Analysis of Published Trials Examining Methods to Change Provider Prescribing Behavior and Child Health Outcomes

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CONTENTS

ABSTRACT

Background: We conducted a systematic review of the literature on the effectiveness of different methods in changing physician prescribing practices and improving child health outcomes.

Methods: We searched four databases that index peer-reviewed literature to find randomized controlled trials (RCTs) published in English that examined the effectiveness of interventions to improve provider prescription of medications. All studies needed to include an objective measure of the impact of the intervention on provider prescribing behavior and ideally, effects one or more patient-level health outcomes. Children were defined as patients aged 0-17 years.

Results: We screened 699 abstracts and identified 98 (14%) for further review Of the 98 potential articles reviewed, 22 articles representing 21 different clinical trials were included for analysis. The 21 trials evaluated 26 different combinations of interventions. The most common types of components included in the interventions were educational materials (n=16), conferences, seminars or lectures (n=14), educational outreach visits (n=12), patient-mediated interventions (n=11), audit and feedback (n=5), reminders (n=3), use of opinion leaders (n=1), policy changes (n=1) and use of a clinical pathway (n=1). There were four main areas of disease focus for these prescribing interventions: asthma (n=9); use of antibiotics (n=9); diarrhea (n=3) and malaria (n=2). We classified interventions as 'individual' 'supplemental' or 'structural'. Those interventions that included multiple interventions and focused on changing systems of care within a practice were more likely to have a positive effect.

Conclusions: Findings from RCTs indicate that a variety of interventions are successful in changing physician prescribing behavior. These interventions have been successfully documented in the context of the treatment of pediatric asthma, antibiotic prescription, treatment

of malaria and treatment of diarrheal disease. Interventions focused on *structural* changes in the design of current practice (e.g., implementation of new asthma clinical pathway, an asthma peer leader with organization change, or restrictions on antibiotic use in a neonatal unit, etc.) were more successful than interventions focused on individual provider change (e.g., an educational conference for providers, or distribution of clinical practice guidelines to physicians). In addition, *multi-faceted* interventions tend to be more successful than single interventions. The majority of interventions that have been developed are persuasive and there are few restrictive interventions that have been evaluated in a rigorous fashion. Although studies examined how the intervention affects provider prescribing behavior, not all studies rigorously evaluate the effect on patient health outcomes. Only one study examined potential unintended consequences of the intervention.

INTRODUCTION

Changing provider prescribing behavior to be consistent with evolving best practices is a challenging task. Pharmaceutical options for providers are constantly changing as there are new data about the effectiveness, side effects, dosing options, indications or contraindications for different medications every day (Schmid, 2005). This dynamic process contributes to the many potential gaps between evidence-based prescribing practice and everyday practice. In addition to under- or over-utilizing of prescription medications, providers may be prescribing medications for inappropriate situations.

In addition, there may be specific issues unique to childhood diseases that may make prescribing medications more challenging. The evidence base for pediatric prescribing may be weaker than the evidence base for adult prescribing because there are limited pharmacodynamic and pharmacokinetic data for medications used in children. In many cases, pediatric doses may be extrapolated from studies performed on adult patients (Dunne, 2007; Rakhamina, 2006). Even with sufficient short-term data, pediatric patients are still developing physically and cognitively and there may be concerns about long-term effects of different medications on childhood development (Hausner, 2008; Rakhamina, 2006). This may lead to provider resistance to adopting new treatment recommendations. In addition, development of a therapeutic plan is more complex due to consideration of parent/caregiver, as well as patient needs, goals and concerns. These priorities may not always be consistent with recommended best prescribing practices and lead to poor provider adherence to clinical practice guidelines (Cabana, 1999).

As a result, a variety of interventions have been attempted to improve provider prescribing practice, such as mailed educational materials, educational programs, feedback and audit, academic detailing, and use of computerized decision support (Soumerai, 1989; Anderson, 1996). Although there are several reviews that focus on methods to change provider practice patterns, as well as reviews on specific techniques (Davis, 1997; Grol, 2003; Grimshaw; 2004; Ranji, 2008; Steinman, 2006; Arnold, 2005); there are none that specifically focus on provider prescribing for pediatric conditions. This report presents a systematic review of rigorous studies that evaluated methods to change provider prescribing behavior for pediatric conditions.

METHODS

Data Sources and Study Selection

We searched four major databases on medical literature: EMBASE, MEDLINE, the Cochrane Central Register of Controlled Trials, and the Cumulative Index to Nursing and Allied Health Literature. A summary of the inclusion criteria is listed in **Table 1** (page 33).

Although we did not limit our search to studies performed in specific countries, we only included articles published in English.

We only included randomized controlled trials (RCTs), as well as other variations including cluster RCTs and cross-over RCTs. In a traditional RCT individual patients are randomized to control and intervention groups, however, many of the studies we used for this analysis included interventions at the provider or clinic level. For these types of studies it may be more appropriate to conduct a cluster randomized controlled trial. Patients may be 'clustered' by specific characteristics to a particular provider, which violates the assumptions of independence for statistical analysis. In addition, contamination may occur at a patient-level, as providers may apply the effects of an intervention to all patients in their panels. RCTs may still be appropriate if the analysis also includes methods to statistically correct for issues of clustering.

We focused on studies that included interventions to change provider prescribing practices. We included all medications that are used to treat diseases and conditions that affect children age < 18 years.

All studies needed to include an objectively measured the impact of the intervention on provider prescribing behavior and ideally, we effects on one or more patient-level health outcomes. We excluded studies that only evaluated the effect of an intervention on changes in provider knowledge or attitudes about prescription of medications.

We defined providers as healthcare professionals responsible for providing patient care to children age < 18 years who have the ability to prescribe medications, such as physicians, nurse practitioners, and pharmacists. Studies that included only health professions students, interns, residents or providers-in-training were excluded.

Since we were focused on provider behavior, we only included medications that were available only by prescription in the country in which the study was conducted (i.e., not available over-the-counter). We included both generic and brand-name drugs.

Interventions to change provider behavior could occur at many different organizational levels. We included studies of any individual, group, or system wide intervention that was intended to affect provider prescribing behavior (as opposed to diagnostic, testing ordering, communication, or documentation behavior). Examples may include education of individual providers, education of groups of providers, clinical practice guidelines, reminder systems, and financial incentives.

Search Process

The literature search was performed by the lead authors (JMC and MDC) in consultation with a medical librarian. The librarian searched the four databases using the MeSH terms and keywords listed in **Table 2** (page 34). The articles were limited by age group to "child" and publication type by "randomized controlled trial."

The titles and abstracts were then reviewed independently by three members of the research team, using explicit criteria to identify articles likely to meet the inclusion criteria. The first and second authors then independently reviewed the full text of these articles to confirm that they met the criteria. Inconsistencies were resolved through informal consensus.

For each article included in the review, information was extracted regarding the research design, sample size, demographic characteristics of the study population, location, type of intervention, setting, type(s) of health professional(s) providing the intervention, the duration of the intervention, and the population that received the intervention (e.g., children, children and parents). We also extracted information regarding the type of outcome(s) measured, the magnitude of the difference in the outcome(s) between the control group and intervention group, the intended direction of the change from the intervention, as well as the actual direction of the change reported.

Analysis

Classification of Interventions

Based on the description of the intervention in the text, we classified the types of interventions using a taxonomy that was modified from classifications used by the Effective Practice and Organization of Care Group (Davey, 2005). A glossary of definitions of the different interventions is listed in **Table 3** (page 36). In addition, we classified the intervention based on two parameters: (a) the 'focus' of the intervention and (b) if the intervention was persuasive or restrictive in nature (or combined).

We classified the intervention as ‘individual’, ‘supplemental’ or “structural’ based on the three different potential foci of the intervention. If the intervention was focused on an individual provider, the intervention was considered ‘*individual*’. If the intervention focused on the addition of supplemental data, skills or services to the practice (vs. the individual provider), but did not attempt to change the original organization of the practice, the intervention was considered ‘*supplemental*.’ If the intervention focused beyond individual providers and incorporated the collection of additional data, skills or services to the practice within the organization of the practice, the intervention was considered ‘*structural*.’

We also classified interventions as restrictive or persuasive. *Restrictive* interventions focused on external methods to decrease or limit provider prescribing behavior to be consistent with best practices (e.g., prohibiting the prescribing of certain medications or requiring prior authorization). *Persuasive* interventions focused on methods to encourage changes in prescribing behavior (e.g., education, audit and feedback). Methods could be both persuasive and restrictive. **Figure 1** (page 30) summarizes the different parameters for classifying interventions, in relation to possible examples.

Combining Data

We encountered a variety of interventions, used in different settings for different types of providers. Due to the heterogeneity of studies, we did not attempt to combine data. We only include simple counts and descriptive statistics of the studies included.

RESULTS

We screened 699 abstracts and identified 98 (14%) for further review Of the 98 articles reviewed, 22 (22%) articles met the inclusion criteria. The 22 studies represented 21 different clinical trials. For one RCT, the results of the patients directly interviewed were published in one article (Lozano, 2004), while the results of all of the patients in the managed care organization using administrative data were published in a separate article (Finkelstein, 2005).

We excluded articles for the following reasons: not original research (e.g., an editorial), no comparison group, enrolled adults, intervention not directed toward providers, intervention did not focus on a prescribing behavior, and did not assess an intervention's effects on prescribing behavior.

Study Findings

Study Design

Information about the research designs of studies included in the review is presented in **Table 4** (page 37)**.** Of the 22 studies included, 14 were cluster RCTs, 7 were RCTs, and 1 was an RCT with a crossover design.

Sampling Frame for the Interventions

The sites were selected from a variety of sampling frames. (See **Table 4**) Larger sampling frames included Medicaid administrative regions in one state (n=1), a group of 16 communities (n=1), a general practice network (n=1), practices located within a city school district (n=1), or practices within a health maintenance organization (n=3).

