline has no impact: a randomised, controlled trial. *Scandinavian Journal of Primary Health Care* 2003;**21**:47-51.

Welschen 2004 *{published data only}*

Welschen I, Kuyenhoven MM, Hoes AW, Verheij TJM. Effectiveness of a multiple intervention to reduce antibiotic prescribing for respiratory tract symptoms in primary care: randomised controlled trial. *BMJ* 2004;**329**:431-5.

Wilson 2003 *{published data only}*

Wilson EJ, Nasrin D, Dear KBG, Douglas RM. Changing GPs' antibiotic prescribing: a randomised controlled trial. *Communicable Disease Intelligence* 2003;**27 (Suppl)**:32-8.

Additional references

Allen 1999

Allen UD, MacDonald N, Fuite L, Chan F, Stephens D. Risk factors for resistance to "first-line" antimicrobials among urinary tract isolates of Escherichia coli in children. *CMAJ* 1999;**160**:1436-40.

Arason 1996

Arason VA, Kristinsson KG, Sigurdsson JA, Stefansdottir G, Molstad S, Gudmundsson S. Do antimicrobials increase the carriage rate of penicillin resistant pneumococci in children?. *BMJ* 1996;**313**:387-97.

Arnold 1999

Arnold SR, Allen UD, Al-Zahrani M, Tan DH, Wang EE. Antibiotic prescribing by pediatricians for respiratory tract infection in children. *Clinical Infectious Diseases* 1999;**29**:312-7.

Baer 1995

Baer M, Vuento R, Vesikari T. Increase in bacteremic pneumococcal infections in children. *Lancet* 1995;**345**:661.

Bauchner 1999

Bauchner H, Pelton SI, Klein JO. Parents, physicians and antibiotic use. *Pediatrics* 1999;**103**:395-401.

Bennett 2003

Bennett JW, Glasziou PP. Computerised reminders and feedback in medication management: a systematic review of randomised controlled trials. *Medical Journal of Australia* 2003;**178**:217-22.

Block 1995

Block SL, Harrison CJ, Hedrick JA, Tyler RD, Smith RA, Keegan E, Chartrand SA. Penicillin-resistant Streptotoccus pneumoniae in acute otitis media: risk factors, susceptibility patterns and antimicrobial management. *Pediatric Infectious Disease Journal* 1995;**14**:751-9.

Brook 1996

Brook I, Gober AE. Prophylaxis with amoxicillin or sulfisoxazole for otitis media: effect on recovery of penicillin-resistant bacteria from children. *Clinical Infectious Diseases* 1996;**22**:143-145.

Brown 2002

Brown PD, Freeman A, Foxman B. Prevalence and predictors of trimethoprim-sulfamethoxazole resistance among uropathogenic Escherichia coli isolates in Michigan. *Clinical Infectious Diseases* 2002;**34**:1061-6.

CDC 2001

Centers for Disease Control and Prevention. Active Bacterial Core Surveillance. Division of Bacterial and Mycotic Diseases 2001.

Cornaglia 1996

Cornaglia G, Ligozzi M, Mazzariol A, Valentini M, Orefici G, Fontana R. Rapid increase of resistance to erythromycin and clindamycin in Streptococcus pyogenes in Italy, 1993-1995. The Italian Surveillance Group for Antimicrobial Resistance. *Emerging Infectious Diseases* 1996;**2**:339-42.

Dagan 1998

Dagan R, Leibovitz E, Greenberg D, Yagupsky P, Fliss DM, Leiberman A. Dynamics of pneumococcal nasopharyngeal colonization during the first days of antibiotic treatment in pediatric patients. *Pediatric Infectious Disease Journal* 1998;**17**:880-5.

Davey 1996

Davey PG, Bax RP, Newey J, Reeves D, Rutherford D, Slack R, et al. Growth in the use of antibiotics in the community in England and Scotland in 1980-93. *BMJ* 1996;**312**:613.

Davey 2002

Davey P. Interventions to improve antibiotic prescribing practices for hospital inpatients. *Cochrane Database of Systematic Reviews* 2005, Issue 4. [DOI: 10.1002/14651858.CD003543.pub2]

Davis 1999

Davis D, Thomson O'Brien MA, Freemantle N, Wolf FM, Mazmanian P, Taylor-Vaisey A. Impact of formal continuing medical education: do conferences, workshops, rounds and other traditional continuing education activities change physician behavior or health care outcomes. *JAMA* 1999;**282**:867-74.

De Vries 1994

De Vries TP, Henning RH, Hogerzeil HV, Fresle DA. Guide to Good Prescribing. World Health Organisation, 1994.

Dowell 1998

Dowell SF, Marcy M, Phillips WR, Gerber MA, Schwartz B. Principles of judicious use of antimicrobial agents for pediatric upper respiratory tract infections. *Pediatrics* 1998;**101 (Suppl)**:163-184.

EARSS 2002

European Antimicrobial Resistance Surveillance System. EARSS Annual Report 2002.

EPOC Module

Bero L, Eccles M, Grilli R, Grimshaw J, Gruen RL, Mayhew A, Oxman AD, Tavender E, Zwarenstein M. Cochrane Effective Practice and Organisation of Care Group. About The Cochrane Collaboration (Cochrane Review Groups (CRGs)) 2007, Issue 1. Art. No.: EPOC.

EPOC Resources

EPOC Resources. Cochrane Effective Practice and Organisation of Care Group website. http://www.epoc.uottawa.ca/resources.htm.

Foster 1994

Foster JA, McGowan KL. Rising rate pneumococcal bacteremia at The Children's Hospital of Philadelphia. *Pediatric Infectious Disease Journal* 1994;**13**:1143-4.

Freemantle 2004

Freemantle N, Harvey EL, Wolf F, Grimshaw JM, Grilli R, Bero LA. Printed educational materials: effects on professional practice and health care outcomes. *Cochrane Database of Systematic Reviews* 2004, Issue 2. [DOI: 10.1002/14651858.CD000172]

Gonzales 1997

Gonzales R, Steiner JF, Sande MA. Antibiotic prescribing for adults with colds, upper respiratory tract infections, and bronchitis by ambulatory care physicians. *JAMA* 1997;**278**:901-904.

Grilli 1997

Grilli R, Freemantle N, Minozzi S, Domenighetti G, Finer D. The impact of mass media on health services utilisation. *Cochrane Database of Systematic Reviews* 2002, Issue 1. [DOI: 10.1002/14651858.CD000389]

Grimshaw 1993

Grimshaw JM, Russell IT. Effect of clinical guidelines on medical practice: a systematic review of rigorous evaluations. *Lancet* 1993;**342**:1317-22.

Hutchinson 1999

Hutchinson JM, Foley RN. Method of physician remuneration and rates of antibiotic prescription. *CMAJ* 1999;**160**:1013-7.

Jackson 1984

Jackson MA, Shelton S, Nelson JD, McCracken GH Jr. Relatively penicillin-resistant pneumococcal infections in pediatric patients. *Pediatric Infectious Disease Journal* 1984;**3**:129-132.

Jamtvedt 2004

Jamtvedt G, Young JM, Kristoffersen DT, Thomson O'Brien MA, Oxman AD. Audit and feedback: effects on professional practice and health care outcomes. *Cochrane Database of Systematic Reviews* 2004, Issue 2. [DOI: 10.1002/14651858.CD000259.pub2]

Kellner 1999

Kellner JD, Ford-Jones EL. Streptococcus pneumoniae carriage in children attending 59 Canadian child care centers. *Archives of Pediatric and Adolescent Medicine* 1999;**153**:495-502.

Ladhani 2003

Ladhani S, Gransden W. Increasing antibiotic resistance among urinary isolates. *Archives of Diseases of Childhood* 2003;**88**:444-5.

Linder 2001

Linder JA, Stafford RS. Antibiotic treatment of adults with sore throat by community primary care physicians: A national survey, 1989-1999. *JAMA* 2001;**286**:1181-6.

Mainous 1997

Mainous AGI, Hueston WJ, Eberlein C. Colour of respiratory discharge and antibiotic use. *Lancet* 1997;**350**:1077.

Mainous 1998

Mainous AGI, Hueston WJ, Love MM. Antibiotics for colds in children; who are the high prescribers?. *Archives of Pediatricsand Adolescent Medicine* 1998;**152**:349-52.

Maruyama 1979

Maruyama S, Yoshioka H, Fujita K, Takimoto M, Satake Y. Sensitivity of group A streptococci to antibiotics. Prevalence of resistance to erythromycin in Japan. *American Journal of Diseases of Children* 1979;**133**:1143-5.

McCaig 1995

McCaig LF, Hughes JM. Trends in antimicrobial drug prescribing among office-based physicians in the United States. *JAMA* 1995;**273**:214-9.

McIsaac 2000

McIsaac WJ, Butler CC. Does clinical error contribute to unnecessary antibiotic use?. *Medical Decision Making* 2000;**20**:33-8.

Murray 2000

Murray S, Del Mar C, O'Rourke P. Predictors of an antibiotic prescription by GPs for respiratory tract infections: a pilot. *Family Practice* 2000;**17**:386-8.

Nasrin 2002

Nasrin D, Collignon PJ, Roberts L, Wilson EJ, Pilotto LS, Douglas RM. Effect of lactam antibiotic use in children on pneumococcal resistance to penicillin: prospective cohort study. *BMJ* 200;**324**:1-4.

Nava 1994

Nava JM, Bella F, Garau J, Lite J, Morera MA, Marti C, et al. Predictive factors for invasive disease due to penicillin-resistant Streptococcus pneumoniae: a population-based study. *Clinical Infectious Diseases* 1994;**19**:884-90.

Nyquist 1998

Nyquist AC, Gonzalez R, Steiner JF, Sande MA. Antibiotic prescribing for children with colds upper respiratory tract infections and bronchitis. *JAMA* 1998;**279**:875-7.

O'Brien 2004a

Thomson O'Brien MA, Oxman AD, Haynes RB, Davis DA, Freemantle N, Harvey EL. Local opinion leaders: effects on professional practice and health care outcomes. *Cochrane Database of Systematic Reviews* 2004, Issue 2. [DOI: 10.1002/14651858.CD000125.pub3]

O'Brien 2004b

Thomson O'Brien MA, Oxman AD, Davis DA, Haynes RB, Freemantle N, Harvey EL. Educational outreach visits: effects on professional practice and health care outcomes. *Cochrane Database of Systematic Reviews* 2004, Issue 2. [DOI: 10.1002/14651858.CD000409.pub2]

O'Brien 2004c

Thomson O'Brien MA, Freemantle N, Oxman AD, Wolf F, Davis DA, Herrin J. Continuing education meetings and workshops: effects on professional practice and health care outcomes. *Cochrane Database of Systematic Reviews* 2004, Issue 2. [DOI: 10.1002/14651858.CD003030]

Oxman 1995

Oxman AD, Thomson MA, Davis D, Haynes B. No magic bullets: a systematic review of 102 trials of interventions to improve professional practice. *CMAJ* 1995;**153**:1423-31.

