

# **Interventions to improve antimicrobial use: evidence from ICIUM 2004**

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## Acronyms

APUA	Alliance for Prudent Use of Antibiotics
ARI	Acute respiratory infection
FUO	Fever of unknown origin
GP	General practitioner
ICIUM	International Conference on Improving Use of Medicines
IMCI	Integrated Management of Childhood Illness
MSH	Management Sciences for Health
MTP	Monitoring, training, planning
OECD	Organization for Economic Co-operation and Development
PDSA	Plan-Do-Study-Act
RCT	Randomized controlled trials
RPM Plus	Rational Pharmaceutical Management Plus Programme
SEAM	Strategies for Enhancing Access to Medicines Programme
SMAC	Standing Medical Advisory Committee, UK
STGs	Standard treatment guidelines
STRAMA	Swedish Strategic Programme for Rational Use of Antimicrobial Agents and Surveillance of Resistance
TB	Tuberculosis
URTI	Upper respiratory tract infection
UTI	Urinary tract infection
WHO	World Health Organization

## Executive summary

Antibiotic resistance is a serious and growing problem. A range of interventions have been developed in various countries to improve the use of antimicrobials. Previous reviews have analysed the evidence on the success of interventions to improve the use of medicines in primary care settings in developing countries (Ross-Degnan et al., 1997), to improve the use of antimicrobials in developing countries (WHO, 2001) and to improve antibiotic prescribing in ambulatory care (Arnold and Straus, 2005). In 2004, the second International Conference on Improving Use of Medicines (ICIUM) was held in Chiang Mai, Thailand, and many papers were presented on antimicrobial use.

The aims of this analysis were to:

- identify papers presented at ICIUM 2004 related to improving antimicrobial use
- review well-designed evaluations of interventions to determine what these add to previous reviews
- review other papers presented at ICIUM looking at the extent and nature of irrational use of antibiotics, the range of interventions being developed around the world and factors which might foster or hinder the success of interventions.

One hundred and twenty-three papers related to antimicrobial use were identified. Sixty-eight papers described 60 evaluations of interventions (in some cases two or three papers described the same study). Of these, 18 studies (referred to as “key studies”) met methodological criteria for study design (pre and post with control, randomized controlled trials (RCT), time series), and adequate follow-up time (at least three months between intervention and follow-up), and were used to provide evidence about the effectiveness of different interventions.

The 26 descriptive studies (including those from 16 different single countries and two multi-country studies) show the extent and nature of problems of antibiotic use, and factors that need to be taken into account in designing interventions. The main issues described were high overall use, use for inappropriate indications, use of inappropriately short courses of antibiotics, lack of knowledge among patients and community members, and extensive supply of antibiotics from outside the formal health care system.

The 18 “key studies” were from seven countries in Asia, three in Latin America and one in Africa. Five studies focused particularly on improving the use of antibiotics while the others had a broader focus, including other medicines issues. Thirteen studies targeted health professionals and one targeted consumers. Others potentially impacted on both. Most studies related to respiratory infections and most used multi-faceted interventions. One was regulatory; one both regulatory and managerial; one regulatory and educational; one regulatory, educational and managerial; four managerial; four managerial and educational; four educational; and two economic. Four studies were randomized controlled trials, six were time series, five were pre and post studies

with a control group, and two were pre and post studies comparing the effect of two interventions. One intervention was evaluated by both a randomized controlled trial and a time series.

Ten studies reported at least one large impact (>30%). Only two studies had small or no impact (<10%) on the only outcome measured and one had a negative impact. All but one of the managerial interventions had a moderate to large impact on the outcome variables. Successful interventions included the teaching of management quality improvement strategies, and complex processes of development and implementation of treatment guidelines which encourage involvement and ownership by those who will use them. The educational interventions evaluated here were also quite effective and frequently involved the use of treatment guidelines.

Overall the interventions described seem more complex, interactive and multi-faceted than those described in previous reviews. They also seem to have been more successful in producing large or moderate changes.

Thirty-six studies evaluated specific interventions but were not judged to be methodologically adequate to provide good evidence of the impact of interventions. However, they do illustrate the type of interventions which are being carried out. Seventeen studies were from Asia, nine from Africa, six from the Russian Federation and the Newly Independent States, two from Europe and two from the USA. Four of the interventions were targeted towards the general public, two towards both the public and health providers, and 29 towards health-care providers. All of the four interventions solely targeted at the general public were aimed at children or young people, although two had adult targets as well. Four studies were directed towards private pharmacies or drug sellers. There were two regulatory interventions, eight managerial, seven managerial and educational, 12 educational, three economic or financial interventions and four concerned national policies. Fifteen interventions were targeted at the treatment of respiratory infections. Among this group of interventions there were many innovative educational initiatives. Although some studies of educational interventions had adequately designed evaluations, with pre and post measurements and control groups, many of the post measurements were taken immediately or very soon after the intervention. Of the eight studies excluded because of short follow-up, five were educational interventions. It is very important to test new innovative strategies appropriately and gather evidence about their long-term effect on knowledge or preferably behaviour.

In their conference presentations, some researchers outlined why they thought their intervention worked or did not. This has some limitations: for example, researchers themselves may not fully know why the intervention worked or not. However, the researchers do know a great deal about the interventions and the context, so their views provide useful additional information. They attributed success to the involvement of stakeholders, stakeholder ownership of the intervention(s), the use of evidence, and the intervention being enjoyable or providing benefits to participants. Most of the reasons given for failure of interventions were constraints on the ability of participants to change their practice. These constraints were said to be due to social and economic considerations, patient demand and organizational factors.

The ICIUM presentations illustrate the extent of excessive and inappropriate use of antibiotics in many countries, and the variety of interventions being carried out. They provide further evidence in support of multi-faceted interventions.

# 1. INTRODUCTION

Antimicrobial resistance costs money, livelihoods and lives and threatens to undermine the effectiveness of health delivery programmes (WHO, 2001a). Resistance has reached worrying levels for many common pathogens. For example, penicillin resistance in *S. pneumoniae* ranges from 5.8% to 54% in different countries (APUA, 2005). The UK Standing Medical Advisory Committee (SMAC) argues that resistance threatens a return to the pre-antibiotic era (SMAC, 1998).

The *WHO Global Strategy for Containment of Antimicrobial Resistance* attributes the growth of resistance to the failure to develop new antimicrobials since the 1980s, and to a combination of overuse, misuse, and under-use (WHO, 2001a). It has been estimated that 50% of antibiotic use is by humans (of which 80% is outside of hospitals), and 20-50% of this is unnecessary (Wise et al., 1998).

A range of interventions has been developed in various countries to address these and other drug use problems. Previous reviews have analysed the evidence about the success of these interventions (Ross-Degnan et al., 1997; WHO, 2001b).

In 2004, the second International Conference on Improving Use of Medicines (ICIUM) was held in Chiang Mai, Thailand. This brought together 472 leading national and international policy-makers, programme managers, researchers, clinicians, patient advocates and others representing 70 countries. Participants reported on the advances made since ICIUM 1997, including presenting a range of new intervention studies. ICIUM 2004 was collaboratively organized by: Boston University School of Public Health Center for International Health and Development; Harvard Medical School Department of Ambulatory Care and Prevention; Karolinska Institutet Division of International Health (IHCAR), the International Network for Rational Use of Drugs; Management Sciences for Health (through the Rational Pharmaceutical Management Plus (RPM Plus), and the Strategies for Enhancing Access to Medicines (SEAM) Programmes); the Thai Network for Rational Use of Drugs, and the World Health Organization (WHO) Department of Essential Drugs and Medicines Policy. This report reviews the presentations concerning antimicrobial use given at ICIUM 2004 and looks at what these add to the conclusions of previous reviews.