Within these sampling frames, studies recruited interested practices, clinics or health centers (n=11) or pharmacies (n=2). One study occurred within two neonatal intensive care units within the same hospital. Another study took place within two different inpatient units within the same children's hospital.

Participants

8 of the 22 studies did not include the total number of prescribing health professionals involved. Of the remaining 14 studies that reported provider data, 1482 prescribing health professionals were included for a median of 73 providers (mean=106 providers) per study. (See **Table 4**.) The providers included pediatricians (n=8), nurse practitioners (n=6), primary care providers, not specified (n=4), general practitioners (n=4); nurses (n=3); physician assistants (n=2), pharmacy salespersons (n=2); as well as neonatologists, medical officers, lab assistants, nurse assistants, mother and child health aides, and 'paramedical prescribers' (n=1 study each). The total number of types of providers is greater than 22, as many studies included more than one provider type for their intervention.

6 of the 22 studies did not include the total number of children cared for by providers enrolled in the study. Of the remaining 16 studies that reported the number of children involved, data was collected for 274, 868 children. (See **Table 4**.) There was a non-normal distribution of children, as two of the studies used data from administrative billing sources from large managed care organizations. The median number of children in these 16 studies was 1922 children (mean=17,179 children).

Geographical Location of the Studies

The 22 studies were from a wide variety of settings and locations. They represented 5 continents and 8 different countries. Studies were conducted in the United States (n=13), Indonesia (n=2), the Netherlands (n=2), Tanzania (n=2), and one study each in Denmark, New Zealand, Scotland and Thailand. (See **Table 5**, page 39).

Types of Intervention

Table 6 (page 43) lists the 13 different types of interventions evaluated in the 21 trials. (Definitions of the different types of interventions are provided in **Table 3**.—page 36). As many of the studies included trials with multiple arms, the total number of different combinations interventions was 26. The most common types of components included in the interventions were educational materials (n=16), conferences, seminars or lectures (n=14), educational outreach visits (n=12), patient-mediated interventions (n=11), audit and feedback (n=5), reminders (n=3), use of opinion leaders (n=1), policy changes (n=1) and use of a clinical pathway (n=1).

Disease Focus of Prescribing Intervention

All the interventions focused on improving prescribing behavior. There were four main areas of disease focus for these prescribing interventions: asthma (n=9); use of antibiotics (n=9); diarrhea (n=3) and malaria (n=2). The totals are greater than 22, as one study focused on use of antibiotics, as well as treatment of diarrhea (Pagaiya, 2005). (See **Table 5**.)

Childhood Asthma

There were nine randomized controlled trials that focused on provider medication prescribing for asthma. Findings from these trials are presented in **Table 7a** (page 45). No restrictive interventions were evaluated. The studies focused on individual provider interventions (n=2); supplemental interventions (n=5) and structural interventions (n=2). We found that those interventions that attempted to change practice organization or systems of care were more successful that those interventions that focused on individual provider prescribing behavior. This is graphically shown in **Figure 2** (page 31).

Individual interventions included a two-hour educational session for general practitioners and provision of algorithms for treatment of acute and chronic asthma (Mitchell, 2005) as well as an 30 minute academic detailing session and feedback about asthma medication prescription (Witt, 2004). Both interventions were not effective.

The only exception was a potential decrease in the use of oral asthma reliever medications for one study (Mitchell, 2005). However, the rate of oral asthma reliever medications decreased for 6.2 to 3.2 inhalers per 1000 patient months. The rate in the control group decreased from 2.8 to 2.0 inhalers per 1000 patient months. Although statistically significant, it is possible that this change in the intervention group is due to regression to the mean (Hayes, 1988; Altman 1991).

When supplemental interventions were evaluated, there was limited, if any success in prescribing changes. Studies that provided supplemental data to providers, such as frequency of asthma symptoms (Halterman, 2005); airway hyperresponsiveness from patient spirometry tests (Hagmolen of ten Have, 2008), or treatment suggestions based on chart review (Bryce, 1995) showed limited effect. Bryce et al. showed some change in oral bronchodilator and cromogylcate prescription, but no significant changes for other twelve other asthma medications such as inhaled bronchodilators and inhaled steroids (Bryce, 1995). Hagmolen of ten Have et al. demonstrated an increase in the prescription of daily inhaled corticoteroids ($p=0.03$), but no changes in beta-agonist use. Halterman, et al. reported no changes in prescription of preventive medications or medication dose.

Supplemental interventions that incorporated more intensive and interactive interventions to change provider skills were somewhat more effective. The intervention by Clark et al. used small group seminars to teach and model specific communication and prescribing skills. The 5 hour intervention encouraged the increased prescription of daily asthma anti-inflammatory medication prescription (Clark, 1998). In addition, the intervention was supplemented with 5 hours of training to improve physician asthma education to parents and communication techniques to improve medication adherence. Similar intensive asthma training was provided in one arm of an intervention reported by Lozano et al. In the intervention, an asthma team leader at each practice was provided with patient education materials and specific feedback on anti-inflammatory prescribing (Lozano, 2004). There was a significant decrease in prescription of oral steroids for exacerbations and decreases in the frequency of asthma symptom days (Lozano, 2004); however, when extrapolated to the broader population of children treated by the physicians (not just the study participants), there was no change in prescription filled for daily inhaled corticosteroids or asthma controller medications (Finkelstein, 2005).

In terms of systematic interventions, both studies reported success in changing prescribing behaviors. The most intense arm of the study by Lozano, et al, included a planned care intervention and organization changes that was facilitated by a trained asthma nurse over a series of 4 to 5 visits to the practice. The intervention encouraged the use of standardized assessments, support in care planning, self-management support to families, and proactive standardized telephone follow-up.

There were decreases in the prescription of oral steroids, decreases in symptomatic days, and periods of asthma exacerbations (Lozano, 2004). Johnson et al. reported the results of a systematic intervention involving redesign of care using an inpatient asthma pathway (Johnson, 2000). Inpatient nurses received additional training for asthma symptom assessment, and the pathway included a protocol for weaning of beta-agonists, based on physician, as well as nurse assessment. As a result, the prescription of beta-agonists for weaning was more efficient and duration of hospitalization was shorter for intervention patients (40.3 hours vs. 53.7 hours, $p<0.01$).

Prescription of Antibiotics for Children

There were nine randomized controlled trials that focused on provider prescribing of antibiotics for children. Findings from these studies are summarized in **Table 7b** (page 48). We found that those interventions that attempted to change practice organization or systems of care were more successful that those interventions that focused on individual provider prescribing behavior. This is graphically shown in **Figure 3** (page 32).

For all the interventions, it is assumed that providers are ‘over-prescribing’ antibiotics or using antibiotics the offer too broad a spectrum of coverage. Five of the studies focused on general antibiotic use (Finkelstein, 2008; Davis, 2007; Doyne, 2004; Finkelstein, 2001; Mainous, 2000). In the remaining studies, the specific focus was antibiotics for otitis media (Bauchner, 2006; Christakis, 2001), antibiotics for upper respiratory infection (Pagaiya, 2005); and use of narrow spectrum empiric therapy for suspected neonatal sepsis (deMan, 2000).

There was only one restrictive intervention evaluated (deMan, 2000). The studies included individual provider interventions (n=2); supplemental interventions (n=6) and systematic interventions (n=1).

Interventions at the individual provider level included the use of an academic detailing program to a designated practice leader (Doyne, 2004). Bauchner et al. used a combined approach of reverse academic detailing, interactive educational sessions (duration not known), chart reminders, and a newsletter to providers (5 times per year). Although the feedback is mentioned as part of the intervention, there are no specific details about the content, timing or delivery of the feedback to providers (Bauchner, 2006). Both studies reported no effect on provider selection or prescription of antibiotics.

Supplemental interventions were more successful and all incorporated specific feedback or educational outreach. Finkelstein et al (2001) evaluated an intervention that incorporated physician education through a peer leader, feedback on prescribing behavior (4 months after the seminar) as well as supporting patient educational materials. In addition, educational materials were also mailed to the families. The intervention was successful in decreasing the antibiotic prescribing rate to children between 3 and 72 months of age. In another study, Finkelstein et al combined a successful physician education program with a broader community-wide program. Similar to the previous study, there is a decrease in antibiotic prescribing for children between 24 and 72 months oaf age, as well as a decrease in the use of second-line penicillins and broad spectrum antibiotics (Finkelstein, 2008).

Mainous et al. describe the use of provider feedback and patient education as successful in decreasing the rate of increase of inappropriate antibiotic prescribing (Mainous, 2000). Finally, use of a three day training course with educational outreach visits was successful in decreasing antibiotic treatment of upper respiratory infections in Thailand (Pagaiya, 2005).

More intensive supplemental interventions included incorporation of a decision support system (DSS) within an existing electronic medical record (EMR) system (Davis, 2007; Christakis, 2001). During the process of completing a prescription through the EMR, additional information about dosing and antibiotic choice appears for specific medical conditions. The supplemental information includes a short summary of evidence for or against medication choice, dosing, or duration. In a university-practice setting, Christakis et al. (2001) reported a decrease in the percentage of prescriptions that were unnecessarily 10 days or longer. Using a similar system in a private practice setting, Davis et al. (2007) reported an increase in the percentage of prescriptions that were consistent with current evidence.

The one structural intervention evaluated the effectiveness of restricting physician access to a specific class of antibiotics. In a crossover RCT design, deMan demonstrated significant decreases in the rates of colonization of resistant bacteria in a neonatal intensive care unit. The intervention prohibited providers from using broad-spectrum antibiotics for neonates with suspected sepsis and instead were only allowed to use narrow-spectrum antibiotics (deMan, 2000).