Pallares 1987

Pallares R, Gudiol F, Lainares J, Ariza J, Rufi B, Murgui L, et al. Risk factors and response to antibiotic therapy in adults with bacteremic pneumonia caused by penicillin-resistant pneumococci. *New England Journal of Medicine* 1987;**317**:18-22.

Palmer 1997

Palmer DA, Bauchner H. Parents' and physicians' views on antibiotics. *Pediatrics* 1997;**99**:e6.

Priest 2001

Priest P, Yudkin P, McNulty C, Mant D, Wise R. Antibacterial prescribing and antibacterial resistance in English general practice: cross sectional study. *BMJ* 2001;**323**:1037-41.

Reichler 1992

Reichler MR, Allphin AA, Breiman RF, Schreiber JR, Arnold JE, McDougal LK, et al. The spread of multiply resistant Streptococcus pneumoniae at a day care center in Ohio. *Journal of Infectious Diseases* 1992;**166**:1346-53.

Scheifele 2000

Scheifele D, Halperin S, Pelletier L, Talbot J. Invasive pneumococcal infection Canadian children, 1991-1998: implications for new vaccine strategies. *Clinical Infectious Diseases* 2000;**31**:58-64.

Seppala 1992

Seppälä H, Nissinen A, Jarvinen H, Huovinen S, Henriksson T, Herva E, et al. Resistance to erythromycin in group A streptococci. *New England Journal of Medicine* 1992;**326**:292-7.

Seppala 1995

Seppälä H, Klaukka T, Lehtonen R, Nenonen E, Huovinen P. Outpatient use of erythromycin: link to increase erythromycin in group A streptococci. *Clinical Infectious Diseases* 1995;**21**:1378-85.

Steinke 2000

Steinke DT, Bain DJG, MacDonald TM, Davey PG. Practice factors that influence antibiotic prescribing in general practice in Tayside. *Journal of Antimicrobial Chemotherapy* 2000;**46**:509-12.

Stephenson 1996

Stephenson J. Icelandic researchers are showing the way to bring down rates of antibiotic-resistant bacteria. *JAMA* 1996;**275**:175.

Stewart 1998

Stewart FM, Antia R, Levin BR, Lipsitch M, Mittler JE. The Population Genetics of Antibiotic Resistance II: Analytic Theory for Sustained Populations of Bacteria in a Community of Hosts. *Theoretical Poplulation Biology* 1998;**53**:152-65.

Tan 1993

Tan TQ, Mason EO, Kaplan SL. Penicillin-resistant systemic pneumococcal infections in children: a retrospective case-control study. *Pediatrics* 1993;**92**:761-7.

Taylor 1977

Taylor B, Abbott GD, McKerr M, Fergusson DM. Amoxycillin and cotrimoxazole in presumed viral respiratory infections of childhood: placebo-controlled trial. *BMJ* 1977;**2**:552-4.

Wang 1999

Wang EE, Einarson TR, Kellner JD, Conly JM. Antibiotic prescribing for Canadian preschool children: evidence of overprescribing for viral respiratory infections. *Clinical Infectious Diseases* 1999;**29**:155-60.

Watson 1999

Watson RL, Dowell SF, Jayaraman M, Keyserling H, Kolczak M, Schwartz B. Antimicrobial use for pediatric upper respiratory infections: reported practice, actual practice and parent beliefs. *Pediatrics* 1999;**104**:1251-7.

Whitney 2000

Whitney CG, Farley MM, Hadler J, Harrison LH, Lexau C, Reingold A, et al. Increasing prevalence of multidrug-resistant Streptococcus pneumoniae in the United States. *New England Journal of Medicine* 2000;**343**:1917-24.

Zenni 1995

Zenni MK, Cheatham SH, Thompson JM, Reed GW, Batson AB, Palmer PS, et al. Streptococcus pneumoniae colonization in the young child: association with otitis media and resistance to penicillin. *Journal of Pediatrics* 1995;**127**:533-7.

Zhanel 2000

Zhanel G, Karlowsky JA, Harding GKM, Carrie A, Mazzulli T, Low DE, et al. A Canadian national surveillance study of urinary tract isolates from outpatients: comparison of the activities of trimethoprim-sulfamethoxazole, nitrofurantoin and ciptrofloxacin. *Antimicrobial Agents and Chemotherapy* 2000;**44**:1089-92.

* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Angunawela 1991

Methods	RCT unit of allocation: district hospitals and health units unit of analysis: episodes of care power calculation: not done concealment of allocation: not clear follow up of professionals: not clear blinded assessment of primary outcomes: not clear baseline measurement: done reliable primary outcome measure: not clear protection against contamination: done analysis appropriate: no
Participants	43 physicians and assistant medical practitioners in 15 outpatient clinics of institutions where drugs prescribed free of charge in Sri Lanka, treating patients of all ages for community acquired infection
Interventions	1. Printed educational materials 2. Printed educational materials + educational meeting

Angunawela 1991 *(Continued)*

	3. No intervention control
Outcomes	Professional practice: change in rate of prescribing several antibiotic classes Patient: none
Notes	Educational materials based upon Drug Information Bulletin produced by the Department of Pharmacology, Peradeniya and the Ministry of Health in Sri Lanka

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Unclear risk	B - Unclear

Arroll 2002

Methods	RCT unit of allocation: patient unit of analysis: patient power calculation: done concealment of allocation: done follow up of patients: done blinded assessment of outcome: not done baseline measurement: not applicable reliable primary outcome measure:done protection against contamination: not applicable analysis appropriate: yes
Participants	129 patients from practices of 15 family physicians in New Zealand with common cold where physician thought patient wanted an antibiotic
Interventions	1. Delayed treatment with antibiotics - patient received prescription for antibiotic and instructed to fill it after 3 days if symptoms not improving 2. Patient received immediate prescription for antibiotic from physician
Outcomes	Professional practice: none Patient: antibiotic use by patient, daily temperature symptom score
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Low risk	A - Adequate

Avorn 1983

Methods	RCT unit of allocation: provider unit of analysis: episode of care power calculation: not done concealment of allocation: not clear follow up of professionals: done blinded assessment of outcome: done baseline measurement: done reliable primary outcome measure: done protection against contamination: done analysis appropriate: no
Participants	435 physicians in Arkansa, Vermont, New Hampshire and District of Columbia, USA treating patients for community acquired infection
Interventions	1. Printed educational materials 2. Printed educational materials + academic detailing by pharmacist 3. No intervention control
Outcomes	Professional practice: Change in rates of prescribing cephalexin (primary outcome) Changes in rate of prescribing of alternative drugs that might be substituted for target drugs Change in costs associated with changes in prescribing
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Belongia 2001

Methods	CBA unit of allocation: community unit of analysis: episode of care (for antibiotic prescribing); childcare center (for antibiotic resistance) power calculation: not done baseline measurement: not done characteristics for studies using second site as control: not done blinded assessment of primary outcome: done protection against contamination: done reliable primary outcome measure: done follow up of professionals: done (for antibiotic prescribing) follow up of patients: not done (for antibiotic resistance) analysis appropriate: no
Participants	185 family practitioners, internists and pediatricians in two communities in Wisconsin, USA and all community residents (particularly parents of young children) being treated for respiratory tract infection

Belongia 2001 *(Continued)*

Interventions	1. Multi-faceted including large and small group educational meetings + printed educational materials for physicians and educational meetings and printed educational materials for childcare providers and parents 2. no intervention control
Outcomes	Professional practice: change in rate of prescribing of oral antibiotics Patient: change in proportion of Streptococcus pneumoniae isolates from children resistant to penicillin
Notes	Campaign message based upon evidence based guidelines: Principles of Judicious Antibiotic Use

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Unclear risk	D - Not used

Bexell 1996

Methods	RCT unit of allocation: general health centers unit of analysis: episodes of care power calculation: not done concealment of allocation: not clear follow up of professionals: not clear blinded assessment of primary outcomes: not clear baseline measurement: done reliable primary outcome measure: not clear protection against contamination: done analysis appropriate: no
Participants	Clinical officers in 16 primary healthcare clinics in Zambia treating patients with acute respiratory infections and diarrhea
Interventions	1. Educational meetings 2. No intervention control
Outcomes	Professinal practice: change in rate of prescribing antibiotics Patient: None
Notes	Content derived from Zambian Essential Drugs Program with support of Swedish International Development Authority

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Unclear risk	B - Unclear

Christakis 2001

Methods	RCT unit of allocation: provider unit of analysis: episode of care power calculation: not done concealment of allocation: done follow up of professionals: not done blinded assessment of outcome: done baseline measurement: done reliable primary outcome measure: done protection against contamination: not done analysis appropriate: yes	
Participants	38 pediatricians, pediatric resident physicians and nurse practitioners in an academic pediatric primary care clinic in Seattle, USA treating children with acute otitis media	
Interventions	1. Physician reminder (online prescription writer which offered summary of evidence for prescribing for acute otitis media) 2. No reminder (online prescription writer with no information on acute otitis media)	
Outcomes	Professional practice: Change in average duration of therapy for acute otitis media Change in rate of prescribing antibiotics for acute otitis media	
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Unclear risk	D - Not used

De Santis 1984

Methods	RCT unit of allocation: post code region unit of analysis: prescriptions power calculation: not clear concealment of allocation: not clear follow up of professionals: not done blinded assessment of outcome: not clear baseline measurement: not clear reliable primary outcome measure: not clear protection against contamination: done analysis appropriate: no
Participants	439 GPs in 8 regions in Victoria, Australia treating patients of all ages with tonsillitis
Interventions	1. Academic detailing by pharmacist + educational materials 2. No intervention control
Outcomes	Professional practice: Change in rate prescribing recommended antibiotics for pharyngitis

De Santis 1984 *(Continued)*

	Patient: none
Notes	Prescribing recommendations Victoria Health Department Prescribing Guidelines