## Previous reviews

Ross-Degnan et al. (1997) reviewed published and unpublished intervention studies from developing countries on improving medicines use. All drug use issues were included, although they found that most studies focused on inappropriate antibiotic use. They developed a method for comparing the impact of various interventions, by looking at the largest percentage point improvement in a key outcome targeted by the intervention. The criteria for the review were that studies must be from developing countries, "broadly defined as countries in

Africa, Asia, and Latin America not on the Organization for Economic Co-operation and Development (OECD) list of industrialized countries; studies had to describe the results of a planned intervention or a clearly delineated policy targeting drug use in a primary care setting; and the studies needed to present clear accounts of methods and measure impacts in terms of defined outcomes". Of the 59 studies meeting these criteria the authors found 36 of satisfactory study design (randomized controlled trials (RCT), pre-post with control, time series). The most common types of intervention were educational (workshops or training courses) or community case management interventions aimed at community health workers. Others were administrative or managerial, such as audit and feedback, or the impacts of a national essential drugs programme. Most interventions targeted prescribing for acute respiratory infections (ARI).

The Ross-Degnan et al. (1997) review found that dissemination of printed materials alone consistently had no impact. Training had more impact if it utilized multiple modalities (for example, lectures, group problem-solving, role playing), repeated sessions, focused on one problem at a time, involved training at the worksite, or used opinion leaders or district-level staff as trainers. Community case management for ARI and diarrhoea was successful in reducing mortality. Administrative interventions based on group processes, effective supervision or monitoring, and regular audit and feedback had consistently moderate to large impacts.

Presentations on interventions to improve medicines use at the 1997 ICIUM conference were summarized and included on the conference website. This summary noted that the best evidence was on interventions to improve primary care prescribing. Similarly to the earlier Ross-Degnan et al. review, it concluded that focused, problem-oriented repeated training; supervision or self-monitoring using simple indicators; and peer group-oriented guideline development were effective.

In 2001, WHO published the report *Interventions and Strategies to Improve the Use of Antimicrobials in Developing Countries* (WHO, 2001b). This reviewed published and unpublished intervention studies on improving antimicrobial resistance. Thirty-six of these were selected on the basis of their methodology (RCT, before and after studies with comparison group, time series), geographical area (Africa, Asia, Latin America, Newly Independent States, or Eastern Europe), target (public and private sector health providers) and focus on antibiotic use in a range of target conditions. Using the methodology developed by Ross-Degnan et al., the authors categorized the interventions by type and reviewed the success of each type of intervention.

Their conclusions about successful interventions were similar to those of Ross-Degnan et al. That is, that simple dissemination of printed guidelines or information was unlikely to be effective, that well-designed educational/training interventions can be effective, and that the use of group processes, such as encouraging peer review, has great potential for improving antimicrobial use and sustaining improvements over time.

Each of these reports also highlighted a range of issues which tended to be neglected. Ross-Degnan et al. suggest that drug use for chronic illness in adults, and in the private sector were under-researched, and evidence was needed about

the cost-effectiveness of interventions. This was echoed in the summary of the first ICIUM conference, which also noted that hospitals in developing countries were under-researched. The 2001 review concluded that few studies had been done in the private sector, especially with drug sellers, or private doctors in out-patient settings and few on hospital in-patients. In addition, the authors concluded that little was known about patient and community use of antibiotics.

A 2005 Cochrane Review reviewed published studies evaluating interventions to improve antibiotic prescribing practices in ambulatory care (Arnold and Straus, 2005). This included interventions directed at either professionals or patients. The authors found 39 studies which met their methodological criteria. Most (35 studies) were conducted in developed countries. Findings were similar to other reviews. They found that printed educational material or audit and feedback alone led to no or only small changes to prescribing. Involving doctors in interactive meetings was more effective than giving lectures. Educational outreach and electronic or written reminders about prescribing produced mixed results. Patient-based interventions, particularly the use of delayed prescriptions, were successful. Multi-faceted interventions were the most successful.

## 2. AIMS AND METHODOLOGY

The aims of this analysis were to:

- identify papers presented at ICIUM 2004 related to improving antimicrobial use
- review well-designed evaluations of interventions in order to see what these add to previous reviews
- review other papers presented at ICIUM looking at the extent and nature of irrational use of antibiotics, the range of interventions being developed around the world, and factors which might foster or hinder the success of interventions.

### Methodology

Relevant studies were identified from the ICIUM website by a single reviewer. All those in the antimicrobial resistance stream were included, and those from other streams were examined to see if they included the use of antibiotics as a descriptor, as a target for intervention, or as an outcome measure for an intervention. One hundred and twenty-three papers were identified at this stage. These were categorized as either descriptive or intervention studies (or some other miscellaneous categories such as descriptions of interventions). The 26 descriptive studies are summarized in Section 4.

Sixty-eight papers were found which evaluate one or more changes or interventions. Summary data were recorded for all of these. These described 60 evaluations of interventions (in some cases two or three papers described the same study).

These studies were evaluated by the same single reviewer. Twenty-six were excluded on the grounds of inadequate study design, or because they were not yet complete (e.g. post-intervention data not yet analysed). As with previous reviews, studies with the following designs were included: RCT, before and after studies with a control group and time series (whether or not a control group was included). A wide definition of time series was used, and studies were included if four or more measures were used including at least one baseline measure. One study was excluded because of large differences between the control group and the intervention group at baseline, (Ofei et al.). A further eight studies were excluded because they had very short follow-up (less than three months between intervention and follow-up), or the follow-up time was unspecified (Cebotarenco et al., Dung et al. (b), Sia et al., Kristiansson et al.(b), Lerner et al.(a), Munawaroh et al., Tumwikirize et al., Th-Akib). Studies were included with shorter follow-up periods, if they had several waves of intervention and several waves of evaluation which meant that the total follow up period exceeded three months. One study was excluded because no antibiotic results were presented (Sharma et

al.). Six studies were excluded because they describe multiple interventions and did not include enough detail about any one to evaluate (Mackson et al. and Pont et al.; Gyansa-Lutterodt et al. and Ofori-Adjei et al.; Suryawati and Santoso; Gunn and Suleiman; Cars, Cars et al.; Qazi). These six are described in Section 7. The other 36 excluded studies are described further in Section 8 and antibiotic-related results are presented in Summary Table 3. The remaining 18 studies (referred to as the “key studies”) are reviewed in Section 5 and results are presented in Summary Table 1.

### 3. DESCRIPTIVE STUDIES

Twenty-six studies presented at ICIUM described the use of antibiotics. These were from 16 different single countries and in addition there were two multi-country studies. These show the extent and nature of problems of antibiotic use, and factors that need to be taken into account when designing interventions. The main issues described are high overall use, use for inappropriate indications, use of inappropriately short courses of antibiotics, lack of knowledge among patients and community members, and extensive supply of antibiotics outside of the formal health care system.

**Table 1: Descriptive Studies**

Country	Number of studies	Studies
Ethiopia	2	Andualem et al. (a) Andualem et al. (b)
Bangladesh	1	Roess et al.
Cambodia	1	Sothearith et al.
India	3	Hiremath et al. Kulkarni et al. Sathyanarayanan and Titus (Murali)
Europe	1	Harbarth et al. (a)
France and Germany	1	Harbarth et al. (b)
Indonesia	1	Hartayu et al.
Iran	1	Cheraghali et al.
Japan	2	Harbarth et al. (c) Okumura et al.
Kenya	1	Orwa et al.
Lao People's Democratic Republic	2	Houamboun et al. Sihavong et al.
Nepal	1	Tamang et al.
Peru	1	Kristiansson et al.
Senegal	1	Diagne et al.
Thailand	3	Suttajit et al. (a), (b) and (c)
United Republic of Tanzania	1	Shija and Malele
Viet Nam	2	Chien et al. Dung et al.
Zimbabwe	1	Trap and Hansen

## Health services measures of antibiotic use

Very high levels of antibiotic use were reported in a wide range of countries. For example, in public health facilities in the United Republic of Tanzania, 42% of patients received antibiotics (Shija et al.). In a free medical service for economically disadvantaged people in Kenya, 46% of patients received antibiotics. In a large sample of prescriptions from Tamil Nadu, India, 54.4% included at least one antibiotic (Murali et al.). A study in a range of both public and private health services in Mumbai, India, found that antibiotics made up 25-30% of drugs dispensed (Kulkarni et al.). The average number of antibiotics per encounter was 0.72 among dispensing doctors and 0.54 in non-dispensing doctors in Zimbabwe (Trap and Hansen).