Malaria

There were two randomized controlled trials that focused on improving prescribing for malaria. (See **Table 7c**, page 50) In one study, a one hour training session was effective in improving provider knowledge of sulfladoxine-pyrimethamine dosing. There was also better dispensing of sulfladoxine-pyrimethamine to mock patients (Nsimba, 2007).

A more intensive, structural intervention included training for medical staff in mircroscopy techniques. Microscopy was thought to increase the likelihood of rational and appropriate prescription of antimalarial medications. For the group randomized to providers with microscropy training, there was a significant decrease in unnecessary antimalarial prescription; however, there was no change in antibiotic or antipyretic prescription. The authors noted that there was 'major variation in accuracy of the microscopy readings" (Ngasala, 2008), which suggests that there may be unintended consequences of microscopy smears that are 'false negatives' and lead to inappropriate undertreatment. Further studies need to consider these potential tradeoffs for this type of intervention.

Oral Rehydration Therapy

There were three randomized controlled trials that focused on provider use of oral rehydration therapy. (See **Table 7d,** page 50) All the interventions used some form of provider education (Pagaiya, 2005; Ross-Degnan, 1996; Santoso, 1996). The use of a three day training course with educational outreach visits was successful in increasing the percentage of cases treated with oral rehydration solution (Pagaiya, 2005). Combining academic detailing for pharmacists with educational materials and posters for parents to increase sales of oral rehydration therapy and decrease the use of anti-diarrheals (Ross-Degnan, 1996). Academic detailing in the form of face-to-face small group sessions or large group lectures was also successful in decreasing the use of anti-diarrheals, but not successful in increasing the use of oral rehydration therapy (Santoso, 1996).

Assessment of Unintended Consequences

All the interventions focused on either increasing or decreasing provider prescription of a medication. As a result, it is possible that potential over- or under-prescription of a medication could have occurred. None of the interventions compared the results to a clinical gold-standard to assess for potential over-prescribing or under-prescribing.

DISCUSSION

The results of this review suggest that RCTS have found that several different types of interventions are successful in changing physician prescribing behavior. These interventions have been successfully documented in the context of the treatment of pediatric asthma, antibiotic prescription, treatment of malaria and treatment of diarrheal disease. Some interventions have been designed to *increase* prescription of certain medications or therapies (e.g., daily inhaled corticosteroids for childhood asthma, oral rehydration therapy for diarrhea), while some interventions have been designed to *decrease* prescription of certain medications (e.g., antibiotic treatment of upper respiratory infections).

Themes

Four themes emerged from this analysis. (1) Interventions focused on structural changes in the design of current practice were more successful than interventions focused on individual provider change. In addition, multi-faceted interventions tend to be more successful than single interventions. (2) The majority of interventions that have been developed are persuasive and there are few restrictive interventions that have been evaluated in a rigorous fashion. (3)

Although studies examined how the intervention affects provider prescribing behavior, not all studies rigorously evaluate the effect on patient health outcomes. Finally, (4) related to the previous point, only one study examined potential unintended consequences of the intervention.

1. Structural Interventions

Similar to previous reviews on changing physician behavior, in general, we found that structural (Grol, 2003) and multifaceted interventions (Grimshaw, 2001) were more likely to be successful than single interventions focused on individual provider change. This pattern was particularly apparent in the analysis of interventions focused on childhood asthma (n=9 studies) and antibiotic use (n=9 studies) where studies of a variety of interventions have been published. Those interventions that incorporated structural change in practices and included multiple types of interventions were more likely to be successful in changing provider prescribing patterns.

For any given disease or condition, a provider must overcome a series of barriers to prescribe in a manner consistent with evidence-based practice (Cabana, 1999). There barriers include a lack of awareness or lack of familiarity with best prescribing practices, or physician attitudes such as lack of agreement with prescribing recommendations, lack of self-efficacy to perform the prescribing behavior, lack of outcome expectancy that prescription of the medication will make a difference, and the inability to overcome the inertia of current practice. In addition, "external barriers" can affect a physician's ability to adhere to best prescribing practices. These barriers occur at different levels: an inter-personal (e.g., peer pressure not to adopt new practices), organizational (e.g., incentives not to prescribe), community (e.g., patient pressure to prescribe or not prescribe recommended medications), or at a policy level (e.g., reimbursement incentives not aligned with best prescribing practices). The potential for multiple barriers at multiple levels (physician, practice, community), may explain the need for multi-faceted interventions at a physician and practice level.

Multifaceted interventions may help address multiple barriers to appropriate prescription. For example, there are different types of barriers to physician prescription on daily controller medications for pediatric asthma. Despite guidelines recommending daily-inhaled corticosteroids for pediatric asthma, they remain underutilized in everyday practice. Physicians may not be aware of prescribing recommendations, may not feel comfortable with assessing side effects or may not feel they will improve outcomes due to poor patient compliance, etc. (Cabana, 2001)

In our analysis, interventions to improve prescription of asthma medication that only included information transfer (Mitchell, 2005; Witt, 2004), were less successful than those interventions that included information transfer, plus interventions to address other potential barriers. For example, Clark et al (1998) included skills training in physician communication to help improve adherence (to address physician self-efficacy), as well as data about the effectiveness of physician communication in improving patient outcomes (to address lack of outcome expectancy). In addition, it has been noted that 'passive' dissemination of information is less likely to be effective than interactive programs (Bero, 1998).

In addition, since physicians have different training, experiences and skills, different barriers may exist that affect different steps of prescribing behavior change for different individual physicians. As a result, multifaceted interventions may have a greater likelihood of overcoming multiple barriers.

Finally, structural interventions that do not rely on a single provider to change prescribing behavior may be more likely to be more successful that interventions that develop systems to improve prescription behavior. For example, Johnson et al. (2000) developed an inpatient clinical pathway that incorporated and trained other health care providers in initiating changes in the frequency of asthma medication timing. Restructuring and training primary health care facilities in rural Tanzania to utilize microscopy data to inform prescribing for malaria led to more judicious medication use (Ngasala, 2008). Although promising, there were a lack of interventions that focused on structural, practice change or redesign.

2. Restrictive Interventions

We noted a dearth of RCTs that evaluated restrictive interventions. There was only one example in our analysis. In this case, banning the use of broad-spectrum antibiotics in a neonatal intensive care unit was effective halting broad-spectrum antibiotic prescription and led to decreased colonization with resistant organisms (deMan, 2000).

Examples of other potential restrictive interventions include pre-approval requirements for the use of certain medications, compulsory order forms, rotation of drugs, therapeutic substitution, or automatic antibiotic stop-order policies. Restrictive interventions may potentially work well to promote the judicious use of certain medications. These types of interventions would also require some ‘leverage’ over the prescriber, either through the ability to control provider reimbursement, reputation, sanction or employment, through a third-party payer or employer.

These types of restrictive interventions may be of interest, as they have been reported as having a quicker impact on prescribing in the short-term compared to persuasive interventions (Davey, 2005).

3. Linking Prescribing Behavior to Patient Outcomes

Evaluation of these interventions to change provider prescribing, with the health care provider as the subject creates a set of challenges unique from traditional RCTs with patients as trial subjects (Cabana, 2003). For example, the downstream impact of such interventions are difficult to measure. Although the focus of an intervention may be to change *provider* prescribing behavior, the outcomes of eventual interest are changes in the *patient* or patient outcomes. Large sample sizes are usually required for data analysis to detect significant changes for patients, especially those related to health care utilization.

The majority of studies evaluated the effect of the intervention on provider prescribing behavior and also examined further effects on health care outcomes and quality of life. Although some studies showed a difference in prescribing behavior that was statistically significant, it is not clear that such changes will have a significant clinical impact. For example, Davis et al. reported that a decision support system incorporated into an electronic health record increased appropriate prescription of antibiotics by 3% compared to controls. This small absolute risk reduction requires a fairly large ‘number needed to treat,’ and for those affected by the prescribing change, there may be an even smaller effect on other downstream effects, such as quality of life or risk of antibiotic resistance. This information may be helpful for those considering incorporating these interventions. Given the small effect of such an intervention on health outcomes and the potentially high cost of certain interventions, the ability to compare the cost-effectiveness of different interventions is helpful.

Another difficulty with this analysis is that interventions may increase health care utilization and affect outcomes normally used to monitor disease severity. For example, with a provider or patient educational component, it is possible that the direction of ED visits or outpatient visits can be increased. Providers and patients become more aware of the signs and symptoms of asthma exacerbations. Although appropriate medication is prescribed, due to earlier recognition of symptoms and increased knowledge about the importance of prompt care, there may be greater numbers of referrals or ED visits for asthma (Bryce, 1995).

4. Evaluating Unintended Consequences

Although some studies explicitly stated goals of increasing or decreasing prescription of certain medications, it is rare that a medication should be prescribed to 100% or 0% of all patients with a specific condition. Assuming that there will always be some individual exceptions or unusual cases for any prescribing guideline, assuming a single direction in change for all patients may lead to unintended consequences.

For example, the prescription of a daily medication for asthma should only occur for those children with persistent asthma symptoms (NHLBI/NIH). Although these medications may be underused, in general (Warman, 1999), greater frequency of prescription may not always be appropriate. It is possible that an intervention may lead to over-treatment or over-prescription of a medication. None of the studies in our analysis examined the potential of 'over-prescription' of daily medications for asthma (e.g., some patients that did not qualify for daily medications were inappropriately prescribed such medications).

The potential for unintended consequences was indirectly assessed in one trial of an intervention to decrease over-prescription of medications for malaria. It is possible that undertreatment for malaria may have occurred. There were no statistically significant differences in rates of re-admission and death reported (Ngasala et al., 2008).