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Dolovich 1999

Methods	RCT unit of allocation: region unit of analysis: prescriptions power calculation: not done concealment of allocation: done follow up of professionals: not clear blinded assessment of primary outcomes: done baseline measurement: done reliable primary outcome measure: done protection against contamination: done analysis appropriate: no
Participants	1215 family physicians and pediatricians in 8 regions in Ontario, Canada prescribing antibiotics for children with acute otitis media
Interventions	1. Academic detailing by pharmaceutical detailer + educational materials 2. Routine pharmaceutical detailing
Outcomes	Professional practice: Change in market share of recommended first line antibiotic (amoxicillin) Change in market share of recommended second line antibiotics (pivampicillin, cotrimoxazole and erythromycin-sulfamethoxazole) Patient: None
Notes	Description of development of the evidence based guideline for management of acute otitis media not provided

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - Adequate

Dowell 2001

Methods	RCT unit of allocation: patient unit of analysis: patient

Dowell 2001 *(Continued)*

	power calculation: done concealment of allocation: done follow up of patients: done blinded assessment of outcome: not clear baseline measurement: not applicable reliable primary outcome measure:done protection against contamination: not applicable analysis appropriate: yes
Participants	191 patients over 16 years of age from 48 general practitioners in Great Britain with uncomplicated respiratory tract infection with cough who were thought to desire antibiotics by the physician
Interventions	1. Delayed treatment with antibiotics - patient received prescription that was kept at physician's office and asked to retrieve it in one week if required 2. Immediate prescription from physician
Outcomes	Professional practice: Subsequent use by GP of delayed prescribing Patient: Proportion of patients who collected prescriptions Duration of symptoms (cough) Patient attitudes
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Low risk	A - Adequate

Finkelstein 2001

Methods	RCT unit of allocation: practice unit of analysis: patient power calculation: done concealment of allocation: not clear follow up of professionals: not clear blinded assessment of outcome: done baseline measurement: done reliable primary outcome measure: done protection against contamination: done analysis appropriate: yes
Participants	129 family physicians, pediatricians and nurse practitioners in 12 practices in the Massachusetts and Washington, USA treating children with respiratory tract infections
Interventions	1. Multi-faceted including local opinion leaders + audit and feedback + educational materials for physicians; printed educational materials for parents 2. No intervention control
Outcomes	Professional practice:

Finkelstein 2001 *(Continued)*

	Change in rate of prescribing antibiotics for respiratory tract infections Patient: None
Notes	Educational materials for clinicials and parents based upon evidence based guidelines: Principles of Judicious Antibiotic Use

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Flottorp 2002

Methods	RCT unit of allocation: practice unit of analysis: practice power calculation: done concealment of allocation: done follow up of professionals: done blinded assessment of outcome: done baseline measurement: done reliable primary outcome measure: done protection against contamination: done analysis appropriate: yes
Participants	General Practitioners and physicians' assistants from 142 practices in Norway treating patients over 3 years of age for sore throat and women between 16 and 55 years of age for urinary tract infection.
Interventions	1. Multi-faceted intervention tailored to overcome identified barriers to change for management of urinary tract infection including printed and electronic educational materials + computer-based decision support and reminders+ increase in fee for telephone consultation + educational with points for continuing medical education for physicians; printed and electronic educational materials for patients 2. Same intervention for the management of sore throat
Outcomes	Professional practice: Changes in rates of prescribing use of antibiotics for both conditions Patient: None
Notes	Guidelines for content published in Journal of the Norwegian Medical Association

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - Adequate

Font 1991

Methods	RCT

Font 1991 *(Continued)*

	unit of allocation: provider unit of analysis: episodes of care power calculation: not done concealment of allocation: not clear follow up of professionals: not clear blinded assessment of primary outcomes: not clear baseline measurement: done reliable primary outcome measure: not clear protection against contamination: done analysis appropriate: no
Participants	244 general practitioners in 26 regions in Spain treating patients of all ages with community acquired infection
Interventions	1. Academic detailing by pharmacist + audit and feedback 2. No intervention control
Outcomes	Professional practice: Change in rate of prescribing of specified antibiotics Patient: None
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Gonzales 1999

Methods	CBA unit of allocation: practice unit of analysis: practice power calculation: not done baseline measurement: done characteristics for studies using second site as control: not done blinded assessment of primary outcome: done protection against contamination: done reliable primary outcome measure: done follow up of professionals: done analysis appropriate: yes
Participants	93 general practitioners and internists in 4 practices in Colorado, USA treating adult patients with acute bronchitis
Interventions	1. Educational meetings + including audit and feedback + patient educational materials 2. Patient educational materials + including audit and feedback 3. No intervention control
Outcomes	Professional practice: Change in rate of prescribing of oral antibiotics for acute bronchitis

Gonzales 1999 *(Continued)*

	Patient: None
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	D - Not used

Harris 1984

Methods	CCT unit of allocation: practices unit of analysis: episodes of care power calculation: not done concealment of allocation: not done follow up of professionals: not clear blinded assessment of primary outcome: done baseline measurement: done reliable primary outcome measure: done protection against contamination: done analysis appropriate: no
Participants	59 general practitioners in 22 practices in Great Britain treating patients of all ages for community acquired infection
Interventions	1. Educational meetings + audit and feedback + printed educational materials 2. No intervention control
Outcomes	Professional practice: Change in rate of prescribing penicillin Patient: None
Notes	No specific prescribing recommendations were made. Feedback data and workshops facilitated discussion of physicians' prescribing in general

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	D - Not used

Hennessy 2002

Methods	CBA unit of allocation: village unit of analysis: nasopharyngeal swab specimen (for Streptococcus pneumoniae resistance assessment), episode of care (for antibiotic prescribing) power calculation: not done baseline measurement: not done

Hennessy 2002 *(Continued)*

	characteristics for studies using second site as control: not clear blinded assessment of primary outcome: not clear protection against contamination: done reliable primary outcome measure: not clear follow up of professionals: not clear analysis appropriate: no
Participants	Physicians and community health aides and community residents in 13 villages in Alaska, USA treating patients for with respiratory tract infection
Interventions	1. Multi-faceted interventions including educational meetings for health care providers and printed educational materials + educational meetings for villagers 2. No intervention control - intervention extended to control villages in second year of study
Outcomes	Professional practice: Change in rate of prescribing of oral antibiotics Patient: Change in proportion of nasopharyngeal Streptococcus pneumoniae isolates resistant to penicillin
Notes	Campaign message based upon evidence based guidelines: Principles of Judicious Antibiotic Use

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Unclear risk	D - Not used

Hux 1999

Methods	RCT unit of allocation: provider unit of analysis: episode of care power calculation: not done concealment of allocation: not clear follow up of professionals: done blinded assessment of outcome: done baseline measurement: done reliable primary outcome measure: done protection against contamination: done analysis appropriate: no
Participants	250 general and family practitioners in Ontario, Canada treating patients over 65 years of age with community acquired infections
Interventions	1. Audit and feedback + printed educational materials 2. No intervention control
Outcomes	Professional practice: Change in rate of use of first- and second-line antibiotics Change in costs of antibiotics prescribed
Notes	recommendations for first and second line therapy based on the Ontario Anti-infective Guidelines for Community-Acquired Infections, 1994, produced by a provincially funded panel

Hux 1999 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Ilett 2000

Methods	RCT unit of allocation: provider unit of analysis: prescriptions power calculation: not done concealment of allocation: not clear follow up of professionals: done blinded assessment of outcome: done baseline measurement: done reliable primary outcome measure: done protection against contamination: not clear analysis appropriate: no
Participants	112 general practitioners in Perth, Australia treating patients with urinary tract infections, bacterial tonsilitis, otitis media, acute bacterial bronchitis and mild pneumonia
Interventions	1. Academic detailing (by therapeutics advisor) 2. No intervention control
Outcomes	Professional practice: Change in rate of prescribing of recommended and non-recommended antibiotics Patient: None
Notes	Guidelines for prescribing developed by expert panel (composition of panel and method of consensus not described) in line with published Australian therapeutic guidelines for antibiotics

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Juncosa 1997

Methods	CBA unit of allocation: health region unit of analysis: episode of care power calculation: not done baseline measurement: not done characteristics for studies using second site as control: not clear blinded assessment of primary outcome: done protection against contamination: done reliable primary outcome measure: done follow up of professionals: done

Juncosa 1997 *(Continued)*

	analysis appropriate: no
Participants	General practitioners and pediatricians in 2 regions in Spain prescribing antibiotics for patients of all ages with community acquired infection
Interventions	1. Financial / health care system changes (primary care reform) 2. No intervention control
Outcomes	Professional practice: Change in mean number of prescriptions for antibiotics Patient: None
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Unclear risk	D - Not used

Lagerlov 2000

Methods	RCT unit of allocation: practice unit of analysis: practice power calculation: not done concealment of allocation: not clear follow up of professionals: not clear blinded assessment of outcome: done baseline measurement: done reliable primary outcome measure: done protection against contamination: done analysis appropriate: yes
Participants	199 general practitioners in 32 groups in Norway treating patients with asthma and urinary tract infection
Interventions	1. Educational meetings + audit and feedback + printed educational materials for asthma management 2. Same intervention for the management of urinary tract infection
Outcomes	Professional practice: Change in rate of prescribing antibiotics for asthma Change in rate of prescribing short course antibiotics for urinary tract infections Patient: None
Notes	Used Norwegian national guidelines for the management of UTI and asthma

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

Lagerlov 2000 *(Continued)*

Allocation concealment?	Unclear risk	B - Unclear

Little 2001

Methods	RCT unit of allocation: patient unit of analysis: patient power calculation: done concealment of allocation: done follow up of patients: done blinded assessment of outcome: not done baseline measurement: not applicable reliable primary outcome measure: not clear protection against contamination: not applicable analysis appropriate: yes
Participants	315 children (6 months to 10 years) with acute otitis media in 42 general practices in Great Britain
Interventions	1. Delayed treatment with antibiotics - patient received a prescription (held at physician's office) and asked to wait 72 hours and fill prescription if there no improvment 2. Parent received and told to fill prescription immediately
Outcomes	Professional practice: None Patient: presence of symptoms (earache, unwell, sleep disturbance) perceived severity of pain number of episodes of distress number of spoonfuls of paracetamol temperature
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Low risk	A - Adequate

Lundborg 1999a

Methods	RCT unit of allocation: physician group unit of analysis: physician group power calculation: done concealment of allocation: not clear follow up of professionals: done blinded assessment of primary outcome: done baseline measurement: done reliable primary outcome measure: done