High levels of prescribing were also found in relation to specific health problems. In Bangkok, Thailand, 63% of patients with upper respiratory tract infections (URTIs) in Bangkok, Thailand, were prescribed an antibiotic. Although patients were more likely to be prescribed antibiotics for bacterial conditions, 60% of those with likely viral conditions were prescribed antibiotics (Suttajit et al. (b)). In Indonesia, 90% of the 273 cases of fever of unknown origin (FUO) were prescribed antibiotics, despite antibiotics not being recommended for this diagnosis (Hartayu et al.).

The only study reporting a low level of antibiotic use as percentage of prescriptions was done in Durban, South Africa, where 12% of prescriptions dispensed in pharmacies were antibiotics (Gray et al.).

The prescribing and dispensing of incomplete doses was reported in several studies. For example, in Zimbabwe, sub-curative doses were prescribed in almost 18% of encounters with dispensing doctors (Trap and Hansen) and in Mumbai, India, 75-100% of antimicrobials were given in incomplete dosages at general practitioner (GP) clinics and municipal dispensaries (Kulkarni et al.).

Some studies were able to investigate which kinds of doctors and patients were more likely to prescribe or be prescribed antibiotics. In the study in Thailand, among patients who were likely to have viral conditions, young male patients who were paying for their own care were more likely to receive antibiotics. Among those with bacterial URTIs, those paying for their own treatment were more likely to get antibiotics than those under national health insurance (Suttajit et al. (a)). In Zimbabwe, Trap and Hansen found more prescribing and less appropriate prescribing of antibiotics among dispensing doctors compared to non-dispensing doctors.

## Interview studies

Some descriptive studies included interviews with providers. Houamboun et al. interviewed drug sellers and their clients, and observed their interactions. They found that drug sellers had limited knowledge of correct drug use and did not provide much information to customers, especially in relation to antibiotics.

Interviews with lay people were more common. Some researchers interviewed people who were receiving health care (i.e. patients). This has the advantage that their prescription medicines can be studied at the point of prescribing/dispensing, but skews the sample towards those that use the kind of health care facility where the interviews occur. In other studies, community members were interviewed in their homes or elsewhere, which can provide a better picture of overall drug use.

In Cambodia, Sothearith et al. interviewed 50 patients at a children's hospital pharmacy. These patients had previously taken drugs for the same illness which they had obtained elsewhere. Among the most common problems found were the use of chloramphenicol and tetracycline without a correct indication, and incorrect duration of antibiotic use. Seventy-nine per cent of antibiotics obtained from pharmacies and 92% of those obtained from drug sellers were incomplete courses.

In a study in Addis Ababa, Ethiopia, 1200 people who came to pharmacies for self-medication were asked about their knowledge of medicines. They were asked which drugs they knew about, and six of the 15 most frequently recalled drugs were antibiotics. Nearly half of the patients reported that they stopped taking medicines when their symptoms were relieved, rather than following the instructions of the health-care provider. The researchers observed that more than 100 different types of drugs were requested, of which 26.4% were antimicrobials (Andualem (a) and (b)). In Mumbai, India, less than 10% of patients knew the reason for the antibiotic prescriptions they were given, nor did they know that incomplete doses can lead to resistance (Kulkarni et al.).

Studies of community members were carried out in Bangkok (Suttajit et al.), eastern Nepal (Tamang et al.), Lao PDR (Sihavong et al.), Bangladesh (Roess et al.), Peru (Kristiansson et al.) and Viet Nam (Dung et al., Larsson et al.). These studies found high levels of antibiotic use, much of it for inappropriate indications and much of it involving little contact with the formal health sector. They also found little understanding of antibiotics and many folk-beliefs about illness and treatment.

In crowded areas of Bangkok, researchers visited households and interviewed 779 people who had had URTIs within the previous two weeks. Based on the symptoms they described, and using established clinical scoring systems, 81% of the infections were likely to be viral. Patients had taken antibiotics for 44% of the viral and 54% of the bacterial infections. Half of the interviewees had sought treatment in drug stores and 65% of these received an antibiotic. Of those who attended doctors, 61% of those with probable viral infections and 71% of those

with probable bacterial infections received antibiotics (Suttajit et al. (b)). In Lao PDR, 500 people who had self-medicated for reproductive tract infections were interviewed. They used drug stores as their first option for seeking treatment. Sixteen per cent reported use of antibiotics, with many using incorrect doses and treatment duration (66%) (Sihavong et al.). In Peru, 36% of children with symptoms of any illness had used antibiotics in the previous two weeks. However this study found low levels of self-medication (Kristiansson et al.). A study in Viet Nam about the treatment of ARIs in children found that about 80-90% of mothers bought antibiotics without prescriptions from drug vendors. Many who received prescription antibiotics did not use them in compliance with the prescription. Over one third of mothers reported using antibiotics for children when they only have a cough and cold (Dung et al.). Another study in Viet Nam found that in 200 children from randomly selected households, 82% had symptoms of ARI, and 75% had used antibiotics within one month of the study. Seventy-eight per cent of the antibiotics were obtained without consulting a doctor (Larsson et al.).

In the Bangkok study, the researchers found that those they interviewed did not distinguish antibiotics from anti-inflammatory drugs and used the same term for both (108b). Similarly, community members in eastern Nepal had poor understanding of antibiotics, using various terms for them such as drug for pneumonia, and fever-reducing drug (Tamang et al.). In a study of people in Lao PDR who had self-medicated for reproductive tract infections, 54% did not know what antibiotic meant (Sihavong et al.). In Peru, people were found to have elaborate theories on diseases, their origin, and proper treatment. Antibiotics were seen as strong medicine so people were concerned about taking a full course. People lacked information about antibiotics and were worried about the quality of drugs they obtained from the public sector. The authors argue that lack of communication between patients and providers, economic constraints, and traditional beliefs lead to low compliance and high levels of self medication (Kristiansson et al.).

Studies carried out in communities, using a variety of qualitative and quantitative methods, provide some very useful insights into antibiotic use. For example, in eastern Nepal a study about the treatment of ARIs in children found that although mothers were the principal care-givers for sick children, they did not make decisions about their treatment. These were made by older and respected members of the community (Tamang et al.). Another study in rural Bangladesh involved field observation, interviews with householders, and a range of different health care providers for people and animals (Roess et al.). This documents the extent of both human and environmental exposure to antibiotics in rural Bangladesh. High levels of animal ownership were found and animals were economically important and therefore prized possessions. More was spent on health care for animals than for humans, and there was a high level of use of antibiotics for animals. Much of this involved sub-optimal doses. Many animals lived inside houses with household members (which the authors suggest would facilitate the transmission of resistant organisms).