Potential Limitations

There are some limitations to this analysis. Our analysis was limited to RCTs. There can be practical, economic and ethical reasons for not conducting RCTs that evaluate broad practice-based interventions (Grimshaw, 2005; Cabana, 2003). We may have excluded important non-RCT studies that evaluated other types of interventions to change provider prescribing patterns. We also limited our search to English language articles. Another potential caveat is that pediatricians play different roles in different countries. In the United States, pediatricians, like general practitioners, are utilized in a primary care role. In other settings, pediatricians serve as consultant physicians. Finally, the majority of studies were conducted in industrialized countries and focused on antibiotic and asthma medication prescription. The applicability of these findings beyond these settings for these indications may be limited.

Summary

The results of this review suggest that there are several different types of interventions that have been evaluated in a randomized controlled trial design, that are successful in changing physician prescribing behavior. These interventions have been successfully documented in the context of the treatment of pediatric asthma, antibiotic prescription, treatment of malaria and treatment of diarrheal disease. Overall, we found that those interventions that were multifaceted and included systemic changes in practice were more likely to be successful in changing provider prescribing behavior.

REFERENCES

Altman DG. *Practical statistics for medical research*. Chapman & Hall. New York, NY. 1991; 285.

Anderson GM, Lexchin J. Strategic for improving prescribing practice. *CMAJ*. 1996; 154: 1013-1017.

Bauchner H, Marchant CD, et al. Effectiveness of Centers for Disease Control and Prevention recommendations for outcomes of acute otitis media. *Pediatrics.* 2006; 117(4): 1009-1017.

Bero L, Grilli R, Grimshaw JM, et al. Closing the gap between research and practice: An overview of systematic reviews of interventions to promote the implementation of research findings. *BMJ*. 1998; 317:465-8.

Bryce FP, Neville RG, et al. Controlled trial of an audit facilitator in diagnosis and treatment of childhood asthma in general practice. *British Medical Journal.* 1995; 310(6983): 838-842.

Cabana MD, Clark NM. Challenges in evaluating methods to improve physician practice. *J Pediatrics*. 2003;143:413-414.

Cabana MD, Rand CS, Becher OJ, Rubin HR. Reasons for pediatrician nonadherence to asthma practice guidelines. *Archives of Pediatrics and Adolescent Medicine.* 2001;155:1057-1062.

Cabana MD, Rand CS, Powe NR, Wu AW, Wilson MH, Abboud PA, Rubin HR. Why don't physicians follow clinical practice guidelines? A framework for improvement. *JAMA.* 1999; 282: 1458-65.

Christakis DA, Zimmerman FJ, et al. A randomized controlled trial of point-of-care evidence to improve the antibiotic prescribing practices for otitis media in children. *Pediatrics.* 2001; 107(2): E15.

Clark NM, Gong M, et al. Impact of education for physicians on patient outcomes. *Pediatrics.* 1998; 101(5): 831-836.

Davey P, et al. Interventions to improve antibiotic prescribing practices for hospital inpatients. Cochrane Database of Systematic Reviews. 2005, Issue 4. No CD003543.

Davis DA, Taylor-Vaisey A. Translating guidelines into practice: a systematic review of theoretic concepts, practical experience and research evidence in the adoption of clinical practice guidelines. *CMAJ.* 1997; 157:408-16.

Davis RL, Wright J, et al. A cluster randomized clinical trial to improve prescribing patterns in ambulatory pediatrics. *PLoS Clin Trials*. 2007; 2(5): E25.

de Man P, Verhoeven BAN, Verbrugh HA, Vos MC, van den Anker JN. An antibiotic policy to prevent emergence of resistant bacilli. *Lancet 2000*; 355:973-8.

Doyne EO, Alfaro MP, et al. A randomized controlled trial to change antibiotic prescribing patterns in a community. *Arch Pediatr Adolesc Med.* 2004; 158(6): 577-83.

Dunne J. The European regulation on medicines for pediatric use. *Ped Respir Rev*. 2007; 8: 177-183.

Finkelstein JA, Huang SS, et al. Impact of a 16-community trial to promote judicious antibiotic use in Massachusetts. *Pediatrics* 2008; 121(1): E15-23.

Finkelstein JA, Lozano P, et al. Practice-level effects of interventions to improved asthmas care in primary care settings: The Pediatrics Asthma Care Patient Outcomes Research Team. *Health Services Research.* 2005; 40(6 I): 1737-1757.

Finkelstein JA, Davis RL, et al. Reducing antibiotic use in children: a randomized trial in 12 practices. *Pediatrics.* 2001; 108(1): 1-7.

Grimshaw J, Eccles M, Campbell M, Elbourne D. Cluster randomized trails of professional and organizational behavior change interventions in health care settings. *Ann Am Acad Pol Soci* Sci. 2005; 599: 71-93.

Grimshaw JM, Thomas RE, MacLennan G, et al. Effectiveness and efficiency of guideline dissemination and implementation strategies. *Health Technology Assessment.* 2004; 8(6): 1-72.

Grimshaw JM, Shirran L, Thomas R, et al. Changing provider behavior: an overview of systematic reviews of interventions. *Med Care*. 2001; 39: II2-II5.

Grol R, Grimshaw J. From best evidence to best practice: effective implementation of change in patients' care. *Lancet*. 2003; 362: 1225-1230.

Hagmolen of ten Have W., van den Berg NJ, et al. Implementation of an asthma guideline for the management of childhood asthma in general practice: A randomised controlled trial. *Prim Care Respir J*. 2008; 17(2): 90-6.

Halterman JS, McConnochie KM, et al. A randomized trial of primary care provider prompting to enhance preventive asthma therapy. *Archives of Pediatrics and Adolescent Medicine. 2005;* 159(5): 422-427.

Hausner E, Fiszman ML, Hanig J et al. Long-term consequences of drugs on the pediatric cardiovascular system. *Drug Safety*. 2008; 31: 1083-96.

Hayes RJ. Methods for assessing whether change depends on initial value. *Stat Med*. 1988; 7: 915-927.

Johnson KB, Blaisdell CJ, et al. Effectiveness of a clinical pathway for inpatient asthma management. *Pediatrics.* 2000; 105(5 I): 1006-1012.

Lozano P, Finkelstein JA, et al. A multisite randomized trial of the effects of physician education and organizational change in chronic-asthma care: health outcomes of the Pediatric Asthma Care Patient Outcomes Research Team II Study. *Arch Pediatr Adolesc Med.* 2004; 158(9): 875-83.

Mainous AG 3rd, Hueston WJ, et al. An evaluation of statewide strategies to reduce antibiotic overuse. *Fam Med.* 2000; 32(1): 22-9.

Mitchell EA, Didsbury PB, et al. A randomized controlled trial of an asthma clinical pathway for children in general practice. *Acta Paediatrica, International Journal of Paediatrics.* 2005; 94(2): 226-233.

National Heart, Blood, Lung Institute. Guidelines for the Management of Asthma. 2007.

Ngasala B, Mubi M, et al. Impact of training in clinical and microscopy diagnosis of childhood malaria on antimalarial drug prescription and health outcome at primary health care level in Tanzania: a randomized controlled trial. *Malar J* 2008; 7: 199.

Nsimba SE. Assessing the impact of educational intervention for improving management of malaria and other childhood illnesses in Kibaha District-Tanzania. *East Afr J Public Health* 2007; 4(1): 5-11.

Pagaiya N and Garner P. Primary care nurses using guidelines in Thailand: a randomized controlled trial. *Trop Med Int Health* 2005; 10(5): 471-7.

Rakhamina NY, van den Anker JN. Pharmacological research in pediatrics: from neonates to adolescents. *Adv Drug Deliv Rev*. 2006; 58: 4-14.

Ranji SR, Steinman MA, Sjohania KG, Gonzales R. Interventions to reduce unnecessary antibiotic prescription. *Med Care*. 2008; 46:847-862.

Ross-Degnan D, Soumerai SB, et al. The impact of face-to-face educational outreach on diarrhoea treatment in pharmacies. *Health policy and planning*. 1996; 1(3): 308-318.

Santoso B, Suryawati S, et al. (1996). Small group intervention vs formal seminar for improving appropriate drug use. *Soc Sci Med*. 1996; 42(8): 1163-1168.

Schmid EF, Smith DA. Is declining innovation in the pharmaceutical industry a myth? *Drug Discov Today*. 2005; 10:1031-1039.

Smabrekke L, Berild D, et al. (2002). Educational intervention for parents and healthcare providers leads to reduced antibiotic use in acute otitis media. *Scand J Infect Dis.* 2002; 34(9): 657-659.

Soumerai SB, McLaughlin TJ, Avorn J. Improving drug prescribing in primary care: a critical analysis of the experimental literature. *Milbank Quarterly*. 1989; 67: 268-317.

Steinman MA, Ranji SR, Shojania KG, Gonzales R. Improving antibiotic selection: a systemic review and quantitative analysis of quality improvement strategies. *Med Care.* 2006; 44: 617-628.

Tumwikirize WA, Ekwaru PJ, et al. Impact of a face-to-face educational intervention on improving the management of acute respiratory infections in private pharmacies and drug shops in Uganda. *East Afr Med J Suppl*: 2004; S25-32.

Warman KL, Silver EJ, McCourt MP, Stein RE. How does home management of asthma exacerbations by parents of inner-city children differ from NHLBI guideline recommendations? *Peds*. 1999; 103;422-7.

Wilson SD, Dahl BB, et al. An evidence-based clinical pathway for bronchiolitis safely reduces antibiotic overuse. *Am J Med Qual* 2002; 17(5): 195-9.

Witt K, Knudsen E, et al. Academic detailing has no effect on prescribing of asthma education in Danish general practice: A 3-year randomized controlled trial with 12-monthly follow-ups. *Family Practice* 2004; 21(3): 248-253.