Lundborg 1999a *(Continued)*

	protection against contamination: done analysis appropriate: yes
Participants	204 general practitioners in 36 practices in Sweden treating adult patients with and urinary tract infection in adults (women only)
Interventions	1. educational meetings + audit and feedback material for asthma 2. Same intervention for the management of urinary tract infection
Outcomes	Professional practice: Change in rate of prescribing first choice antibiotics and short courses of antibiotics for urinary tract infection Change in rate mean number of antibiotic courses per patient for asthma Patient: None
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

MacCara 2001

Methods	ITS unit of allocation: not applicable unit of analysis: prescriptions protection against secular changes: not clear sufficient data points to enable reliable statistical inference: done formal test for trend: not applicable protection against detection bias: done intervention unlikely to affect data collection: done blinded assessment of primary outcome: done completeness of data set: done reliable primary outcome measure: done analysis appropriate: no
Participants	Physicians of any specialty in Nova Scotia, Canada treating patients over 65 years of age for any community acquired infection
Interventions	1. Financial / health care system change by instituting fluoroquinolone reimbursement guidelines (limitations on prescribing)
Outcomes	Professional practice: Frequency of prescribing fluoroquinolones Frequency of prescribing other antibiotic classes Patient: None
Notes	

MacCara 2001 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	D - Not used

Macfarlane 2002

Methods	RCT unit of allocation: patient unit of analysis: patient power calculation: done concealment of allocation: not clear follow up of patients: done blinded assessment of outcome: done baseline measurement: not applicable reliable primary outcome measure: not clear protection against contamination: not applicable analysis appropriate: yes
Participants	212 adult patients with acute bronchitis from 3 general practices in Great Britain who were felt by the physician to desire but not require antibiotics
Interventions	1. Given standard verbal reassurance and prescription for antibiotics to use if they got worse along with leaflet outlining why antibiotics were not necessary for treatment of acute bronchitis 2. Given standard verbal reassurance and prescription for antibiotics to use if they got worse along with blank leaflet
Outcomes	Professional practice: None Patient: Proportion of patients who filled prescription Reconsultation for same symptoms in next month
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Mainous 2000

Methods	RCT unit of allocation: provider unit of analysis: episode of care power calculation: not done concealment of allocation: not clear follow up of professionals: done blinded assessment of outcome: done baseline measurement: not done

Mainous 2000 *(Continued)*

	reliable primary outcome measure: done protection against contamination: not clear analysis appropriate: no
Participants	269 family or general practitioners, pediatricians or general internists in Kentucky, USA treating children for upper respiratory tract infection
Interventions	1. Patient educational materials 2. Audit and feedback to physicians 3. Audit and feedback +patient educational materials 4. No intervention controls
Outcomes	Professional practice: change in rate of prescribing antibiotics for upper respiratory infection Patient: None
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Unclear risk	B - Unclear

McConnell 1982

Methods	RCT unit of allocation: provider unit of analysis: prescriptions power calculation: not done concealment of allocation: not clear follow up of professionals: done blinded assessment of outcome: done baseline measurement: not done reliable primary outcome measure: done protection against contamination: not clear analysis appropriate: no
Participants	33 physicians in New Mexico, USA treating patients of all ages for upper respiratory infection/streptococcal throat infection
Interventions	1. Academic detailing by physician 2. No intervention control
Outcomes	Professional practice: Change in rate of prescribing of tetracycline Patient: None
Notes	

McConnell 1982 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

McIsaac 1998

Methods	RCT unit of allocation: provider unit of analysis: provider/episode of care (each provider contributed only one patient) power calculation: done concealment of allocation: not clear follow up of professionals: not done blinded assessment of outcome: not clear baseline measurement: not done reliable primary outcome measure: not clear protection against contamination: not done analysis appropriate: yes
Participants	396 family practitioners in Ontario, Canada treating patients over 15 years of age for sore throat
Interventions	1. Reminder (interactive component of scoring system) + Printed educational materials (sore throat scoring system with explicit management recommendations) 2. Printed educational materials (sore throat scoring system with explicit management recommendations)
Outcomes	Professional practice: Difference in rate of prescribing of oral antibiotics for sore throat Difference in rate of prescribing first- and second-line antibiotics
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

McIsaac 2002

Methods	RCT unit of allocation: provider unit of analysis: provider power calculation: done concealment of allocation: not clear follow up of professionals: not done blinded assessment of outcome: not clear baseline measurement: not done reliable primary outcome measure: not clear protection against contamination: not done analysis appropriate: yes

McIsaac 2002 *(Continued)*

Participants	169 family practitioners in Ontario, Canada treating patients over three years of age for sore throat
Interventions	1. Printed educational materials (clinical score management approach for sore throat) + reminders (stickers to apply to patient encounter form encouraging use of the score) 2. Printed educational materials (clinical score management approach for sore throat)
Outcomes	Professional practice: Rate of prescribing unnecessary antibiotics (prescription given to a patient who subsequently has negative throat culture for Group A Strep) Rate of overall antibiotic use Association between prescription rates and physician practice and demographic characteristics
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	D - Not used

McNulty 2000

Methods	CBA unit of allocation: community unit of analysis: episodes of care power calculation: not done baseline measurement: not done characteristics for studies using second site as control: done blinded assessment of primary outcome: done protection against contamination: done reliable primary outcome measure: done follow up of professionals: not clear
Participants	339 general practitioners from 84 practices in Great Britain treating patient of all ages for any community acquired infection
Interventions	1. Educational meetings (small group)+ printed educational materials + audit and feedback 2. Educational meetings (microbiology tutorial)
Outcomes	Professional practice: Change in number of antibiotics prescribed per 1000 prescribing units Change in cost of antibiotics prescribed per 1000 prescribing units Patient: None
Notes	Gloucestershire antibiotic prescribing guidelines created and reviewed annually by local pharmacy advisors, specialist consultatns and GPs and are approved by the local Drug and Therapeutics Committees and Local Medical Committees. They are based upon local antimicrobial sensitivity patterns and trials on antibiotic use in general practice.

Risk of bias

McNulty 2000 *(Continued)*

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	D - Not used

Meyer 2001

Methods	RCT unit of allocation: primary healthcare clinics unit of analysis: episodes of care power calculation: done (available in How to investigate drug use in health facilities: selected drug use indicators. Geneva: World Health Organisation 1993) concealment of allocation: not clear follow up of professionals: not clear blinded assessment of primary outcomes: not clear baseline measurement: done reliable primary outcome measure: not clear protection against contamination: done analysis appropriate: no
Participants	457 primary healthcare nurses in 22 clinics in South Africa treating patients of all ages with upper respiratory infection and diarrhoea
Interventions	1. Educational meetings 2. No intervention control
Outcomes	Professional practice: Change in rate of prescribing antibiotics Patient: None
Notes	Content of workshop based on World Health Organisation Guide to Good Prescribing

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

O'Connell 1999

Methods	RCT unit of allocation: postal code regions unit of analysis: episodes of care power calculation: done concealment of allocation: not clear follow up of professionals: not clear blinded assessment of primary outcome: done baseline measurement: done reliable primary outcome measure: done protection against contamination: done analysis appropriate: no

O'Connell 1999 *(Continued)*

Participants	2440 general practitioners grouped by postal code region in rural Australia treating patients of all ages with any community acquired infection
Interventions	1. Printed educational materials + audit and feedback 2. No intervention control
Outcomes	Professional practice: Change in rate of prescribing antibiotics Patient: None
Notes	Specific prescribing guidelines and recommendations not made

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Perez-Cuevas 1996

Methods	CBA unit of allocation: family medicine clinics and health centers unit of analysis: episodes of care power calculation: not done baseline measurement: not clear characteristics for studies using second site as control: done blinded assessment of primary outcome: not clear protection against contamination: done reliable primary outcome measure: not clear follow up of professionals: not clear analysis appropriate: no
Participants	119 physicians in 18 primary healthcare clinics in Mexico City, Mexico treating patients of all ages with rhinopharyngitis
Interventions	1. Educational meetings + audit and feedback + participation in peer review 2. No intervention control
Outcomes	Professional practice: Change in rate of prescribing antibiotics Change in rate of prescribing symptomatic medications
Notes	Content of workshop derived from review of current bibliography on rhinopharyngitis

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	D - Not used

Perz 2002

Methods	CBA unit of allocation: county unit of analysis: episode of care (? account for clustering by having a variable for county in the binomial regression model) power calculation: not done baseline measurement: not done characteristics for studies using second site as control: done blinded assessment of primary outcome: done protection against contamination: done reliable primary outcome measure: done follow up of professionals: not clear analysis appropriate: no (yes?)
Participants	Family practitioners and pediatricians (250 in intervention region, unknown in control regions) in 4 counties in Tennessee, United States treating children under 15 years of age for respiratory tract infection
Interventions	1. Multi-faceted including educational meetings + printed educational materials for physicians, printed educational materials for parents and patients. 2. No intervention control
Outcomes	Professional practice: Change in rate of prescribing of oral antibiotics Patient: Change in proportion of invasive Streptococcus pneumoniae isolates that are antibiotic resistant
Notes	Campaign message determined by East Tennessee Drug Resistance Task Force and based upon evidence based guidelines: Principles of Judicious Antibiotic Use

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	D - Not used

Peterson 1997

Methods	CBA unit of allocation: region unit of analysis: episodes of care power calculation: not done baseline measurement: done characteristics for studies using second site as control: not clear blinded assessment of primary outcome: done protection against contamination: done reliable primary outcome measure: done follow up of professionals: done analysis appropriate: no
Participants	250 general practitioners in 2 regions of Tasmania, Australia prescribing treating adult women for urinary tract infection
Interventions	1. Printed educational materials + academic detailing

Peterson 1997 *(Continued)*

	2. Printed educational materials
Outcomes	Professional practice: Change in rate of prescribing recommended antibiotics Opinions of general practitioners regarding program
Notes	Rational prescribing guidelines written in consultation with memeber of the Management Committee, Division of General Practice (Tasmania - Southern region) and a clinical microbiologist emphasizing the recommendations of the Antibiotic Guidelines Sub-Committee, Victorian Drug Usage Advisory Committee.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	D - Not used