## Country level studies

Studies comparing different countries provide insights into national-level cultural and social factors which affect antibiotic use. Harbarth et al. (b) compare France, where there is a much higher level of antibiotic resistance, with Germany, where resistance is lower. For example, the rate of penicillin-nonsusceptible pneumococci is 43% in France, compared with 7% in Germany. Retail sales of antibiotics are about three times higher in France than in Germany and in Germany narrow-spectrum antibiotics are used more frequently. Harbarth et al. (b) explore possible reasons for these differences. These include higher prescribing for respiratory tract infections in France, patient demand and health beliefs, differing childcare and breastfeeding practices and regulatory differences. National variations in Europe are explored more quantitatively in Harbarth et al. (a), which explores variation in rates of macrolide-resistant *streptococcus pneumoniae* in 14 European countries. Factors positively correlated with this variation were: total macrolide use, use of broad-spectrum antibiotics, misuse of antibiotics, attendance at preschool, and foreign travel (the latter two facilitate transmission of resistant bacteria). Negative correlates were: breastfeeding, general vaccination coverage, physical activity of adults, the responsiveness of the health care system (a measure of how well the health system performs relative to non-health aspects, such as choice of providers and client orientation), and high use of narrow-spectrum penicillins. Population density and low socio-economic status were not correlated with levels of resistance.

## Levels of resistance

Some studies describe patterns of resistance. For example a Japanese study (Okumara et al.) reported the results of testing of samples of *Shigella sonnei* from quarantine stations. Ninety per cent were resistant to at least one antimicrobial, and 80% were resistant to more than two. In 1999, 47% of the Indonesian strains tested were resistant to more than four antimicrobials. Chien et al. (129) describe a resistance surveillance programme in Viet Nam. High levels of resistance to cotrimoxazole and ampicillin were found in bacteria causing UTIs and ARIs, and high resistance among *pseudomonas aeruginosa* and *staphylococcus aureus*.

## Summary of descriptive studies

Descriptive studies are very important for showing the dimensions of the problem of irrational use of antibiotics, providing insights into possible causes of the problem and targets for change. The studies reviewed here describe very high levels of antibiotic use in a range of settings and countries, a great deal of use for inappropriate indications, considerable use of incomplete courses of treatment, wide availability of antibiotics from pharmacies and drug sellers, and little understanding of antibiotics among lay people. They suggest that lay people may not have a distinct category of "antibiotics" which they distinguish from other drugs and that folk beliefs about health and illness are an important influence on how people use antibiotics. One study points out that patients or their carers may not make their own decisions about treatment. Other important

people in the community may make these decisions. In general these studies point to the importance of understanding people's lives, (such as the importance of animal husbandry, childcare practices, etc.) in order to develop interventions to improve antibiotic use in both developed and developing countries.

## 4. INTERVENTION STUDIES

Eighteen studies evaluated interventions and met the methodological criteria set out above. They are summarized in the Summary Table 1. These 18 studies were from 11 countries, and were described in 22 conference presentations.

**Table 2: Intervention studies**

Country	Number of studies	Studies
Indonesia	5	Hidayati and Munawaroh Sunartono Suryawati Wan Dwiprahasto and Kristin Yudatiningsih et al. (a) and (b)
Philippines	3	Alejandria et al.; Berba et al. Saniel et al. Valera et al.
Nepal	3	Holloway et al. Kafle et al. Shrestha et al.
Chile	1	Bavestrello and Cabello
Viet Nam and Thailand	1	Chalker et al.; Chuc et al.; Larsson et al.
Iran (Islamic Republic of)	1	Darbooy et al.
Lao PDR	1	Kounnavong et al.
Colombia	1	Perez et al.
Mexico	1	Reyes et al.
South Africa	1	Summers et al.

Five studies focused particularly on improving the use of antibiotics (Bavestrello and Cabello, Alejandria et al., Perez et al., Saniel et al., Yudatiningsih et al.), while the other 10 had a broader focus, including other medicines issues. Three involved general changes which impacted on other medicines as well as antibiotics (Sunartono, Suryawati, Valera et al.). Thirteen studies targeted health professionals and one targeted consumers (Darbooy et al.). Others (Bavestrello, Cabello, Holloway et al., Suryawati, Valera et al.) potentially impacted on both health professionals and consumers. The health professionals included hospital staff (Alejandria et al., Kounnavong et al., Perez et al.), doctors in primary care (Reyes et al., Saniel et al.), other primary health care providers (Dwiprahasto and Kristin, Hidayati et al., Kafle et al., Shrestha, Yudatiningsih et al., Summers et al., Holloway et al.), and drug sellers (Chalker et al.).

Most studies related to respiratory infections (Dwiprahasto and Kristin, Hidyati et al., Kafle et al., Kounnavong et al., Reyes et al., Shrestha, Yudatiningsih et al., Summers et al.). Four studies were on general use of antibiotics (Bavestrello and Cabello, Chalker et al., Darbooy et al., Holloway et al.), three on diarrhoea (Dwiprahasto and Kristin, Kafle et al., Kounnavong et al.) and one looked at diarrhoea and vomiting (Summers et al.). Two studies covered issues in hospitals (infection control (Alejandria et al.), and parenteral use (Perez et al.)). Other issues addressed were urinary tract infections (Saniel et al.), and fever of unknown origin (Kafle et al.). Some of the studies also addressed other illnesses, such as diabetes.

As in previous reviews, interventions were classified as regulatory, educational, managerial or economic. In some cases classification was difficult because, for example, the distinction between educational and managerial interventions is sometimes blurred. Interventions were classified as educational if they involved teaching about antibiotics, appropriate prescribing, etc. If they involved teaching about a managerial strategy, such as the PDSA (Plan-Do-Study-Act) cycle, they were classified as managerial, since the main aim was to implement a new management strategy.

Most studies used multi-faceted interventions. No attempt was made to classify interventions according to one dominant type. Thus each study had up to three different types of interventions.

**Table 3: Types of interventions**

<b>Types of interventions</b>	<b>Number</b>	<b>Reference</b>
Regulatory	1	Valera et al.
Regulatory and managerial	1	Sunartono
Regulatory and educational	1	Bavestrello and Cabello
Regulatory, educational and managerial	1	Chalker et al.; Chuc et al.; Larsson et al.
Managerial	4	Alejandria et al.; Berba et al. Hidyati et al. Kounnavong et al. Yudatiningsih et al. (a) and (b)
Managerial and educational	4	Dwiprahasto and Kristin Kafle et al. Perez et al. Reyes et al.
Educational	4	Darbooy et al. Saniel et al. Shrestha Summers et al.
Economic	2	Holloway et al. Suryawati

Five studies involved development or implementation of treatment guidelines (Hidyati et al., Kafle et al., Reyes et al., Saniel et al., Shrestha). Four studies were randomized controlled trials (Chalker et al., Hidayati et al., Kounnavong et al., Shrestha, Yudatiningsih et al. (b)), six were time series (Bavestrello and Cabello, Alejandria et al., Perez et al., Sunartono, Suryawati, Valera et al.), five were pre and post studies with a control group (Darbooy et al., Dwiprahasto and Kristin, Reyes et al., Summers et al., and Holloway et al.), and two were pre and post studies comparing the effect of two interventions (Kafle et al., Saniel et al.). One intervention was evaluated by both a randomized controlled trial and a time series (Yudatiningsih et al. (a)).

## **Outcome measures:**

For one study evaluating the impact of a regulatory measure (Bavestrello and Cabello), aggregate consumption for the whole country was the outcome measure. In seven other studies the proportion of prescriptions (for the target condition(s) where appropriate) which included an antibiotic was the outcome measure (Dwiprahasto and Kristin, Hidayati et al., Shrestha, Yudatiningsih et al., Summers et al., Sunartono, Suryawati). Two of these studies (Shrestha et al., Sunartono) and seven others, used an indicator of prescribing appropriateness as their outcome measure(s), such as following a treatment guideline, appropriate timing of antibiotics in relation to surgery (Alejandria et al., Kafle et al., Kounnavong et al., Perez et al., Reyes et al., Saniel et al.). One of these (Alejandria et al.) used a range of outcomes set by the participating hospitals themselves. Other outcome measures included the number of medicines stored in people's homes (Darbooy et al.), the sale of an inappropriately small amount of antibiotics and the questions asked and advice given by drug sellers (Chalker et al.). Holloway et al. looked at the prescribing of inappropriately small quantities of antibiotics as well as the proportion of prescriptions which included an antibiotic. Valera et al. included costs of antibiotics as a percentage of monthly drug costs.