	Persuasive	**Potentially Persuasive OR Restrictive**	**Restrictive**
Individual Intervention focused on the individual prescriber	Individual CME for provider. Topics include how to collect diagnostic data to aid with appropriate Rx	Distribution of clinical practice guidelines to individual providers	Individual physicians are restricted from use of specific medications
Supplemental Current practice system not changed. Intervention focused on supplementing practice with additional data or service	Additional diagnostic data (meant to aid with appropriate Rx) is collected and sent to practice	Rx patterns of individual providers are audited. External feedback sent to providers.	Additional 'prior approval' must be obtained from consultant subspecialist for approval of medication during Rx process
Structural Intervention focused on changing the system of care within the practice	Either new system developed, practice staff or provider trained to collect new diagnostic data to aid with appropriate Rx	Training and implementation of care pathway that defines new roles for team members. If no provider available, RN can use default rules for Rx.	All Rx orders for specific medications have an 'automatic stop order' or restrictions on use

Figure 1: Scheme for Classifying Types of Interventions

	Persuasive	**Potentially Persuasive OR Restrictive**	**Restrictive**
Individual Intervention focused on the individual prescriber		Mitchell, 2005 (no effect) Witt, 2004 (no effect)	
Supplemental Current practice system not changed. Intervention focused on supplementing practice with additional data or service	Bryce, 1995 (no effect) Halterman, 2005 (no effect) Hagmolen, 2008 (some effect) Lozano, 2004 (some effect for intervention A)	Clark, 1998 (+ effect)	
Structural Intervention focused on changing the system of care within the practice	Lozano, 2004 (some effect for intervention B)	Johnson, 2000 (+ effect)	

Figure 2: Studies that Included Interventions to Address Prescribing for Childhood Asthma

	Persuasive	**Potentially Persuasive OR Restrictive**	**Restrictive**
Individual Intervention focused on the individual prescriber	Doyne, 2004 (no effect)		
Supplemental Current practice system not changed. Intervention focused on supplementing practice with additional data or service	Christakis, 2001 (+ effect) Davis, 2007 (+ effect)	Bauchner, 2006 (no effect) Finkelstein, 2001 (+ effect) Finkelstein, 2008 (+ effect) Pagaiya, 2005 (+ effect)	
Structural Intervention focused on changing the system of care within the practice			deMan, 2000 (+ effect)

Figure 3: Studies that Included Interventions to Address Antibiotic Prescribing

Table 1: Inclusion Criteria for Studies Used in the Analysis

Full text of the article was published in English

The study used a randomized controlled trial (RCT) design

The intervention addressed a prescribing behavior

The intervention was directed towards physicians or other health professionals with prescribing authority (e.g., nurse practitioners, pharmacists) – may be combined with an intervention directed toward parents or the community

Table 2: MeSH Terms and Keywords Used in Search Strategy

MeSH Terms:

Anti-Bacterial Agents/ therapeutic use
Anti-Infective Agents/ therapeutic use
Bacterial Infections/drug therapy/prevention & control
Drug Prescriptions
Drug Resistance, Bacterial
Drug Utilization
Education, Continuing
Education, Medical, Continuing
Evaluation Studies as Topic
Evidence-Based Medicine/ standards
Feedback
Guideline Adherence
Health Personnel/education
Infection Control/organization & administration
Inservice Training
Intervention Studies
Medical Audit
Nurse Practitioners/education
Outcome and Process Assessment (Health Care)
Pediatrics/education
Pediatrics/education/standards
Pharmacists
Physicians
Physician's Practice Patterns
Practice Guidelines as a Topic
Professional Practice/standards
Program Evaluation
Prospective Studies
Quality Assurance, Health Care
Quality of Health Care
Reimbursement, Incentive
Reminder Systems
Treatment Outcome

Keywords:

Assess*, develop*, education, effect*, evaluat*, evidence*, feedback, financial incentive*, guideline adherence, impact*, implement*, improve*, intervention*, medical edit, promot*, reminder, strateg*, training

(antibiotics AND (prescribing OR prescription*)), anti bacterial, anti infect*, bacterial Infections, infection control, nurse practitioner*, pediatric*, pharmacist*, physician*, physician's practice pattern*, treatment outcome*,

Infant*, newborn*, child*

* truncation to retrieve various words with the same root e.g. child*➔ to retrieve child, children, childbearing

Table 3: Glossary of Definitions of Interventions*

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
Conferences	Participation of health care providers in conferences, lectures, workshops or traineeships
Local Consensus Process	Inclusion of participating providers in discussion to ensure that they agree that the chosen clinical problem is important and the approach to managing the program (i.e., the clinical practice guideline or definition of adequate care) is appropriate. The consensus process might also address the design of an intervention to improve performance.
Educational outreach visits	Use of a trained person who meets with providers in their practice settings to provide information with intent of changing the provider's performance. The information given may include feedback on the provider's performance. *Academic detailing was considered a type of educational outreach visit
Local opinion leaders	Use of providers nominated by their colleagues as 'educationally influential.' The investigators must explicitly state that 'the opinion leaders were identified by their colleagues.'
Patient-mediated interventions	Any intervention aimed at changing the performance of health care providers where specific information was sought from or given to patients: for instance, direct mailings to patients, patient counseling delivered by someone other than the targeted providers, clinical information collected from patients by others and given to the provider, educational materials given to patients or placed in waiting rooms.
Audit and feedback	Any summary of clinical performance over a specified period of time. Summarized information may include the average number of medications prescribed, etc. The summary may also include recommendations for clinical care. The information may be given in a written or verbal format.
Reminders	May be manual or computerized. Any intervention that prompts the health care provider to perform a patient- or encounter-specific clinical action.
Multifaceted Interventions	Any intervention that includes two or more of the above.

***** Based on Effective Practice and Organization of Care (EPOC) definitions of interventions. (Modified from Grimshaw, 2001)

Table 4. Research Design Characteristics

Citation	Type of Study (e.g., RCT)	Sampling Frame & Sites	Sample Size —Health Professionals	Sample Size --Children	Type of Comparison
Bauchner, 2006	RCT (Cluster)	12 pediatric practices	Not reported	2584	Intervention vs. no intervention
Bryce, 1995	RCT	12 general practices	Not reported	3148	Intervention vs. no intervention
Christakis, et al., 2001	RCT	University-based primary care pediatric clinic	38	Not reported (14,414 visits, 1339 for otitis media)	Intervention vs. no intervention
Clark, et al., 1998	RCT	Primary care pediatric practices	74	637	Intervention vs. no intervention
Davis, et al., 2007	RCT (Cluster)	University-based and private primary care pediatric clinics	44	Not reported (3561 prescriptions; 12,195 visits)	Intervention vs. no intervention
deMan, 2000	RCT (Crossover)	2 Neonatal Intensive Care Units	Not reported	436	Intervention A vs. Intervention B
Doyne, et al., 2004	RCT (Cluster)	Health centers and private practices	Not reported	Not reported	Intervention vs. no intervention
Finkelstein, et al., 2001	RCT (Cluster)	12 practices affiliated with 2 HMOs	157	8,815	Intervention vs. no intervention
Finkelstein, 2005 (reanalysis of Lozano)	RCT (Cluster)	42 Primary care practices with 4 HMOs	28	5169	Intervention A, B and no intervention
Finkelstein, 2008	RCT (Cluster)	16 communities	207	143,884 (223,135 person-yrs)	Intervention vs. no intervention, before and after
Hagmolen of ten Have et al., 2008	RCT (Cluster)	18 health care centers	105	404	Intervention vs . no intervention
Halterman et al., 2005	RCT	Rochester City School District	72	151	Intervention vs. no intervention
Johnson et al., 2000	RCT	Children's Hospital	Not reported	110	Intervention vs. no intervention
Lozano et al., 2004	RCT (Cluster)	42 Primary care practices with 4 HMOs	28	638	Intervention A, B and no intervention
Mainous et al., 2000	RCT	8 Medicaid administrative regions in Kentucky	216	Not reported 124,092 patient encounters	Intervention A, B, A+B, and no intervention
Mitchell et al, 2005	RCT (Cluster)	General practitioner network	270	104,501	Intervention vs. no intervention

Table 4. Research Design Characteristics (cont'd.)

Citation	Type of Study (e.g., RCT)	Sampling Frame & Sites	Sample Size —Health Professionals	Sample Size --Children	Type of Comparison
Ngasala et al., 2008	RCT (Cluster)	16 Primary Health Centers	Not reported	3,131	Intervention A, B and no intervention
Nsimba, 2007	RCT	Drug stores	40	Not reported	Intervention A vs B
Pagaiya and Garner, 2005	RCT (Cluster)	18 rural health centers	18	1260	Intervention vs. no intervention
Ross-Degnan, et al., 1996	RCT (Cluster)	87 pharmacies	Not reported	Not reported	Intervention vs. no intervention
Santoso et al., 1996	RCT	90 health centers	Not reported	Not reported	Interventions vs. no intervention
Witt et al., 2004	RCT (Cluster)	84 general practices	185	Not reported	Intervention vs. guideline and prescription profile mailing only