Ray 1985

Methods	CBA unit of allocation: region unit of analysis: episode of care power calculation: not done baseline measurement: done characteristics for studies using second site as control:not clear blinded assessment of primary outcome: done protection against contamination: done reliable primary outcome measure: done follow up of professionals: done analysis appropriate: no
Participants	372 physicians in 4 counties in Tennessee, USA treaing patients of all ages with any community acquired infections
Interventions	1. Printed educational materials 2. Academic detailing by pharmacist + printed educational materials 3. Academic detailing by physician counselor + printed educational materials 4. No intervention control
Outcomes	Professional practice: Change in mean number of prescriptions for contraindicated antibiotics and oral cephalosporins. This study examines the persistence of the effects of the intervention one year after completion. Patient: None
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	D - Not used

Rokstad 1995

Methods	CBA unit of allocation: region unit of analysis: episodes of care power calculation: not done baseline measurement: done characteristics for studies using second site as control: done blinded assessment of primary outcome: not clear protection against contamination: done reliable primary outcome measure: not clear follow up of professionals: done analysis appropriate: no
Participants	111 general practitioners from 2 regions of Norway treating adult women with urinary tract infection
Interventions	1. Audit and feedback + printed educational materials for treatment of urinary tract infection 2. Same intervention for treatment of insomnia
Outcomes	Professional practice: Change in rate of prescribing recommended antibiotics Patient: None
Notes	Recommendations for prescribing made by local experts

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Unclear risk	D - Not used

Santoso 1996

Methods	RCT unit of allocation: health districts unit of analysis: episodes of care power calculation: not done concealment of allocation: not clear follow up of professionals: not clear blinded assessment of outcome: not clear baseline measurement: not clear reliable primary outcome measure: not clear protection against contamination: done analysis appropriate: no
Participants	Physicians and para-medical prescribers in 90 health centers in Indonesia treating patients under 5 years of age for gastroenteritis
Interventions	1. Small group educational meetings + written educational materials 2. Large-group educational meetings + written educational materials
Outcomes	Professional practice: change in rate of prescribing antibiotics

Santoso 1996 *(Continued)*

	Patient: None
Notes	Data from focus group meetings included in content of meetings and educational materials

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Schaffner 1983

Methods	CBA unit of allocation: region unit of analysis: episode of care power calculation: not done baseline measurement: done characteristics for studies using second site as control:not clear blinded assessment of primary outcome: done protection against contamination: done reliable primary outcome measure: done follow up of professionals: done analysis appropriate: no
Participants	372 physicians in 4 counties in Tennessee, USA treating patients of all ages with any community acquired infections
Interventions	1. Printed educational materials 2. Academic detailing by pharmacist + printed educational materials 3. Academic detailing by physician counselor + printed educational materials 4. No intervention control
Outcomes	Professional practice: Change in mean number of prescriptions for contraindicated antibiotics and oral cephalosporins Patient: None
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	D - Not used

Seppala 1997

Methods	ITS unit of allocation: not applicable unit of analysis: prescriptions

Seppala 1997 *(Continued)*

	protection against secular changes: not done sufficient data points to enable reliable statistical inference: done formal test for trend: not done protection against detection bias: done intervention unlikely to affect data collection: done blinded assessment of primary outcome: done completeness of data set: done reliable primary outcome measure: done analysis appropriate: no
Participants	Physicians in Finland treating patients of all ages with respiratory or skin infections
Interventions	1. Printed educational materials (published national guidelines)
Outcomes	Professional practice: Frequency of prescribing macrolide antibiotics Patient: Frequency of isolation of erythromycin resistant Group A streptococci
Notes	Guideline prepared by members of The Finnish Study Group for Antimicrobial resistance

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	D - Not used

Stewart 2000

Methods	CBA unit of allocation: community unit of analysis: episode of care power calculation: not done baseline measurement: not clear characteristics for studies using second site as control: not done blinded assessment of primary outcome: done protection against contamination: done reliable primary outcome measure: done follow up of professionals: not clear analysis appropriate: no
Participants	Physicians in Ontario, Canada treating patients of all ages for any community acquired infections
Interventions	1. Mulit-faceted including educational meetings + printed educational materials for physicians and nurses and the community (different meetings and materials) 2. No intervention control
Outcomes	Primary outcome Change in rate of prescribing of oral antibiotics Change in rate of prescribing first- and second-line antibiotics
Notes	Recommendations for first and second line therapy based on the Ontario Anti-infective Guidelines for Community-Acquired Infections, 1997 (2nd Edition), produced by a provincially funded panel

Stewart 2000 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	D - Not used

Veninga 2000

Methods	RCT unit of allocation: physician group unit of analysis: physician group power calculation: done concealment of allocation: not clear follow up of professionals: not clear blinded assessment of primary outcome: done baseline measurement: done reliable primary outcome measure: done protection against contamination: done analysis appropriate: yes
Participants	181 general practitioners from 24 pharmacotherapy counselling groups in the Netherlands treating adult patients for asthma and urinary tract infection (women only)
Interventions	1. Educational meetings + audit and feedback + printed educational materials for asthma management 2. Same intervention for the management of urinary tract infection
Outcomes	Professional practice: Change in rate of prescribing antibiotics for asthma Changes in rate of prescribing first-choice antibiotics and average duration of treatment for urinary tract infection:
Notes	Prescribing messages based on Dutch GP guidelines

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Armstrong 1999	ITS with insufficient datapoints
Armstrong 2001	ITS with insufficient datapoints
Barwitz 1999	Inappropriate study design
Braybrook 1996	Inappropriate control group

Study	Reason for exclusion
Bryars 1991	ITS with insufficient data points
Bush 1979	Data for intervention and control groups collected for different times
Cates 1999	Intervention not appropriate for inclusion
Chalker 2001	ITS with insufficient datapoints
Cohen 2000	Outcome measure not objective
Damsgaard 2001	Outcome measure not objective
Deiderichsen 2000	Intervention not appropriate for review
Ekedahl 1995	No objective outcome measure
Erramouspe 1989	ITS with insufficient datapoints
Fagan 2001	Intervention not appropriate for review
Farris 1996	Inappropriate control group
Faryna 1987	ITS with insufficient datapoints
Friis 1989	ITS with insufficient datapoints
Friis 1993	ITS with insufficient datapoints
Garica Lirola 1999	Inappropriate control group
Goode 2000	ITS with insufficient datapoints
Guiscafre 1988	Inappropriate control group
Guiscafre 1995	No control group
Gutierrez 1994	Antibiotic data not extractable
Hueston 1997	No intervention
Ibrahim 1997	No baseline data
Ives 1987	ITS with insufficient datapoints
Kafle 1995	Outcome measure not objective
Klein 1981	Inappropriate control group (intervention group trainees, control group fully trained physicians)
Leach 1999	Full antibiotic data not available (authors contacted)
Lohr 1980	No control group
Lundborg 1999b	Reported physician's evaluation of intervention only
Mallet 2001	ITS with insufficient datapoints

Study	Reason for exclusion
Margolis 1992	No control group
Melander 1999	In appropriate control group; no objective outcome measure
Molstad 1989	ITS without enough datapoints
Molstad 1994	
Molstad 1999	ITS but no specified point in time where intervention occurred
Motheral 1999	Antibiotic data not extractable
Munck 1998	Outcome measure not objective
Needham 1988	No control group
North England 1992	Appropriate baseline data not available
O'Connor 1996	ITS with insufficient datapoints
Ochoa 1996	No baseline data available
Ornstein 1997	ITS not analysed appropriately and datapoints not available (author contacted) for reanalysis
Perez Rodriguez 1994	Data for controls not available
Poses 1995	Data for intervention and control groups collected for different time periods
Putnam 1985	Antibiotic data not available (authors contacted)
Raz 1995	Inappropriate control group
Saint 1999	Appropriate baseline data not available
Stuart 1997	Antibiotic data not extractable
Suchyta 2001	No control group
Temte 1999	ITS with insufficient data points, trainees only
Vedsted 1997	Antibiotic data not extractable
Walley 2000	Inappropriate study design
Wood 1997	No control group, no extractable antibiotic data
Wyatt 1992	ITS with insufficient datapoints
Zuriguel 1993	Inappropriate control group
Zwar 1995	Included trainees only
Zwar 1999	Included trainees only
Zwar 2002	Follow up data from Zwar 1999

ADDITIONAL TABLES

Table 1. Printed educational materials versus other intervention or no intervention

Study	Targeted behaviour	Main process effect	Absolute change	Relative change	Notes
Schaffner 1983 Ray 1985 (2 year follow up of Schaffner 1983)	Reducing prescribing of contraindicated antibiotics and oral cephalosporins	Comparison: Printed educational materials vs control Mailed brochure reported as having no detectable effect and data combined with control group for other comparisons			For comparison of academic detailing vs control see Table 4
Avorn 1983	Reducing prescribing of cephalexin	Comparison: printed educational materials vs control Mean number of units of cephalexin prescribed Before: 1403 vs 1101 After: 1434 vs 1240	Absolute change: 194 Difference in absolute change from baseline: -100 (by linear regression)	Relative percent change (post): 16%	Change in prescribing not statistically significant by linear regression For comparison of academic detailing vs control see Table 4
Angunawela 1991	Reducing prescribing of oral antibiotics	Comparison: printed educational material vs control Proportion of patients prescribed an antibiotic Before: 31.5% vs 32.2% After: 24.1% vs 31.8%	Absolute change (post): -7.7% Difference in absolute change from baseline: -7.0%	Relative per cent change (post): -24.2%	P value >0.05 by Wilcoxon Rank Sum test for difference in prescribing from pre to post-test period between intervention and control groups For comparison of educational meetings vs control see Table 3
Seppala 1997	Reducing prescribing of macrolide antibiotics for Group A Streptococcal infections	Comparison: Before and after printed educational materials (Interrupted time series study) Number of defined daily doses (DDD) per 100 inhabitants Before: 2.40 After: 1.38			P value 0.007 for difference between prescribing in 1991 and 1992. By time series analysis (not performed by study authors) there was a significant change in the level of prescribing at point of intervention (-1.59, SE=0.268, p<0.001) but no signficant change in slope (-0.5, SE 0.129, P value 0.691) suggesting the effect of intervention would be maintained over time (more time points further out would clarify) For effect of prescribing change on antibiotic resistance see Table 9