## **Effectiveness of different interventions**

The table below follows the methodology developed by Ross-Degnan et al. in presenting the largest reported improvement in a drug use indicator targeted by the interventions. In this table, only impacts on antibiotics are presented (although some studies addressed other medicines as well). Fuller details about the impact of each intervention are in the Summary Table 1 and the limitations of this methodology are discussed in the Conclusion.

Ten studies reported at least one large impact (>30%). Only two studies had a small or no impact (<10%) on outcomes measured. One had a negative impact.

**Table 4: Effect of different types of interventions**

<b>Type of Intervention</b>	<b>Reference</b>	<b>Measure</b>	<b>Effect (percentage points)</b>
<b>Regulatory</b>			
Expanded insurance coverage for medicines	Valera et al.	Antibiotic costs as percentage of monthly expenditure	No change
<b>Regulatory and managerial</b>			
Responses to decentralization, including Monitoring-Training-Planning (MTP), training, recruitment, incentives for prescribers	Sunartono	% of antibiotic prescriptions for less than 5 days	-75
<b>Regulatory and educational</b>			
Restricting antibiotics to prescription only, posters and leaflets	Bavestrello and Cabello	Sales from private pharmacies in USD millions	-32.5
<b>Regulatory, educational and managerial</b>			
Enforcement of regulations about prescription-only medicines, education, peer review	Chalker et al.; Chuc et al.; Larsson et al.	Sale without asking questions or giving advice	One site: -30
<b>Managerial</b>			
Workshop on PDSA (plan-do-study-act) rapid cycle model	Alejandria et al.; Berba et al.	Adherence to appropriate antibiotic prophylaxis in elective caesarean sections	+90
Small group discussions, self-assessment discussions, feedback seminar to improve compliance with STGs	Hidayati et al.	% ARI prescriptions including antibiotics	-41
Monthly audit sessions	Kounnavong et al.	Treatment indicator scores	+4
Monitoring-Training-Planning approach, followed up by feedback	Yudatiningsih et al. (a) and (b)	% child ARI prescriptions including antibiotics	-37

Table 4 continued

<b>Managerial and educational</b>			
Training, followed by self-monitoring, supervision and feedback	Dwiprahasto and Kristin	% prescriptions for diarrhoea which include antibiotics	-63.7
Small group training OR small group training plus peer-group discussion to improve use of STGs	Kafle et al.	Use of co-trimox+ paracetamol for pneumonia % non-pneumonia cases given antibiotics	not enough detail provided to calculate  not enough detail provided to calculate
Structured antibiotic order form, educational campaign, posters	Perez et al.	Aminoglycosides in dose intervals less and 24 hours	-47
Developing clinical guidelines, training, peer review sessions	Reyes et al.	Following of clinical guidelines for ARI	+37.7
<b>Educational</b>			
Public education sessions	Darbooy et al.	Number of antibiotics stored at home	-63
Interactive session with feedback to disseminate guidelines	Saniel et al.	Appropriate antibiotic prescriptions for acute cystitis	+26
Training in guidelines	Shrestha et al.	Correct prescriptions for lung disease	+50
Training in effective prescribing	Summers et al.	% URTI prescriptions including antibiotics	-31.3
<b>Economic</b>			
Fee for drug unit versus fee for drug item	Holloway et al.	% antibiotics prescribed in under-dose	+12
Currency crisis	Suryawati	% of prescriptions including antibiotics	+8.5

All of the studies succeeded in improving antibiotic use, apart from Holloway et al. which was monitoring how a change in prescription fees affected prescribing. In this case there was a significant increase in the prescribing of incomplete courses of antibiotics with a fee per unit as compared to a fee per drug item (covering a full course). National policy changes and economic crises mostly had

no, or a negative effect, on antibiotic use. Although the decentralization of drug management allowed one province in Indonesia to introduce a range of measures to improve antibiotic prescribing, it did not have this effect in other provinces. The currency crisis in Indonesia in 1998 did not lead to any decrease in the proportion of prescriptions which included antibiotics. Expanded insurance coverage for medicines in the Philippines did not lead to any increase in the appropriateness of antibiotic prescribing.

The prohibition of over-the-counter sales of antibiotics in Chile (with an accompanying educational campaign) (Bavestrello and Cabello) had a seemingly moderate impact on the consumption of antibiotics from private pharmacies. However, because this was a nationwide measure, its overall impact may have been extremely large. Further data are needed on the impact of the strategy on consumption in the public sector (hospital and 'primary attention' pharmacies (Cabello, personal communication).

All but one of the managerial interventions evaluated had a moderate to large impact on the outcome variables. Successful interventions included the teaching of management quality improvement strategies, and complex processes of development and implementation of treatment guidelines which encourage involvement and ownership by those who will use them. The educational interventions evaluated here were also quite effective, and frequently involve the use of treatment guidelines.

## Summary

These eighteen studies provide the best evidence about the impact of various interventions. Consistent with previous reviews, they report success from multifaceted strategies. Studies presented at ICIUM suggest that managerial interventions can be particularly successful.

## 5. EVALUATION OF PACKAGES OF INTERVENTIONS

Nine papers described the implementation and effect of six different broad approaches to improving medicines use. These papers did not include enough information about any particular intervention or its effect to be included in the 18 key papers (Section 5).

**Table 5: Studies of packages of interventions**

Country	Number of approaches studied	Studies
Australia	1	Mackson et al., Pont et al.
Ghana	1	Gyansa-Lutterodt et al., Ofori-Adjei et al.
Indonesia	1	Suryawati and Santoso
Oman	1	Gunn and Suleiman
Sweden	1	Cars, Cars et al.
International	1	Qazi

The six intervention types were the Swedish Strategic Programme for the Rational Use of Antimicrobial Agents and Surveillance of Resistance (STRAMA) (Cars, Cars et al.), the Directorate of Rational Drug Use in Oman (Gunn and Suleiman), the Antibiotic Campaign of the National Prescribing Service in Australia (Pont et al., Mackson et al.), the Comprehensive Pharmaceutical Sector Development Programme in Ghana (Ofori-Adjei et al., Gyansa-Lutterodt et al.), IMCI (Integrated Management of Childhood Illness) (Qazi), and the MTP approach (Suryawati and Santoso).

STRAMA (Cars, Cars et al.) is a cross-sectoral initiative which operates at both national and local levels. At national level, media and information campaigns have been carried out. Groups within each county in Sweden also carry out their own initiatives, evaluating use and resistance in their region and working to improve prescribing patterns. Their activities have included the development of local treatment guidelines and the implementation of these using strategies such as feedback to prescribers and patient information leaflets. Free return visits are offered for patients with respiratory tract infections, so that patients know that if their condition worsens they can return to get an antibiotic prescription. STRAMA appears to have been successful in reducing antibiotic use in Sweden, particularly in children. National sales of antibiotics decreased by 22% from 1993 to 2002 and resistance levels are generally stable and low.

In Oman, the Directorate of Rational Drug Use was established to address rapidly escalating drug expenditure. The Directorate undertakes studies of drug use, distributes information, and carries out workshops, courses and a Rational Drug Use exam for new GPs. It has also created an Omani National Formulary.

In 2002, a 7% reduction in the national use of antibiotics was achieved (Gunn and Suleiman).

The National Prescribing Service in Australia carried out a five year intervention programme to encourage appropriate prescribing of antibiotics for URTIs in primary care (Pont et al., Mackson et al.). GPs could participate in academic detailing, clinical audit, case studies and small group discussions. All GPs were sent printed publications and feedback about their prescribing. A consumer awareness campaign included media advertising and small grassroots meetings. The number of antibiotic prescriptions per 100 URTI encounters fell from 42.1 to 33.1. An increase in the use of first-line agents for URTI, acute otitis media, sinusitis and tonsillitis was also observed.