Table 5. Characteristics of the Intervention and the Study Population

Citation	Medication	Disease or Condition	Type of Intervention	Populations Receiving Intervention	Type(s) of Health Professionals	Patient Population for with Outcomes Assessed	Location
Bauchner, 2006	Antibiotics	Otitis media	Reverse academic detailing (use of local opinion leaders who meet with clinicians in small group discussions), interactive educational sessions, feedback, and enabling tools (physician reminders).	Health professionals	Physicians	Children, between 3 and 36 months of age with a clinical diagnosis of AOM, with no underlying major medical illness, no history of premature birth, not allergic to penicillin.	Practices within 30 miles of Boston, MA, USA.
Bryce, 1995	Asthma medications (inhaled bronchodilators, oral bronchodilators, cromoglycate, inhaled steroids, theophyllines, anticholincergics, oral steroids	Asthma	An audit facilitator ('acts as a catalyst to assist change within practices.'). Audit facilitator placed sticker on chart, placed protocol for managing acute asthma attacks, a letter suggesting review, and guidelines on treatment with prophylactic drugs. Practices supplied with inhaler devices, patient education materials, portable nebulizers. Audit facilitator had no direct patient contact or meetings with doctors or nurses.	Health professionals	General physicians	Children 1 to 15 years of age with asthma.	Tayside Region, Central Scotland, UK.
Christakis, et al., 2001	Antibiotics	Otitis media	Evidence-based "action trigger screens" that appear in Electronic Health Record when the provider is about to write an electronic prescription. Actions focused on reducing antibiotic treatment to 5 days (versus longer periods) and use of antibiotic treatment for otitis media.	Health professionals	Residents, nurse practitioners, attendings	Children diagnosed with acute otitis media	US—University of WA
Clark, et al., 1998	Inhaled corticosteroids	Asthma	2 interactive continuing medical education seminars each 2.5 hours	Physicians	Pediatricians	Children with hx asthma 1-12yo, otherwise healthy, at least 1 emergency visit for asthma in past year.	MI—Ann Arbor & NY—New York
Davis, et al., 2007	Various	Multiple—otitis media, allergic rhinitis, sinusitis, constipation, pharyngitis, croup, urticaria, bronchiolitis	Evidence-based medicine prompts that appear ("just-in-time") at point of electronic prescription writing. Focus included otitis media, allergic rhinitis, sinusitis, constipation, croup, urticaria, and bronchiolitis.	Health care providers	Residents, nurse practitioners, attendings	Children diagnosed with diseases as listed in previous column.	US—University of WA & Skagit, WA
deMan, 2000	Antibiotics (empiric broad spectrum antibiotics vs. more narrow spectrum antibiotics)	Neonatal infection	Policy change: restriction on type of antibiotics that can be ordered for initial antibiotic therapy (amoxicillin cefotaxime regimen compared to penicillin-tobramycin regimen)	Health professionals (via a policy change in the treatment unit)	Neonatologists	Premature infants requiring empiric intravenous antibiotics	Sophia Children's Hospital, Rotterdam, Netherlands

Table 5. Characteristics of the Intervention and the Study Population (cont'd.)

Citation	Medication	Disease or Condition	Type of Intervention	Populations Receiving Intervention	Type(s) of Health Professionals	Patient Population for with Outcomes Assessed	Location
Doyne, et al., 2004	Antibiotics	Various	Academic detailing program (created by leaders for study). Practice leader at each intervention site attended seminar, received educational materials (for parents, posters, flyers), and created an academic detailing program by meeting with an expert every other month. Academic detailing was presented by leader to each practice every other month. (Control: received copy of guidelines, and practice-specific report cards)	Physicians	Pediatricians	All patients prescribed antibiotics.	US—Ohio, Kentucky
Finkelstein, et al., 2001	Antibiotics – excluded topical anti-microbials, anti-tuberculosis drugs, and anti-helminthics	Multiple – otitis media accounted for 62% of prescriptions	Physician education intervention over 1 year. Trained 'peer leader' led 90 minute small group educational session with member of practice. Pamphlets and poster placed in office and waiting room. Four months after initial session, peer leaders visited physicians to give feedback (bar graphs of practitioner and practice-level antibiotic prescribing rates). For parents, written materials were mailed to families	Health professionals, Parents	Physicians, Nurse Practitioners	Children < 6 yrs. who had at least on antibiotic dispensing and at least one ambulatory care visit during the period – most enrolled in commercial health plans	United States – urban and suburban areas of Massachusetts and Washington
Finkelstein, 2005 (reanalysis of Lozano)	Asthma medications	Asthma	Asthma team leader peer education, planned care intervention with peer leader and organization change (trained asthma nurse),	Providers and health care organization	Physicians, nurse practitioners, nurses, physician assistants	Children ages 3-17 with mild to moderate persistent asthma	United States- Urban and suburban areas of Seattle, Chicago and eastern Massachusetts
Finkelstein, 2008	Antibiotics	Otitis media, URI, sore throat	Guideline dissemination, small group education, written material, Rx feedback. Parent written material. Child care center written material	health professionals	Physicians	Children 36-72 months	Massachusetts
Hagmolen of ten Have et al., 2008	Inhaled corticosterioids	Asthma	Health professionals: dissemination of guideline, educational session, individual treatment advice based on patient airway hyper-responsiveness (AHR) data	Health Professionals	Physicians	Children 7-17 years old with mild to severe persistent asthma	Almere, Netherlands

Table 5. Characteristics of the Intervention and the Study Population (cont'd.)

Citation	Medication	Disease or Condition	Type of Intervention	Populations Receiving Intervention	Type(s) of Health Professionals	Patient Population for with Outcomes Assessed	Location
Halterman et al., 2005	Preventive medications for asthma	Mild to severe persistent asthma	Notification of primary care providers about patient asthma symptoms and NHLBI guidelines	Health professionals	Primary care physicians	Children 3-7 years old entering the Rochester School District with mild to severe persistent asthma	Rochester, NY
Johnson et al., 2000	Beta-agonists	Asthma	Clinical pathway Nurses: Staff training, weaning bronchodilator protocol Patients: asthma teaching, pre-discharge prescriptions	Health professionals	Nurses	2-18 years old admitted to pediatric hospital with asthma exacerbation (non-ICU)	Baltimore, MD
Lozano, et al., 2004	Asthma medications	Asthma	One of three interventions: (A) Asthma team leader peer education (i.e., training one physician in each practice site to serve as an asthma champion, sharing guidelines with colleagues and encouraging implementation), Champions were provided with 2 workshops, an educational coordinator, ongoing learning network for peer leaders and a toolkit. Educational coordinator contacted physician champion every 1 to 2 months. (B) planned care intervention with peer leader and organization change (trained asthma nurse); 4 to 5 trained asthma nurse visits included standardized assessments, support in care planning, self-management support to families, and proactive standardized phone follow-up or (C) usual care	Providers and health care organization	Physicians, nurse practitioners, nurses, physician assistants	Children ages 3-17 with mild to moderate persistent asthma	United States- Urban and suburban areas of Seattle, Chicago and eastern Massachusetts
Mainous et al., 2000	Antibiotic usage	Acute otitis, sinusitis, strep phyaryngitis, pharyngitis, rhinitis, URI, bronchitis.	Performance feedback to physicians of data of prescribing practices for pediatric upper respiratory infections, acute bronchitis and purulent rhinitis for the last year. Patient education material was mailed to parents with letter. Each office also received copies of pamphlets for distribution.	Providers and patients	Physicians	Children < 18 years of age	Kentucky, urban and rural
Mitchell et al., 2005	Short acting beta agonists, methyl-xanthines, inhaled cortico-steroids, mast cell stabilizers	Asthma	Clinical pathway and physician education (2 hour group education)	Health professionals	General practitioners	Children ≤ 18 years of age	Waitemata and Auckland, New Zealand

Table 5. Characteristics of the Intervention and the Study Population (cont'd.)

Citation	Medication	Disease or Condition	Type of Intervention	Populations Receiving Intervention	Type(s) of Health Professionals	Patient Population for with Outcomes Assessed	Location
Ngasala et al., 2008	Anti-Malarial (sulphadoxine/pyrimeth-amine, amodiaquine and quinine)	Malaria	One of three interventions: (A) Group training on management of malaria using clinical algorithm, (B) Group training on management of malaria using clinical algorithm plus malaria microscopy or (C) No training	Providers, staff, laboratory assistants	Assistant medical officers, assistant clinical officers, clinical officers, health aids, trained nurses, nurse auxiliaries and laboratory assistants	Age < 5years	Rural Tanzania (Kibaha and Bagamoyo)
Nsimba, 2007	Anti-Malarial drugs (sulfadoxine/ pyrimeth-amine)	Malaria	Poster compared to Poster plus 1 hour training session	Drug sellers	Drug seller/ attendant	n/a	Rural Tanzania (Kibaha district)
Pagaiya and Garner, 2005	Antibiotics and oral rehydration solution	(1) Acute respiratory infections and (2) diarrhea	Three day training course followed up with educational outreach visits by nurse supervisors. Guidelines and educational outreach visits.	Health professionals.	Nurses	Children 0-5 years with presenting to nurse staffed health centers with acute respiratory infections and diarrhea	Khon Kaen Province, Thailand
Ross-Degnan, et al., 1996	Antidiarrheals and oral rehydration salts	Diarrhea	Pharmacists: Back counter display and face-to-face education ("academic detailing"). Parents: posters promoting oral rehydration salts and feeding	Health professionals	Pharmacists	Hypothetical population of children (actors posing as parents of children with diarrhea visiting pharmacies for care)	Indonesia
Santoso et al., 1996	Oral rehydration solution, antidiarrheals, antibiotics and polypharmacy (defined as mean number of drugs prescribed per patient)	Diarrhea	Academic detailing in the form of (1) face-to-face small group sessions at health centers (2) large group lectures Both supplemented with an educational booklet	Health professionals	Paramedical Prescribers	Children <5 years old	Indonesia (Java)
Witt et al., 2004	Inhaled steroids and beta agonists	Asthma	Academic detailing (guideline and prescription profile discussed with practice)	Health professionals	General practitioners	Pediatric patients <16 years old	Vestsjaelland, Denmark

Table 6. Number of Different Interventions Used

Citation	EDUC. MATERIALS	CONF	EDUCATIONAL OUTREACH	OPINION LEADER	PATIENT-MEDIATED	AUDIT & FEEDBACK	REMINDER SYSTEM	OTHER	
Bauchner, 2006	1	1	1				1		
Bryce, 1995			1		1				
Christakis 2001							1		
Clark, et al., 1998	1	1							
Davis, et al., 2007							1		
deMan, 2000								1	Policy change
Doyne, et al., 2004	1		1	1	1				
Finkelstein, 2001	1	1	1		1	1			
Finkelstein, 2008	1	1	1		1	1			
Hagmolen of ten Have et al., 2008	1	1			1				
Halterman et al., 2005	1				1				
Johnson et al., 2000								1	Clinical pathway
Lozano, et al., 2004 A intervention	1	1	1						
Lozano, et al B intervention	1	1	1		1				
Mainous et al., 2000 A intervention					1	1			
Mainous et al., 2000 B intervention					1				
Mainous et al., 2000 C intervention						1			
Mitchell et al., 2005	1	1							
Ngasala et al., 2008 A intervention	1	1							
Ngasala et al., 2008 B intervention	1	1			1				Microscopy training
Nsimba, 2007		1							
Pagaiya, 2005 For Abx	1	1	1						
Pagaiya, 2005 for ORS	1	1	1						

Table 6. Number of Different Interventions Used (cont'd.)