Table 2. Audit and feedback versus other intervention or no intervention

Study	Targeted Behaviour	Main Process Effect	Absolute Change	Relative Change	Notes
Rokstad 1995	Increasing prescribing of recommended antibiotics for urinary tract infection Reducing number of days of therapy for urinary tract infection (3 days recommended)	Comparison: Audit and feedback vs control (same intervention, different condition) Number of prescriptions for first-line antibiotics (mean for 2 recommended antibiotics) Before: 40.5 vs 51.0 After: 63.5 vs 39.5 Duration of antibiotic therapy in defined daily doses (DDD) (mean for 2 recommended antibiotics) Before: 10.0 vs 8.2 After: 7.4 vs 12.3	First line agents: Absolute change (post) for first line agents: 24 Difference in absolute change from baseline for first line agents: 34.5 Defined daily doses: Absolute change (post) for DDD: -4.9 Difference in absolute change from baseline for DDD: -7.7	First line agents: Relative percent change (post): 60.7% Defined daily doses: Relative percent change (post): -39.8%	Authors also reported on reductions in prescriptions for non-recommended antibiotics No between group comparisons performed
O'Connell 1999	Reducing prescribing of oral antibiotics for any condition	Comparison: Audit and feedback vs control Prescribing rate per 100 medicare services Before: 10.7 vs 10.7 After: 10.5 vs 10.1	Absolute change (post): 0.4 Difference in absolute change from baseline: 0.4	Relative percent change (post): 4.0%	No significant difference between groups reported
Hux 1999	Increasing proportion of episodes of care with first-line antibiotic Reducing median antibiotic cost	Comparison: Audit and feedback vs control Proportion of episodes with first-line antibiotic Before: 67.2 vs 68.5 After: 69.8 vs 66.8 Median antibiotic cost ($) per physician Before: 11.5 vs 10.78 After 11.55 vs 14.15	First line antibiotics: Absolute change (post): 3.0 Difference in absolute change from baseline: 5.1 Median cost: Absolute change (post): -2.6 Difference in absolute change from baseline: -3.32	First line antibiotics Relative percent change (post): 4.5% Median cost: Relative percent change (post): -18.3%	P value <0.01 by ANOVA for improvement in first-line antibiotic use between group comparison P value <0.002 by ANOVA for reduction in antibiotic cost between group comparison
Mainous 2000	Reducing prescribing of antibiotics for upper respiratory infection	Comparison 1 Audit and feedback vs control Proportion (%) of viral (RTI) episodes with antibiotics Before: 28.4 ± 16.8% vs 31.0 ± 17.6% After: 43.6 ± 28.0% vs 53.5 ± 26.8% Comparison 2 Audit and feedback + patient educational materials vs control Proportion (%) of viral (RTI) episodes with antibiotics Before: 34.4 ± 13.8% vs 31.0 ± 17.6%	Comparison 1 Absolute change (post): -9.9 % Difference in absolute change from baseline: -7.3% Comparison 2 Absolute change (post): -3.8% Difference in absolute change from baseline: -7.2%	Comparison 1 Relative percent change (post): -18.5% Comparison 2 Relative percent change (post): -7.1%	All groups showed increase in proportion of patients receiving antibiotics. Gain scores for patient educational materials groups (with or without audit and feedback) were significantly less that control (T=2.374, P value <0.05) For comparison of patient educational materials vs control see Table 7

Table 2. Audit and feedback versus other intervention or no intervention *(Continued)*

		After: 49.7 ± 22.3% vs 53.5 ± 26.8%			

Table 3. Educational meetings versus other interventions or no intervention

Study	Targeted Behaviour	Main Process Effect	Absolute Change	Relative Change	Notes
Harris 1984	Reducing prescribing of oral antibiotics	Comparison: Educational meetings + audit and feedback vs control Prescriptions per 1000 registered patients Before: 16.5 vs 16.0 After 16.7 vs 18.9	Absolute change (post): -2.2 Difference in absolute change from baseline: -2.7	Relative percent change (post): -6.9%	Practice level audit and feedback provided four times over two years. Two interactive discussions of audit material
Angunawela 1991	Reducing prescribing of oral antibiotics	Comparison: educational meetings + printed educational materials vs control Proportion of patients prescribed an antibiotic Before: 38.8% vs 32.2% After: 31.5% vs 31.8%	Absolute change (post): -0.3% Difference in absolute change from baseline: -6.9%	Relative percent change (post): -0.009%	No before and after differences within study group were statistically significant by Wilcoxon rank sum test One meeting per prescriber lasting 3 hours reinforcing printed materials. Not clear if interactive For comparison of patient educational materials vs control see Table 1
Bexell 1996	Reducing prescribing or oral antibiotics	Comparison: educational meeting vs control Proportion of patients prescribed an antibiotic Before: 41.2% vs 41.0% After: 34.2% vs 42.1%	Absolute change (post): -7.9% Difference in absolute change from baseline: -8.1%	Relative percent change (post): -18.8%	Three, interactive, two day seminars discussing prescribing guidelines
Perez-Cuevas 1996	Improving appropriateness of antibiotic prescribing	Comparison: educational meeting + peer review vs control (intervention and controls selected from two groups of physicians, SSA and IMSS; results reported separately for these two groups) Proportion of patients prescribed antibiotics SSA Before: 80.7% vs 97.1% After: 62.7% vs 86.5% IMSS Before: 88% vs 95.7% After: 56.3% vs 96.9%	SSA Absolute change (post): -23.8% Difference in absolute change from baseline: -7.4% IMSS Absolute change (post)(IMSS): -40.6% Difference in absolute change from baseline (IMSS): -32.9%	SSA Relative percent change (post): -27.5% Relative percent change (post): -41.9%	Follow up of prescribing practices at 18 months showed: persistent positive change (continued improvement in prescribing) for 17.5% of study physicians (from both groups) vs 2.6% of control physicians and a stable positive change (maintained improvement after training but no additional improvement) in 25% of study physicians and 0.0% of control physicians Five, interactive, two hour, small-group workshops

Table 3. Educational meetings versus other interventions or no intervention *(Continued)*

Santoso 1996	Reducing prescribing of antibiotic prescribing for diarrhoea	Comparison 1: small group educational meeting vs control Proportion of patients prescribed an antibiotic Before: 77.4% vs 82.6% After: 60.4% vs 79.3% Comparison 2: large group educational meeting vs control Proportion of patients prescribed an antibiotic Before: 82.3% vs 82.6% After: 72.3% vs 79.3%	Comparison 1: Absolute change (post): -18.9% Difference in absolute change from baseline: -13.7% Comparison 2: Absolute change (post): -7.0% Difference in absolute change from baseline: -6.7%	Comparison 1: Relative percent change (post): -23.8% Comparison 2: Relative per cent change (post): -8.4%	Change in prescribing in intervention compared with control not statistically significant by chi square Small group meetings interactive with 8 to 12 participants Large group meetings were formal, non-interactive seminars
Lundborg 1999	Increasing prescribing of first line antibiotics and reducing duration of therapy for urinary tract infection (UTI). Reducing antibiotic prescribing for asthma exacerbations	Comparison: education meetings + audit and feedback vs control (UTI and asthma groups acted as controls for each other) Proportion of patients prescribed first-line antibiotic (UTI) Before: 52% vs 70% After: 57% vs 58% Average duration of treatment (UTI) (days) Before: 7.51 vs 7.41 After: 7.60 vs 7.44 Number of antibiotic courses per asthma patient Before: 0.26 vs 0.27 After: 0.32 vs 0.26	First line UTI antibiotics Absolute change (post): -1.0% Difference in absolute change from baseline: 17.0% Average duration of treatment: Absolute change (post): 0.16 Difference in absolute change from baseline: 0.06 Number of antibiotic courses per asthma patient Absolute change (post): 0.08 Difference in absolute change from baseline: 0.07	First line UTI antibiotics Relative percent change (post): -1.7% Average duration of treatment: Relative percent change (post): 2.2% Number of antibiotic courses per asthma patient Relative percent change (post): 30.7%	Using multilevel regression and paired t-statistic: change in proportion of patients prescribed first-line antibiotics for UTI significant (P value <0.001) change in average duration of treatment not significant (p> 0.2) change in number of antibiotic prescriptions per asthma patient not significant (P value >0.2) Interactive small group (3 to 12 participants), 1.4 hours long discussing audit material, case simulations and guidelines
Lagerlov 2000	Increasing the proportion of appropriately treated UTI patients (short course therapy)	Comparison: educational meetings + audit and feedback vs control (similar intervention for different condition - asthma) Mean proportion of short courses of therapy Before: 0.12 vs 0.12 After: raw data not available	Not calculable or provided	Relative percent change (post): 13.1%	Using hierarchical regression, the 13.1% increase in prescribing of short courses of antibiotics for UTI in intervention compared with control was statistically significant (P value <0.0001) 2 interactive, 2 to 3 hour long, small-group (4 to 8 participants) meetings

Table 3. Educational meetings versus other interventions or no intervention *(Continued)*

McNulty 2000	Reducing prescribing of antibiotics	Comparison: educational meetings + audit and feedback vs microbiology tutorials Number of prescriptions for antibiotics Before: 71 657 vs 53 867 After: 69 199 vs 52 658	Absolute change (post): 16541 Difference in absolute change from baseline: -1249	Relative percent change (post): 31.4%	P value 0.09 for the change in overall antibiotic between intervention and control groups by Mann-Whitney U test One, small-group, interactive workshop, 1.5-2 hours long discussing audit material and guidelines vs One, large, formal, non-interactive, microbiology lecture
Veninga 2000	Increasing prescribing of first-choice antibiotics and reducing duration of therapy for urinary tract infection	Comparison: educational meetings + audit and feedback vs control (same intervention for asthma) Proportion of first-choice antibiotics dispensed for all UTI antibiotics Before: 89% vs 86% After: 89% vs 85% Average duration of UTI therapy (in defined daily doses - DDD) Before: 6.07 vs 5.40 After: 4.29 vs 5.51	First choice antibiotics Absolute change (post): 4.0% Difference in absolute change from baseline: 1.0% Duration of therapy Absolute change (post): -1.22 Difference in absolute change from baseline: -1.89	First choice antibiotics Relative percent change (post): 4.7% Duration of therapy Relative percent change (post): 22.2%	Change in duration of UTI therapy significant at P value 0.05 level by hierarchical regression Self-learning auditing program for peer groups - small-group (8 participants), interactive workshops discussing audit material, cases and guidelines
Meyer 2001	Reducing prescribing for upper respiratory infection and diarrhea	Comparison: educational meeting vs control Proportion of prescriptions with an antibiotics (mean value for 2 conditions) Before: 47.2% vs 32.6% After: 18.8% vs 25.8%	Absolute change (post): -7.0% Difference in absolute change from baseline: -21.6%	Relative percent change (post): -27.1%	One, effective prescribing workshops for 20 participants 4 days long, not clear if interactive