The Ghana National Drugs Programme was established in 1997 (Ofori-Adjei et al., Gyansa-Lutterodt et al.). The core of this programme was the promotion of the rational use of drugs. A National Drugs Policy was developed and implemented, standard treatment guidelines were developed and distributed, and training programmes for clinical pharmacy and Drug and Therapeutics Committees were established. Rational use of drugs focal persons were appointed for each region. The use of antibiotics had been rising (46.6% of prescriptions in 1993 to 56.0% in 1998), but after five years of the programme it dropped to 42.5% (2002).

The WHO/UNICEF Integrated Management of Childhood Illnesses (IMCI) programme involves, among other things, case management training of health workers. It addresses a range of the most common childhood illnesses. The programme has been implemented and evaluated in Bangladesh, Brazil, Peru, Uganda and the United Republic of Tanzania, using a variety of study methods. Evidence presented at ICIUM suggests that this has led to an increased proportion of children needing antibiotics being prescribed them correctly, a large increase in the proportion of caregivers advised how to administer oral antibiotics and reductions in misuse of antibiotics (Qazi).

The MTP (Monitoring-Training-Planning) approach has been mentioned above and specific evaluations of it are included in the 18 key studies (Section 5). In the MTP approach, a team is set up within a hospital or health centre. This team identifies a priority problem and then plans a series of meetings involving people who contribute to the problem. The MTP cycle involves describing the situation, reflection on previous experience and problem solving, and setting targets for improvement. One problem is usually addressed by three to five meetings. Evidence from a range of hospitals and health centres in three Asian countries suggests that MTP can be very effective in addressing problems of inappropriate antibiotic use (Suryawati and Santoso).

## Summary

These papers described programmes that involved a coordinated range of initiatives, targeted at improving either prescribing and use of medicines in general, or antibiotics in particular. These initiatives appear to have been very successful in reducing consumption at a national level.

## 6. OTHER INTERVENTION STUDIES

Thirty-six studies evaluated specific interventions but were excluded from the analysis in Section 5 because of problems with their study design or because they (or the reporting of them) were incomplete (27 studies), short follow-up period (8), or large differences between intervention and control groups at baseline (1). While these studies cannot provide reliable evidence about the impact of interventions, they do illustrate the type of interventions which are being carried out.

**Table 6: Other intervention studies**

Country	Number of interventions	Studies	Reason for exclusion from 5
Bangladesh	1	Akter et al.	Abstract only
Cambodia	1	Srun and Sokhan	Study design
People's Republic of China	2	Ran and Tomson Qing et al.	Study design Study design
Ghana	1	Ofei et al.	Large differences between control and intervention groups, pre-intervention
India	1	Sharma et al.	Study design
Indonesia	3	Munawaroh et al. Suryawati et al. Th-Akib	Short or unspecified follow-up period Study design Short or unspecified follow-up period
Kazakhstan	2	Gulaev et al. (presented by Lobyntsev) Nurgozhin	Study design Study design
Kenya	2	Gitau and Kiambuthi Kiambuthi	Study design Study design
Republic of Korea	1	Park et al.	Study design
Kyrgyz Republic	1	Toktobaeva and Karymbaeva	Study design
Lao PDR	1	Sisounthone et al.	Study design
Malaysia	1	Babar et al.	Study design
Moldova	1	Cebotarenco et al.	Short or unspecified follow-up period
Namibia	1	Lates and Shiyandja	Study design

Nepal	4	Holloway and Gautam (a) Holloway and Gautam (b) Karkee et al. Prasad et al.	Study design Study design Study design Incomplete
Nigeria	2	Abu Isah et al.	Study design Study design
Philippines	1	Sia et al. (presented by Galang)	Short or unspecified follow-up period
Russian Federation	1	Ziganshina et al.	Study design
South Africa	1	Cassimjee et al.	Study design
Sweden	2	Kristiansson et al. (b) Stålsby Lundborg et al.	Short or unspecified follow-up period Study design
Tajikistan	1	Makhmudova	Study design
Uganda	1	Tumwikirize et al.	Short or unspecified follow-up period
USA	2	Lerner et al. (a) Lerner et al. (b)	Short or unspecified follow-up period Study design
Viet Nam	1	Dung et al. (b)	Short or unspecified follow-up period
Zambia	1	Kandeke et al.	Study design

Seventeen studies were from Asia, nine from Africa, six from the Russian Federation and the Newly Independent States, two from Europe and two from the USA. Four of the interventions were targeted towards the general public (Cebotarenco et al., Kristiansson et al. (b), Lerner (b), Th-Akib) two towards both the public and health providers (Abu, Karkee et al.), and 29 towards health care providers. One study on privatization of the medicines procurement and distribution agency was not targeted directly at providers or public. All of the four interventions solely targeted at the general public were aimed at children or young people, although two (Cebotarenco et al., Th-Akib) had adult targets as well. Four studies were directed towards private pharmacies or drug sellers (Sia et al. (presented by Galang), Stålsby-Lundborg et al., Holloway and Gautum (b), Tumwikirize et al.). Interventions directed towards hospital staff often did not specify whether hospitals were public or private.

The types of intervention described are outlined in the table below. These were often simpler and less multi-dimensional than those described in Section 5. A large proportion were purely educational interventions.

**Table 7: Types of interventions in studies which did not meet methodological criteria**

Type of interventions	Number of studies	Studies
Regulatory	2	Stålsby-Lundborg et al. Park et al.
Managerial	8	Cassimjee et al. Dung et al. Munawaroh et al. Prasad et al. Sisountho et al. Srun and Sokhan Surywati et al. Toktobaeva and Karymbaeva
Managerial and educational	7	Akter et al. Kiambuthi Makhmudova Nurgozhin Ofei et al. Qing et al. Sharma et al.
Educational	12	Cebotarenco et al. Gitau and Kiambuthi Gulaev et al. (presented by Lobyntsev) Kandeke et al. Karkee et al. Kristiansson et al. (b) Lerner et al. (a) Lerner et al. (b) Sia et al. (presented by Galang) Tumwikirize et al. Ziganshina et al. Th-Akib
Economic/ financial	3	Holloway and Gautam (a) Holloway and Gautam (b) Ran and Tomson
National policy (national drug policy, health services provision)	4	Abu Isah et al. Lates and Shiyandja Babar et al.

As in the eighteen key studies, many interventions related to respiratory infections (Dung et al. (b), Karkee et al., Munawaroh et al., Nurgozhin, Tumwikirize et al., Abu, Sia et al. (presented by Galang), Cebotarenco et al., Ofei et al., Gitau and Kiambuthi, Akter et al., Suryawati et al., Lerner (a), Ziganshina et al., Sharma et al., Gulaev et al. (presented Lobyntsev), Prasad). Thirteen were on the general use of antibiotics (Cassimjee et al., Holloway and Gautam (a) and (b), Isah et al., Kandeke et al., Kiambuthi, Kristiansson et al. (b), Lates and Shiyandja, Lerner et al. (b), Makhmudova, Ran and Tomson, Toktobaeva and Karymbaeva, Th-Akib), and four on diarrhoea (Abu, Akter et al., Prasad et al. Suryawati et al., Sharma et al.). Four papers included the use of antibiotics in surgery (Qing et al., Gulaev et al. (presented Lobyntsev), Suryawati et al., Srun and Sokhan). Some of the studies also addressed other illnesses, such as malaria, hypertension and asthma.