Citation	EDUC. MATERIALS	CONF	EDUCATIONAL OUTREACH	OPINION LEADER	PATIENT-MEDIATED	AUDIT & FEEDBACK	REMINDER SYSTEM	OTHER	
Ross-Degnan, et al., 1996			1		1				
Santoso et al., 1996	1	1	1						
Witt et al., 2004	1		1			1			

Table 7a. Outcomes Assessed for Interventions Focused on Asthma Medications

Citation	Outcome	Intended Direction	Difference	P value	Notes
Bryce, 1995	Hospital admissions for asthma **	Decrease	0.53 (0.11, 1.26)		
	ED visits for asthma **	Not clear	1.19 (0.76, 1.18)		
	Outpatient visits for asthma **	Not clear	0.42 (0.09. 1.94)		
	Rx for inhaled bronchodilator	Not clear	1.16 (0.93, 1.45)		
	Rx for oral bronchodilator	Not clear	1.43 (1.06, 1.94)	p<0.05	
	Rx for sustained relief bronchodilator	Not clear	1.69 (0.54, 5.26)		
	Rx for cromoglycate	Not clear	1.52 (1.02, 2.25)	p<0.05	Appropriateness of Rx not evaluated
	Rx for inhaled steroids	Not clear	1.02 (0.71, 1.47)		Appropriateness of Rx not evaluated
	Rx for theophyllines	Not clear	1.30 (0.78, 2.15)		Appropriateness of Rx not evaluated
	Rx for spacer devices	Not clear	1.68 (1.06, 2.66)		
	Rx for peak flow meters	Not clear	1.99 (0.86, 4.60)		
	Rx for oral steroids	Not clear	1.03 (0.58, 1.81)		
	Rx for Emergency nebulization	Not clear	0.78 (0.44, 1.37)		
	Rx for Emergency injection	Not clear	1.17 (0.13, 10.2)		
	Rx for antibiotics	Not clear	1.07 (0.91, 1.26)		
	Rx for cough linctus	Not clear	1.01 (0.77, 1.32)		
	Rx for nasal spray	Not clear	1.43 (0.94, 2.17)		
Clark, et al., 1998	Hospital admissions for asthma	Decrease	0.08 for intervention versus 0.08 for control	NS	
	ED visits for asthma	Decrease	0.65 for intervention versus 0.67 for control	NS	
	Scheduled outpatient visits for asthma	Not clear	1.24 for intervention versus 2.25 for control	p=0.005	
	Unscheduled follow-up outpatient visits for asthma after symptoms	Decrease	0.94 for intervention versus 1.61 for control	p=0.005	
	Frequency of treating newly diagnosed patients with inhaled anti-inflammatory medication (physician report)	Not clear	67% for intervention versus 56% for control	p=0.044	Appropriateness of Rx not evaluated
Finkelstein, et al. 2005 (reanalysis of Lozano)	Mean change in proportion of persistent asthma patients with 1 ED or hospitalization	Decrease	0 (-0.06, 0.06) for Group A vs. Grp C		
	Mean change in proportion of persistent asthma patients with 1 ED or hospitalization	Decrease	0.03 (-0.003, 0.06) for Group B vs. Grp C		
	Mean change in proportion of persistent asthma patients with ambulatory visit	Increase	0.06 (-0.02, 0.14) for Group A vs. Grp C		
	Mean change in proportion of persistent asthma patients with ambulatory visit	Increase	-0.08 (-0.01, 0.18) for Group B vs. Grp C		
	For persistent asthmatic patients in practice				
	Mean change in proportion receiving > 1 controller	Increase	0.01 (-0.07, 0.08) for Group A vs. Grp C		
	Mean change in proportion receiving > 1 controller	Increase	-0.03 (-0.09, 0.02) for Group B vs. Grp C		
	Mean change in proportion receiving > 3 controllers	Increase	0.02 (-0.06, 0.10) for Group A vs. Grp C		
	Mean change in proportion receiving > 3 controllers	Increase	0.03 (-0.04, 0.10) for Group B vs. Grp C		
	Mean change in proportion receiving > 1 inhaled corticosteroid	Increase	0.03 (-0.11, 0.16) for Group A vs. Grp C		
	Mean change in proportion receiving > 1 inhaled corticosteroid	Increase	-0.02 (-0.13, 0.09) for Group B vs. Grp C		
	Mean change in proportion receiving > 3 inhaled corticosteroids	Increase	0.07 (-0.02, 0.15) for Group A vs. Grp C		
	Mean change in proportion receiving > 3 inhaled corticosteroids	Increase	0.03 (-0.04, 0.10) for Group B vs. Grp C		

Table 7a. Outcomes Assessed for Interventions Focused on Asthma Medications (cont'd.)

Citation	Outcome	Intended Direction	Difference	P value	Notes
Finkelstein, et al. 2005 (reanalysis of Lozano) – cont'd.	For all asthmatic patients in practice				
	Mean change in proportion receiving > 1 controller	Increase	0.03 (-0.08, 0.15) for Group A vs. Grp C		
	Mean change in proportion receiving > 1 controller	Increase	0.04 (-0.06, 0.14) for Group B vs. Grp C		
	Mean change in proportion receiving > 3 controllers	Increase	0.02 (-0.05, 0.09) for Group A vs. Grp C		
	Mean change in proportion receiving > 3 controllers	Increase	0.04 (-0.02, 0.09) for Group B vs. Grp C		
	Mean change in proportion receiving > 1 inhaled corticosteroid	Increase	0.05 (-0.08, 0.17) for Group A vs. Grp C		
	Mean change in proportion receiving > 1 inhaled corticosteroid	Increase	0.04 (-0.06, 0.14) for Group B vs. Grp C		
	Mean change in proportion receiving > 3 inhaled corticosteroids	Increase	0.04 (-0.02, 0.10) for Group A vs. Grp C		
	Mean change in proportion receiving > 3 inhaled corticosteroids	Increase	0.03 (-0.02, 0.07) for Group B vs. Grp C		
Hagmolen of ten Have et al., 2008	Rx for inhaled corticosteroids (based on parent report)	Not clear	83% for intervention versus 70% for control	p=0.018	Appropriateness of Rx not evaluated
	Change in Log Methacholine Provocation Dose for a 20% fall in forced expiratory flow at second (PD-20)	Increase	+ 0.3 for A; + 0.2 for B; + 0.7 for C	p=0.09	
	Change in forced expiratory flow at second (FEV-1)	Increase	+ 0.1 for A; - 1.0 for B; + 0.2 for C		
	Change in Peak expiratory flow (PEF) variability %	Decrease	- 1.3 for A; - 1.7 for B; - 1.6 for C		
	Change in total symptom score	Decrease	- 0.6 for A; - 0.3 for B; - 0.5 for C		
	Change in nocturnal symptom score	Decrease	- 0.24 for A; - 0.07 for B; - 0.15 for C	p=0.02	
	Change in number of symptom free days	Increase	+ 1.5 for A; + 1.3 for B; + 1.9 for C		
	Change in Rx of puffs per day of inhaled corticosteroids	Increase	- 0.1 for A; - 0.01 for B; + 0.1 for C	p=0.03	** All pts had mild to severe asthma that required daily controller medication.
	Change in Rx of puffs per day of beta agonist	Decrease	+ 0.06 for A; - 0.2 for B; - 0.4 for C		
	Change in Rx of puffs per day of beta agonist (based on diary period)	Decrease	- 0.07 for A; - 0.09 for B; - 0.24 for C		
Halterman et al., 2005	% patients with hospitalization for asthma	Decrease	1.5% for intervention, vs. 4.2% for control		
	% patients with emergency visit for asthma	Decrease	32 % for intervention vs. 44% for control		
	% patients with office visit	Not clear	85% for intervention vs. 79% for control		
	% with Rx or change in asthma medication	Increase	22% for intervention vs. 26% for control		
	% with Rx for preventive medication	Increase	7% for intervention vs. 9% for control		
	% with Rx for change in medication dose	Increase	15% for intervention vs. 17% for control		
Johnson et al., 2000	Duration of hospitalization	Decrease	53.7 hrs for control vs. 40.3 hrs for interv.	p<0.01	
	Rx mean # of beta agonists at q2 hr interval	Decrease	4.5 for intervention vs. 6.5 for control	p=0.02	
	Rx mean # of beta agonists at q3 hr interval	Decrease	3.7 for intervention vs. 5.9 for control	p=0.002	
	Rx mean # of beta agonists at q4 hr interval	Decrease	3.5 for intervention vs. 4.7 for control	p=0.044	
	Rx mean # of beta agonists at q6 hr interval	Decrease	1.4 for intervention vs. 2.2 for control	p=0.01	
	Rx mean # of beta agonists at q8 hr interval	Decrease	0.1 for intervention vs. 0.0 for control		
	Post-discharge unscheduled health care encounters related to asthma	Decrease	No differences		

Table 7a. Outcomes Assessed for Interventions Focused on Asthma Medications (cont'd.)