Table 4. Academic detailing versus other intervention or no intervention

Study	Targeted behaviour	Main process effect	Absolute change	Relative change	Notes
McConnell 1982	Reducing prescribing of tetracycline	Comparison: academic detailing vs control Mean number of prescriptions per provider Before: 12.6 vs 7.6 After:1.8 vs 3.2	Absolute change (post): -1.4 Difference in absolute change from baseline: -6.4	Relative percent change (post): -43.8	By ANCOVA, reduction in mean number of prescriptions greater in intervention compared with control (P value <0.05) One 30 minute meeting by physician detailer

Table 4. Academic detailing versus other intervention or no intervention *(Continued)*

Avorn 1983	Reducing prescribing of cephalexin	Comparison: Academic detailing + Printed educational materials vs control Mean number of units of cephalexin prescribed Before: 1272 vs 1101 After: 1029 vs1240	Absolute change: -211 Difference in absolute change from baseline: -382 (by regression)	Relative percent change (post): -17%	Change in prescribing significant with P value 0.0006 by linear regression model One meeting with pharmaceutical educator
Schaffner 1983 Ray 1985 (2 year follow up of Schaffner 1983)	Reducing prescribing of contraindicated antibiotics and oral cephalosporins	Comparison 1: academic detailing (physician counsellor) vs. control/mailer Number of prescriptions per physician (mean value for contraindicated antibiotics and oral cephalosporins reported baseline: 117.9 vs 102.2 Postintervention year 1: 59.8 vs 35.4 Postintervention year 2: 61 vs 38.8 Comparison 2: academic detailing (drug educator) vs control/mailer Number of prescriptions per physician (mean value for contraindicated antibiotics and oral cephalosporins) Baseline: 75.8 vs 52.2 Postintervention year 1: 48.3 vs 35.4 Postintervention year 2: 53.4 vs 38.8	Comparison 1 year 1 Absolute change (post): 24.4 Difference in absolute change from baseline: 8.7 year 2 Absolute change (post): 22.2 Difference in absolute change from baseline: 6.5 Comparison 2 year 1 Absolute change (post): 12.9 Difference in absolute change from baseline: -10.4 Year 2 Absolute change (post): 14.6 Difference in absolute change from baseline: -9.0	Comparison 1 Relative percent change (post): year 1: 68.9% year 2: 57.2% Comparison 2 Relative percent change (post): year 1: 36.4% year 2: 37.6%	One meeting with either physician or pharmacist detailer
Font 1990	Reducing prescribing of antibiotics	Comparison: academic detailing vs control Mean number of containers per doctor per month (mean value for antibiotics combined with symptomatic agents, oral cephalosporins and injectable cephalosporins) Before: 32.69 vs 39.38 After: 29.92 vs 37.92	Absolute change (post): -8.00 Difference in absolute change from baseline: -1.31	Relative percent change (post): 21.1%	3 meetings, each 15 minutes long by pharmacist detailer
De Santis 1994	Increasing prescribing of first-line antibiotics for tonsillitis	Comparison: academic detailing +printed educational materials vs control Median proportion of prescriptions for first-line antibiotics	Absolute change (post):13.1% Difference in absolute change from baseline: -3.3%	Relative percent change (post): 15.0%	Relative improvement between intervention and control groups not statistically significant

Table 4. Academic detailing versus other intervention or no intervention *(Continued)*

		Before: 78.3% vs 61.9% After: 100.0% vs 86.9%			One meeting with pharmacist detailer
Peterson 1997	Increasing prescribing of recommended antibiotics for UTI	Comparison: academic detailing + printed educational materials vs control Proportion of defined daily doses (DDD) that were for recommended antibiotics Before: 73.5% vs 81.7% After: 84.4% vs 83.1%	Absolute change (post): 1.3% Difference in absolute change from baseline: 9.5%	Relative percent change (post): 1.6%	Relative improvement between intervention and control groups statistically significant (P value <0.0001) using normal approximation of binomial distribution One meeting with pharmacist detailer
Dolovich 1999	Changing market share of for a set of antibiotics for acute otitis media	Comparison: academic detailing vs routine pharmaceutical detailing Market share of amoxicillin Before: 31.7% vs 27.6% After: not reported as raw data	Absolute change (post): cannot calculate Difference in absolute change from baseline: 1.35%	Relative percent change (post): cannot calculate	Preintervention to postintervention change in market share no statistically significant (by ANOVA adjusting for sex, years since graduation and location of prescriber) One meeting with pharmaceutical detailer
Ilett 2000	Increasing prescribing of recommended antibiotics for upper and lower respiratory tract infection, acute otitis media and urinary tract infections	Comparison: academic detailing + printed educational materials vs control Number of prescriptions (mean value for the 4 recommended first-line antibiotics) Before: 221.8 vs 411.6 After: 481.2 vs 518.4	Absolute change (post): -37.2 Difference in absolute change from baseline: 152.6	Relative percent change (post): -7.2%	One meeting with therapeutics advisor

Table 5. Financial/health care system changes vs other intervention or no intervention

Study	Targeted Behaviour	Main Process Effect	Absolute Change	Relative Change	Notes
Juncosa 1997	Reducing prescribing of antibiotics	Comparison: Primary care reform vs control Monthly average packages of antibiotics Change (intervention): -56.6% Change (control): -32.5%	Absolute change: cannot calculate Difference in absolute change from baseline: -24.1%	Relative per cent change (post): cannot calculate	

Table 5. Financial/health care system changes vs other intervention or no intervention *(Continued)*

MacCara 2001	Reducing prescribing of fluoroquinolones	Comparison: Before and after change in reimbursement policy for fluoroquinolones Average number monthly fluoroquinolone prescriptions Before: 1798.1 After: 356.6	Absolute change: -1441.5 Difference in absolute change from baseline: cannot calculate	Relative percent change (post): cannot calculate	Another interpretation of data, by time series analysis (not performed by study authors), is that the pre-intervention slope is 3.95 prescriptions per month (SE 3.68; P value 0.29), there is a large decrease in number of prescriptions of -1532.34 (SE 88.10; P value <0.001) followed by a postintervention slope of 10.74 prescriptions per month (SE 10.86; P value 0.33). Although slopes are not statistically significant there may be a trend toward an increasing the number of prescriptions postintervention such that the initial effect of the intervention wanes over time and is less than -1532.34 by the end of the study period.

Table 6. Reminders versus other intervention or no intervention

Study	Targeted Behaviour	Main Process Effect	Absolute Change	Relative Change	Notes
McIsaac 1998	Reducing prescribing of antibiotics for sore throat	Comparison: physician reminder + printed educational material vs printed educational materials Proportion of patients prescribed an antibiotic intervention: 35.7% control: 27.8%	Absolute difference: 7.8%	Relative per cent difference: 28.4%	In a multiple logistic regression model (controlling for patient characteristics), use of reminder associated with reduced antibiotic prescribing with OR 0.44 (95% CI 0.21 to 0.92)
Christakis 2001	Reducing duration of antibiotics for acute otitis media	Comparison: physician reminder vs control Proportion of prescriptions for less than 10 days of antibiotics Before: 50.7% overall (all providers combined) After: 69.7% overall (44.43% increase for intervention and 10.48% increase for control providers)	Absolute change (post): cannot calculate Difference in absolute change from baseline: 33.95%	Relative per cent change (post): cannot calculate	Change in intervention group compared with control group statistically significant by t-test (P value 0.000)
McIsaac 2002	Reducing prescribing of antibiotics for sore throat	Comparison: physician reminder + printed educational material vs printed educational materials Proportion of patients prescribed an antibiotic intervention: 27.9% control: 28.1%	Absolute difference: -0.2%	Relative per cent difference: -0.7%	In a multiple logistic regression model (controlling for physician characteristics), use of reminder not associated with reduced antibiotic prescribing with OR 0.57 (95% CI 0.27 to 1.17)

Table 7. Patient based interventions versus other interventions or no intervention

Study	Targeted Behaviour	Main Process effect	Absolute Change	Relative Change	Notes
Mainous 2000	Reducing prescribing of antibiotics for viral respiratory tract infection	Comparison 1: Patient educational materials vs control Proportion of episodes with antibiotic prescription Before: 31.9 ± 16.8% vs 31.0 ± 17.6% After: 44.5 ± 25.6% vs 53.5 ± 26.8% Comparison 2: Patient educational materials + audit and feedback vs control Proportion of episodes with antibiotics Before: 34.4 ± 13.8% vs 31.0 ± 17.6% After: 49.7 ± 22.3% vs 53.5 ± 26.8%	Comparison 1: Absolute change (post):-9.0% Difference in absolute change from baseline: -9.9% Comparison 2: Absolute change (post): -4.1% Difference in absolute change from baseline: -7.2%	Comparison 1: Relative percent change (post): -16.8% Comparsion 2: Relative percent change (post): -7.6%	Change in prescribing different across all study groups (all groups had increase in prescribing). Gain scores significantly lower in these two groups compared with control (Dunnett's T=2.374, P value <0.05) (not so for audit and feedback alone)
Dowell 2001	Reducing use of antibiotics by patients for viral respiratory tract infection	Comparison: Delayed prescription vs immediate prescription Proportion of patients collecting prescription Delayed: 45.0% Immediate: 100%	Absolute difference: -55.0%	Relative difference: -55%	From unpublished data, 28.3% in delayed arm took antibiotics vs 75.0% in immediate arm (absolute difference: 46.7%, relative difference:62.3%) Proportion of patients filling prescription not available
Little 2001	Reducing use of antibiotics by patients for acute otitis media	Comparison: Delayed prescription vs immediate prescription Proportion of patients taking antibiotics Delayed: 24.0% Immediate: 98.5%	Absolute difference: -74.5%	Relative difference: -75.6%	For effect of intervention on clinical outcomes see Table 10
Arroll 2002	Reducing use of antibiotics by patients for common cold	Comparison: Delayed prescription vs immediate prescription Proportion of patients taking antibiotics Delayed: 43.5% Immediate: 88.5%	Absolute difference: 45.0%	Relative difference: 50.8%	Odds ratio for taking antibiotics for delayed group 0.12 (95% CI 0.05 to 0.29) For effect of intervention on clinical outcomes see Table 10
Macfarlane 2002	Reducing use of antibiotics by patients for acute bronchitis	Comparison: Patient educational materials vs control Proportion of patients taking antibiotics Intervention: 47.1% Control: 62.3%	Absolute difference: -15.2%	Relative difference: 24.3%	Hazard ratio for taking antibiotics up to 14 days post consultation for intervention compared with control 0.66 (95% CI 0.46 to 0.96)