Among this group of interventions there were many innovative educational initiatives. For example, Cebotarenco et al. carried out a school-based project in Moldova which aimed to involve school children in reducing unnecessary antibiotic use for colds and flu. Students were trained to train other students and parents about antibiotic use. Meetings with opinion leaders and focus group discussions with parents, students, teachers and doctors were used to develop the intervention. In Indonesia, Th-Akib reported on a poster competition to promote rational use in the community. Women from women's associations and students from high schools were given written information about either rational use of antibiotics or about generic drugs and asked to make posters based on this information. In the Philippines, Sia et al. (paper presented by Galang) reported on an intervention to improve the practices of drug sellers. Mothers and drug sellers participated together in group discussions about TB, ARI and influenza. Drug sellers were given copies of leaflets on the rational use of these conditions to share with other sellers and clients.

Although some studies of educational interventions had adequately designed evaluations, with pre and post measurements and control groups, many of the post measurements were taken immediately or very soon after the intervention. Of the eight studies excluded because of short follow-up, six were educational interventions, and these included two targeted at drug sellers, one at doctors, and three at children (one of these included parents, and another women in women's groups). It is very important to test new innovative strategies appropriately and gather evidence about their long-term effect on knowledge or preferably behaviour.

## Summary

Limitations in study design mean that these studies cannot provide evidence of the impact of interventions. However they provide a good picture of the range of interventions being carried out to improve antibiotic use. Most interventions were from developing countries and most were targeted at health professionals. Those that targeted the general public included innovative educational initiatives often aimed at children and young people. It is important that good studies are designed to evaluate these.

## 7. RESEARCHERS' ACCOUNTS OF WHY INTERVENTIONS WORKED OR NOT

As well as showing the range of interventions tried and providing evidence of the quantitative impact of various interventions, the ICIUM 2004 papers provide qualitative data giving reasons why interventions might succeed or fail. In the discussion section, some researchers outline why they think their intervention worked or not. This has some limitations: researchers themselves may not know exactly why the intervention worked or not and not all of them discuss this in their papers as so much data is missing. However the researchers do know a great deal about the interventions and the context, so their views provide useful additional information.

### Reasons for success

The researchers who evaluated successful interventions attributed the success to involvement of stakeholders, stakeholder ownership of the intervention(s), the use of evidence, and the intervention being enjoyable or providing benefits to participants.

In managerial interventions, such as MTP, or the use of guidelines, researchers stressed the involvement of the prescribers in the development of initiatives or in guidelines as an ingredient for success (Suryawati and Santoso, Sisounthone, Srun and Sokhan). For educational initiatives, such as the Swedish programme teaching children about antibiotics and resistance, the involvement of children in the design of the material was given as a reason for success of the programme (Kristiansson et al.). The involvement of participants such as prescribers in the delivery of the intervention provided a range of benefits. In Indonesia, an intervention targeted at paramedics used trained paramedics as facilitators of group discussion about standard treatment guidelines. They suggest that this allowed participants to talk more freely and reduced their resistance to new ideas (Munawaroh). Similarly in Cambodia, the involvement of stakeholders in the hospital allowed any potential negative consequences of rational drug use to be discussed within the hospital and interventions to be designed accordingly (Srun and Sokhan).

The ownership of interventions by participants was regarded as important and this is a particular feature of the MTP approach. This allows participants (e.g. MTP groups within hospitals or health centres) to set their own goals and work on projects that are important to them. This and other successful managerial interventions also allow participants to find solutions that are feasible and achievable within their practice setting (Suryawati and Santoso, Sisounthone, Srun and Sokhan, Alejandria et al.). Similarly, encouraging community ownership and participation in educational interventions was regarded as important. In Moldova, the parents of students who had been trained as peer and parent educators were reported to be very proud of them and to encourage their activities (Cebotarenco et al.).

Interventions in which participants developed their own solutions to drug use problems, or their own practice guidelines, may increase commitment to these solutions and guidelines. In Indonesia, it was reported that when groups of paramedics agreed how they would treat ARI, there was group pressure on individual paramedics to stick to these guidelines (Munawaroh). In an educational initiative for children in the US, the researchers also asked children to commit to being deputy 'resistance rangers' (Lerner (b)).

The use of good evidence was also suggested by some researchers as an ingredient for success. This included use of evidence-based interventions, the use of individual or group prescribing data, and the use of immediate feedback of the impact of the intervention. (Alejandria et al., Hidayati).

Some researchers attributed the success of their programmes to the benefits gained by the participants. These included team development and empowerment in some managerial approaches. Educational initiatives were described as fun and easy to use. The researchers from the Moldovian programme of peer education for children reported that students like to be taught by peers and that peers use simple language and attractive teaching methods and create a positive, friendly atmosphere (Cebotarenco et al.).

## Reasons for failure

Most of the reasons given for failure of interventions were constraints on the ability of participants to change their practice. These constraints were the result of social and economic considerations, patient demand and organizational factors.

Social considerations were mentioned in two studies. In the Philippines an educational initiative among drug sellers did not affect drug sellers' decisions about whether to dispense an erroneous prescription. This was thought to be because drug sellers (who were less educated and often young) were not able to question the decisions of those with higher knowledge (doctors) (Sia et al.). In Viet Nam, researchers found that drug sellers were reluctant to recommend condom use because of sensitivities about this topic (Chuc et al.).

Economic considerations were frequently mentioned for failures of interventions in the private sector. In the Philippines it was difficult to reduce use of antibiotics for flu because pre-pack combinations of antibiotic and analgesics for flu symptoms were very profitable for drug sellers, so store owners encouraged their sale (Sia et al). Competition limited the success of several interventions targeted at drug sellers. In Nepal, shops supported by the British Nepal Medical Trust could not stop selling prescription only drugs without prescription, non-EDL drugs, and incomplete courses, because of competition from commercial shops (Holloway and Gautum (b)).

Economic considerations may also be important in the public sector. In Tajikistan, Makhmudova attributed the failure of a training intervention to change prescribing habits to, among other things, prescribers' self-interest.

Strong consumer demand for irrational use of antibiotics (due to cultural understandings of illness and medicine, habit, and economic constraints) was one reason identified for the failure of some interventions. For example, in Nigeria mothers perceived danger signs of ARI or diarrhoea as normal consequences of these illnesses and thus did not seek appropriate treatment (Abu), in the Philippines consumers demanded pre-pack combinations of antibiotics and analgesics (Sia et al.), in Uganda the recommended dose was unaffordable to most clients (Tumwikirize).

Organizational and health services factors were also mentioned as constraints on participants' ability to change their practice. In India doctors reported that they did not comply with guidelines because of lack of organizational support, heavy patient load and complexities in clinical presentation (Sharma et al.). In Nigeria, attempts to encourage rational use of medicines were hampered by the lack of public health services available in the wet season. When lanes were flooded, itinerant drug peddlers on motorbikes or bicycles provided the only health services available and they sold irrational combinations of medicines (Abu).

## Summary

Interventions which involve participants fully, increase their sense of ownership, and provide benefits to participants seem to be successful. Interventions which do not take into account the social, economic or organizational constraints on participants' behaviour are unlikely to be successful.

## 8. CONCLUSION

Descriptive studies of antibiotics in developing countries continue to show high levels of use, inappropriate use, wide availability of antibiotics without prescriptions and little understanding of antibiotics among lay people. The descriptive studies presented at ICIUM 2004 provide useful insights into how antibiotics are used in the community. The intervention studies presentations at ICIUM 2004, suggest that researchers have responded to gaps identified in previous reviews. There are more studies on the private sector and more involving complex and multi-faceted interventions. Fifteen of the 18 studies which met methodological criteria succeeded in improving antibiotic use. All but one of the managerial interventions evaluated had a moderate to large impact on the outcome variables. Successful interventions included the teaching of management quality improvement strategies, and complex processes of development and implementation of treatment guidelines which encourage involvement and ownership by those who will use them. The educational interventions evaluated here were also quite effective and frequently involve the use of treatment guidelines.