Citation	Outcome	Intended Direction	Difference	P value	Notes
Lozano et al., 2004	Asthma symptom days	Decrease	- 13.3 (-24.7, -2.1) for Group B vs. Grp C		
	Asthma symptom days	Decrease	- 6.5 (- 16.9 -3.6) for Group A vs. Grp C		
	Odds of period of frequent symptoms	Decrease	OR: 0.69 (0.50, 0.96) for Group B vs. Grp C		
	Odds of period of frequent symptoms	Decrease	OR: 1.15 (0.86, 1.55) for Group A vs. Grp C		
	Physical health based on CHSA	Increase	3.29 (-1.39, 7.97) for Group A vs. Grp C		Child Health Survey for asthma (CHSA)
	Physical health based on CHSA	Increase	3.68 (0.06, 7.30) for Group B vs. Grp C		
	Child Activity based on CHSA	Increase	3.89 (0.29, 7.70) for Group A vs. Grp C		
	Child Activity based on CHSA	Increase	2.90 (-0.57, 6.37) for Group B vs. Grp C		
	Family Activity based on CHSA	Increase	1.58 (-1.31, 4.48) for Group A vs. Grp C		
	Family Activity based on CHSA	Increase	0.12 (-2.52, 2.75) for Group B vs. Grp C		
	Child Emotional Score based on CHSA	Increase	6.47 (0.72, 12.2) for Group A vs. Grp C		
	Child Emotional Score based on CHSA	Increase	6.42 (0.80, 12.0) for Group B vs. Grp C		
	Family Emotional Score based on CHSA	Increase	0.36 (-1.86, 2.58) for Group A vs. Grp C		
	Family Emotional Score based on CHSA	Increase	1.02 (-1.34, 3.39) for Group B vs. Grp C		
	Rx of oral steroids for asthma exacerbations	Decrease	- 36% (-11%, -54%) for Group A vs. Grp C		"use of steroids in exacerbations…serves as a rough proxy for exacerbations."
	Rx of oral steroids for asthma exacerbations	Decrease	- 39% (-11%, -58%) for Group B vs. Grp C		
	Parent adherence to controller medications	Increase	1.05 (1.00, 1.09) for group B vs. GrpC		Based on multivariate model
	Parent adherence to controller medications	Increase	'not significant for Group A vs. Grp C.		Based on multivariate model
Mitchell et al., 2005	Hospital admissions for asthma	Decrease	No difference	p=0.70	
	ED visits for asthma	Decrease	No difference	p=0.30	
	Rx for inhaled corticosteroids	Not clear	No difference	p=0.40	
	Rx for inhaled relievers	Not clear	No difference	p=0.20	
	Rx for methylxanthines	Not clear	No difference	p=0.30	
	Rx for dry powder relievers	Not clear	No difference	p=0.30	
	Rx for mast cell stabilizers	Not clear	No difference	p=0.50	
	Rx for oral relievers	Decrease	Intervention 6.2 to 3.2 Rx per 1000 patient months, versus 2.8 to 2.0 Rx per 1000 patient months.	p<0.001	Could be due to regression to the mean (large baseline differences between control and intervention groups)
Witt et al., 2004	Rx of beta agonists (daily defined dose)	Decline	No difference in prescription	p=0.60	
	Rx of inhaled steroids (daily defined dose)	Increase	No difference in prescription	p=0.90	Appropriateness of Rx not evaluated

Table 7b. Outcomes Assessed for Interventions Focused on Antibiotic Prescription

Citation	Outcome	Intended Direction	Difference	P value	Notes
Bauchner, et al. 2006	Rx with appropriate antibiotic at initial episode	Increase	OR 1.29 (0.69, 2.41)		
	Rx with appropriate antibiotic at second episode	Increase	OR 1.06 (0.59, 1.93)		
Christakis, et al., 2001	Rx of prescription for otitis media less than 10 d duration	Increase	44% for intervention, 10% for control	p<0.01	
	Rx for otitis media	Decrease	+4% for intervention; +17% for control	p=0.095	
Davis, et al., 2007	% of Rx that increased in accordance with evidence provided by electronic prompt	Increase	1% for control, vs. 4% for intervention (adjusted difference was reported as 8%; 95% CI: 1%, 15%)		"A small percentage of the data includes data previously published in the earlier report by Christakis, et al." Data from each site presented separately. No other combined results.
deMan, 2000	Risk of colonization for broad-spectrum group				
	Gram negative bacillus resistant to cefotaxime	Increase	RR 3.14 (1.76, 5.56) for broad spectrum grp.		
	Gram negative bacillus resistant to cefotaxime or tobramycin	Increase	RR 2.42 (1.41, 4.15) for broad spectrum grp.		
	Enterobacter spp. resistant to cefotaxime	Increase	RR 2.98 (1.64, 5.38) for broad spectrum grp.		
	Gram negative bacillus resistant to empiric therapy of unit	Increase	RR 17.98 (5.57, 58.0) for broad spectrum grp.		
Doyne, et al., 2004	Antibiotic prescription rate	Decrease	Decrease to 0.82 (95% CI: 0.71, 0.95) for intervention. Decrease to 0.86 (95% CI: 0.77, 0.95) for control. No difference between control and intervention.		
Finkelstein et al., 2001	Adj. effect of intervention on prescribing rate for 8815 patients in analysis				Adjusted for clustering, baseline rate and age.
	3 months to <36 months	Decrease	-16% (95% CI: 8%, 23%)		
	36 months to < 72 months	Decrease	-12% (95% CI: 2%, 21%)		
Finkelstein, et al., 2008	Difference in adjusted percentage change in rate of antibiotics, in general				Study assumes that only 'inappropriate' use decreased
	3 to < 24 months	Decrease	-20.7 for control; -21.2 for inter; - 0.5% diff	p=0.69	
	24 to < 48 months	Decrease	-10.3 for control; -14.5 for inter; -4.2% diff	p<0.01	
	48 to < 72 months	Decrease	-2.5 for control; -9.3 for inter; -6.7% diff	p<0.001	
	Difference in adjusted percentage change in rate between intervention and control for use of second line penicillins				
	3 to < 24 months	Decrease	5.0 for control; 2.8 for inter; - 2.2% diff	p=0.48	
	24 to < 48 months	Decrease	10.1 for control; 0.9 for inter; -9.2% diff	p=0.03	
	48 to < 72 months	Decrease	19.7 for control; -1.6 for inter; -21.3% diff	p<0.001	
	Difference in adjusted percentage change in rate between intervention and control for use of broad-spectrum abx				
	3 to < 24 months	Decrease	-10.2 for control; -16.9 for inter; - 6.7% diff	p=0.02	
	24 to < 48 months	Decrease	13.4 for control; 0.7 for inter; -12.7% diff	p<0.01	
	48 to < 72 months	Decrease	29.5 for control; 7.0 for inter; -22.5% diff	p<0.001	
Mainous et al., 2000	Mean percentage of episodes receiving antibiotics	Decrease	Overall increase in antibiotic prescribing, but less in the patient education group (B) and feedback with patient education group (C) compared to control group (D)		

Table 7b. Outcomes Assessed for Interventions Focused on Antibiotic Prescription (cont'd.)

Citation	Outcome	Intended Direction	Difference	P value	Notes
Pagaiya and Garner, 2005	% of upper respiratory infection cases with antibiotic Rx	Decrease	-14.6 for intervention; 2.8 for control	p=0.022	
	% of diarrhea cases with antibiotic Rx	Decrease	-1.8 for intervention; -2.1 for control	p=0.308	

Table 7c. Outcomes Assessed for Interventions Focused on Malaria Prescription

Citation	Outcome	Intended Direction	Difference	P value	Notes
Ngasala et al., 2008					
	% of patients with antimalarial prescription	Decrease	95% for A; 61% for B; 99% for C	p<0.01	
	% of patients with antibiotic prescription	Decrease	55% for A; 46% for B; 34% for C		
	% of patients with antipyretic prescription	Decrease	97% for A; 96% for B; 95% for C		
	Recovery rate	Increase	78% for A; 74% for B; 67% for C		
	Death rate	Decrease	Only one death in study (Group A)		"…Major variation in accuracy of the microscopy readings was found. Lack of qualified laboratory technicians at PHS facilities and the relatively short training period may have contributed to the shortcomings."
Nsimba, 2007	Dispensing of SP for mock patients	Increase	85% for intervention vs 55% for control	p<0.01	
	Received correct drug and correct dose	Increase	40% for intervention; 13% for control	p<0.01	

Table 7d. Outcomes Assessed for Interventions Focused on Oral Rehydration Therapy

Citation	Outcome	Intended Direction	Difference	P value	Notes
Pagaiya and Garner, 2005	% of diarrhea cases with Rx for oral rehydration solution	Increase	2.2 for intervention; -8.6 for control	p=0.026	
Ross-Degnan, et al., 1996	Sales of ORS	Increase	34% increase in intervention; 13% for control; 21% difference (95% CI: 3%, 39%)		
	Sales of antidiarheals	Decrease	-29% for intervention, -9% for controls; -20% difference (95% CI: -39%, -3%)		
Santoso et al., 1996	Use of ORS	Increase	+ 7.1% for A; + 5.7% for B; +2.4% for control	p>0.05	
	Use of Antimicrobials	Decrease	- 17% for A; -10% for B; -3.3% for control	p<0.01	
	Use of Antidiarrheals	Decrease	-7.8% for A; -21.5% for B; -0.4% for control	p<0.01	
	Use of polypharmacy	Decrease	-0.1% for A; -0.2% for B; -0.2% for control		