Table 8. Multi-faceted intervention versus other intervention or no intervention

Study	Targeted Behaviour	Main Process Effect	Absolute Change	Relative Change	Notes
Gonzales 1999	Reducing antibiotic prescribing for acute bronchitis	Comparison 1: Patient and physician printed educational materials vs control Proportion of episodes with antibiotics Before: 82% vs 78% After: 77% vs 76% Comparison 2: Patient and physician printed educational materials + physician education (educational meetings + audit and feedback + academic detailing) vs control Proportion of episodes with antibiotics Before: 74% vs 78% After: 48% vs 76%	Comparison 1: Absolute change (post): 1.0% Difference in absolute change from baseline: -3.0% Comparison 2: Absolute change (post): -28.0% Difference in absolute change from baseline: -24.0%	Comparison 1: Relative percent change (post): 1.3% Comparison 2: Relative percent change (post): -36.8%	Between group comparisons demonstrated that the full intervention (comparison 2) group had a statistically significant reduction in monthly prescription rates compared with the control and limited intervention sites (P value 0.02)
Stewart 2000	Reducing antibiotic prescribing	Comparison: Educational meetings +printed educational materials (physicians) and educational meetings + printed educational materials (community) vs control Number of antibiotic claims (data for intervention community only available) Before: 10 071 After: 9125	Not available	Not available	Odds ratio for prescribing recommended first-line antibiotics before and after intervention in community vs remainder of province 1.02 (95% CI 0.99 to 1.06) Odds ratio for prescribing second-line antibiotics before and after intervention in community vs remainder of province 1.40 (95% CI 1.32 to 1.49) Comparison group is remainder of province (raw data not available)
Finkelstein 2001	Reducing antibiotic prescribing to children under 6 years old	Comparison: Printed education materials +opinion leader led educational meetings (physicians) + printed educational materials (parents and families) Antibiotic courses per person-year ages 3 to <36 months Before: 2.20 vs 2.90 After: 1.80 vs 2.57 Antibiotic courses per person-year ages 36 to 72months Before: 1.43 vs 1.74 After: 1.21 vs 1.57	Age 3 to <36 months Absolute change (post): -0.77 Difference in absolute change from baseline: -0.07 Age 36 to 72 months Absolute change (post): -0.36 Difference in absolute change	Age 3 to <36 months Relative percent change (post): -30.0% Age 3 to <36 months Relative percent change (post): -22.9%	Controlling for clustering and patient covariates, relative intervention effect seen for both 3 to <36 months of age (16%, 95% CI 8% to 23%) and 36 to 72 months of age (12%, 95% CI 2% to 21%)

Table 8. Multi-faceted intervention versus other intervention or no intervention *(Continued)*

			from baseline: -0.05		
Belongia 2001	Reducing antibiotic prescribing to children	Comparison: Educational meetings + printed educational materials (physician) and educational meetings + printed educational materials (community/parents) vs control Median number of prescriptions per clinician (liquid preparations) Before: 146 vs 69 After: 112 vs 55 Median number of prescriptions per clinician (solid preparations) Before: 48 vs 30.5 After: 38 vs 35.5	Liquid preparation Absolute change (post): 57 Difference in absolute change from baseline: -20.0 Solid preparation Absolute change (post): 2.5 Difference in absolute change from baseline: -15.0	Liquid preparation Relative percent change (post): 103.6% Solid preparation Relative percent change (post): 0.07%	Between area difference P value 0.042 for liquid preparations and P value 0.019 for solid preparations by Wilcoxon rank sum test. Effect of intervention on rate of carriage of penicillin resistant pneumococci in table 9
Perz 2002	Reducing antibiotic prescribing to children	Comparison: Educational meetings + printed educational materials (physicians) and printed educational materials + mass media (parents and community) vs control Antibiotic prescription rate (per 100 person-years) Before: 175 vs 150 After: 144 vs 139	Absolute change (post): 5 Difference in absolute change from baseline: -20	Relative percent change (post): 3.6%	Percent change in prescriptions for intervention region -19% and for control regions -8% for intervention attributable effect of -11% (95% CI, -14% to -8%), P value <0.001 using negative binomial regression controlled for county and study year. Effect of intervention on infections due to penicillin resistant pneumococci in table 9
Hennessy 2002	Reducing antibiotic prescribing among all community residents	Comparison: Educational meetings + printed educational materials (health care workers) and printed educational materials (community) vs control Number of antibiotic courses per person Year 1 Before: 1.24 vs 0.63 After: 0.85 vs 0.57 Year 2 (compared pre-intervention; intervention expanded to control regions) Before: 1.24 vs 0.63 After: 0.81 vs 0.41	Year 1 Absolute change (post): 0.28 Difference in absolute change from baseline: -0.33 Year 2(compared to end of year 1) Absolute change (post): 0.4 Difference in absolute change from baseline: -0.21	Year 1 Relative percent change (post): 49.1% Year 2 Relative percent change (post): 97.5%	Reduction in antibiotic use sustained over 2 years in initial intervention region. Regions receiving intervention in second year experienced reduction in antibiotic use that year. Effect of intervention on infections due to penicillin resistant pneumococci in table 9
Flottorp 2002	Reducing antibiotic prescribing for sore throat	Comparison: Printed and electronic educational materials + computer-based decision support + interactive educational courses + financial/system change (change i fees for phone consult) (physicians)	Absolute change (post): -5.7% Difference in absolute change from baseline: -3.0%	Relative percent change (post): -11.5%	Using hierarchical logistic regression, pvalue for difference among groups 0.032 (representing significance of time-intervention interaction)

Table 8. Multi-faceted intervention versus other intervention or no intervention *(Continued)*

		and printed educational materials (patients) vs control (same intervention for urinary tract infection) Rate of use of antibiotics for sore throat Before: 48.1% vs 50.8% After: 43.8% vs 49.5%

Table 9. Effect of intervention on bacterial resistance

Study	Organism/antibiotic	Main Process Effect	Absolute Change	Relative Change	Notes
Seppala 1997	Macrolide resistance in clinical group A streptococcus isolates	Comparison: Before and after printed educational materials recommending reduced usage of macrolide antibiotics for group A streptococcal respiratory and skin infections (issued in 1991/92) Percent of isolates resistant to erythromycin Before: 16.5% (1992) After: 8.6% (1996)	-7.9%	-47.9%	Odds ratio for GAS isolate being erythromycin resistant in 1996 0.5 (95% CI 0.4 to 0.5) compared with 1992
Belongia 2001	Penicillin nonsusceptible Streptococcus pneumoniae (PNP) nasopharyngeal isolates in children attending daycare	Comparison: Educational meetings + printed educational materials (physician) and educational meetings + printed educational materials (community/parents) vs control Proportion of children colonized with PNP Before: 12.8% vs 24.7% After: 12.0% vs 18.6%			Residence in intervention region during intervention year not associated with reduced odds of nasopharyngeal carriage of PNP (OR 0.46, 95% CI 0.18 to 1.18)
Hennessy 2002	PNP nasopharyngeal isolates in village residents of all ages	Comparison: Educational meetings + printed educational materials (health care workers) and printed educational materials (community) vs control Proportion of tested villagers colonized with PNP Before: 41% vs 24% Year 1: 29% vs 22% Year 2: 43% vs 26% (intervention expanded to control regions in this year)	Absolute change (post): Year 1: 7% Year 2: 17% Difference in absolute change from baseline: Year 1: -10% Year 2 (compared with baseline year): 0%	Relative per cent change (post): Year 1: 31.8% Year 2: 65.3%	

Table 9. Effect of intervention on bacterial resistance *(Continued)*

Perz 2002	PNP invasive isolates	Comparison: Educational meetings + printed educational materials (physicians) and printed educational materials + mass media (parents and community) vs control Proportion of invasive S. pneumoniae isolates that are PNP (only reported for intervention region Before: 60% Year 1: 74% Year 2: 70%	Year 1: 14% Year 2 (compared to baseline): 10%	

Table 10. Effect of intervention on patient clinical outcome

Study	Patient Outcome	Main Process Effect	Absolute change	Relative change	Notes
Little 2001	Otitis media symptom resolution (with and without immediate antibiotic treatment)	Comparison: Delayed prescription vs immediate prescription Duration of symptoms(mean days) Immediate: 2.56 Delayed: 3.57	Absolute difference: -1.10 days		Absolute difference of -1.10 days, 95% CI -0.54 to -1.48), p<0.01by t-test
Arroll 2002	Common cold symptom resolution (with and without immediate antibiotic treatment)	Comparison: Delayed prescription vs immediate prescription Symptom score at days 3, 7, 10 Day 3 Immediate: 2.9 Delayed: 3.6 Day 7 Immediate: 1.8 Delayed: 2.0 Day 10 Immediate: 1.4 Delayed: 1.5			General linear model for repeated measures shows no significance for the symptom score (p=0.29)

WHAT'S NEW

Date	Event	Description
12 November 2008	Amended	Minor changes

HISTORY

Protocol first published: Issue 1, 2002
Review first published: Issue 4, 2005

Date	Event	Description
30 July 2008	Amended	Converted to new review format.
1 August 2005	New citation required and conclusions have changed	Substantive amendment

CONTRIBUTIONS OF AUTHORS

Sandra Arnold wrote the protocol, performed the searching, read the abstracts and retrieved and appraised relevant evidence. Sharon Straus retrieved and appraised relevant evidence. Sandra Arnold and Sharon Straus selected trials for inclusion in the review and extracted the data using the Cochrane Effective Practice and Organisation of Care Group (EPOC) checklist. Sandra Arnold wrote the review and Sharon Straus reviewed and edited it.

DECLARATIONS OF INTEREST

None known

SOURCES OF SUPPORT

Internal sources

- University of Tennessee, USA.
- University of Toronto, Canada.

External sources

- No sources of support supplied

INDEX TERMS

Medical Subject Headings (MeSH)

*Drug Resistance, Bacterial; Ambulatory Care; Anti-Bacterial Agents [*therapeutic use]; Education, Medical, Continuing [methods]; Practice Patterns, Physicians' [*standards]; Randomized Controlled Trials as Topic; Virus Diseases [*drug therapy]

MeSH check words

Humans