Caution should be exercised in generalizing from these conclusions. While an intervention may work well in one setting, it may not work in another. For example, the Chalker et al. study found that their multi-component intervention worked well in one context, but not another. This suggests the context of the intervention and the process of implementation may be critical in determining success. This echoes the messages from the authors of the ICIUM papers: that qualitative aspects such as involvement of stakeholders and awareness of social, economic and other barriers to change in a particular setting may be crucial.

Other intervention studies demonstrated the range of different strategies being used around the world to improve antibiotic use. There were many innovative approaches studied, particularly in the area of community education. However evaluations of these tended to be immediate and to focus on improvements in knowledge, rather than behaviour. It is important to improve evaluations of these methods. These should examine their long-term impact on knowledge and ideally behaviour.

This report has reviewed conference presentations rather than published papers (although some studies have subsequently been published elsewhere). Conference papers tend to be shorter and contain less information than published papers. Results tend to be presented either graphically or text form, but not both. Thus numbers sometimes had to be estimated from graphs. Conference papers have not been peer reviewed and there is less information available from which to assess quality. There could be also be a bias towards presenting interventions that work, and presenting indicators which show significant changes rather than those that show small or no changes. It is extremely important that interventions that do not work continue to be reported, in the same way that clinical trials which show drugs are not effective must be reported so that the published literature does not over-estimate their effect.

The method of comparing effect sizes used here and elsewhere has some limitations. Some outcomes may be easier to change than others, and therefore studies which measure outcomes that are difficult to change may be disadvantaged. In particular, studies which target indicators which are very high are likely to produce bigger changes than those that target indicators which are smaller, because the figures used for comparison are percentage point changes rather than percentage changes. A further problem with the method is that an intervention which produces a large change in one outcome (such as prescribing for ARI) is regarded as more significant than an intervention which produces modest changes in many outcomes. Thus interventions which are extremely successful in one way, but not successful in others, are advantaged over those which make many modest changes. Previous reviews (Ross-Degnan et al., 1998, WHO 2001b) have taken no account of the time dimension in comparing interventions. It is likely that the effect of most interventions decays over time. Thus it is not ideal to compare the immediate effect of one intervention with the long-term impact of another. In this review only interventions which were followed up for at least three months have been included, but this only partially addresses this problem. In addition, the scope of the intervention is not taken into account by comparing percentage point changes. Some interventions are very large scale (such as national changes in legislation or regulation), while others are small local initiatives. Small percentage point changes in the former may have more impact overall than large percentage point changes in the latter.

The need to improve antibiotic use continues to be an important and urgent public health priority. The ICIUM 2004 papers contribute to a growing body of evidence about successful interventions. It is extremely important to continue to collect evidence about the interventions that work and in what settings. It is also vital to continue to gather descriptive information about the dynamics underlying inappropriate use in order to develop and refine successful interventions.

## KEY MESSAGES

- The need to improve antibiotic use continues to be an important and urgent public health priority.
- The interventions reviewed here are more complex and multi-faceted than those in previous reviews, suggesting that researchers have responded to lessons from previous reviews.
- Very successful results were achieved by implementing management strategies.
- Novel educational interventions look promising, but their long-term impact on behaviour needs to be evaluated.
- Interventions need to take account of context and constraints on people's behaviour. Therefore they may work in one setting, but not in another.

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## Appendix 1: Explanation of study designs

**An intervention is designed to change an outcome variable, such as the proportion of children treated with antibiotics in health centre X or the number of people dying from pneumonia in community Y. How can we measure the effect of the intervention?**

We need to measure the outcome variable (thing we want to change), both before and after the intervention. We can provide better evidence if we use one of the following research designs.

### **Pre and post with control group:**

What is a control group? A group which is not the target of the intervention, but which is included in the study.

Why use a control group? This is to provide stronger evidence about whether it was our intervention that produced any changes we found. For example, we might find that fewer children are being treated with antibiotics after our intervention. If we have a control group we can see whether this also happened in other health centres at the same time. If it did, it could be because of a general change such lack of availability of antibiotics, rather than our intervention.

Who could be a control group? A group which is similar to the intervention group, such as another health centre, hospital, region.

In a pre and post study with control group we measure the thing we want to change (e.g. the proportion of children treated with antibiotics) before we do the intervention in the experimental group (e.g. health centre X) and the control group (e.g. health centre Z)

We carry out the intervention, and again measure the thing we want to change in both the experimental group (e.g. health centre X) and the control group (e.g. health centre Z)

### **Randomized controlled trial:**

The same as above except: each participant (person, hospital, health centre) is randomly assigned to either

- the experimental group (the group with which the intervention is carried out) or
- the control group (the group which has 'normal treatment')

This means that any individual participant (e.g. person, health centre or hospital) has an equal chance of ending up in the control group, or experimental group, and the allocation is done by chance, rather than as a result of the researchers' (or anyone else's) decision.

**Time series**

The outcome variable (the thing we want to change) is measured repeatedly before and after the intervention. For example, we might measure the percentage of antibiotic prescriptions every month for several months before and after the intervention.

Time series studies also provide stronger evidence if they include a control group.

## Annex 1: Summary tables

Summary table 1: 18 key studies (all reported outcomes)

	Region	Study design	Target group	Target condition	Sample size	Intervention	Outcome measure	Change
	Latin America	Time series	Whole population	Not specific	Entire country	Restricted sales of antibiotics to prescription only, educational campaign	Total consumption in DDDs (private pharmacies)  Total sales in USD (private pharmacies)	Approx .35 to .25 DDD/1000 inh/day  Average 43.1 million in 3 years before intervention Average 29.1 million in 3 years after
	Asia	Time series	Tertiary hospitals	Infection control	5 hospitals	Workshop to teach QI principles, tools and Plan-Do Study Act (PDSA) rapid cycle model	% adherence to hand hygiene (MICU)  % adherence to hand hygiene (ICU)	$\Delta I: 7 \rightarrow 67 = +60$  $\Delta I: 25 \rightarrow 71 = +46$

	Region	Study design	Target group	Target condition	Sample size	Intervention	Outcome measure	Change
							% inappropriate urine catheter use % adherence to appropriate antibiotic prophylaxis in elective caesarean section  % adherence to appropriate preoperative antibiotic prophylaxis in general surgery and urology  % adherence to proper timing of preoperative antibiotic prophylaxis	$\Delta I: 32 \rightarrow 15 = -17$ $\Delta I: 0 \rightarrow 100 = +100$  $\Delta I: 28 \rightarrow 52 = +24$  $\Delta I: 0 \rightarrow 90 = +90$
	Asia	RCT	Private pharmacies	Illegal steroids,	I: 34 pharmaci	Enforcement of regulations,	Dispensing of illegal steroids	After regulatory: Hanoi

	Region	Study design	Target group	Target condition	Sample size	Intervention	Outcome measure	Change
				low-dose antibiotics	es in Hanoi, 39 in Bangkok C:34 in Hanoi, 39 in Bangkok	education, peer review		$\Delta I - \Delta C = -4$ Bangkok $\Delta I - \Delta C = -19$  After Education: Hanoi $\Delta I - \Delta C = -33$ Bangkok $\Delta I - \Delta C = -16$  After peer review: Hanoi $\Delta I - \Delta C = -40$ Bangkok $\Delta I - \Delta C = -18$  Steroids: Asking no questions and giving no advice  After regulatory: Hanoi $\Delta I - \Delta C = +6$ Bangkok $\Delta I - \Delta C = -7$  After Education: Hanoi $\Delta I - \Delta C = -24$ Bangkok $\Delta I - \Delta C = -3$

	Region	Study design	Target group	Target condition	Sample size	Intervention	Outcome measure	Change
							Dispensing of low dose antibiotics	<p>After peer review: Hanoi <math>\Delta I - \Delta C = -19</math> Bangkok <math>\Delta I - \Delta C = 0</math></p> <p>After regulatory: Hanoi <math>\Delta I - \Delta C = 0</math> Bangkok <math>\Delta I - \Delta C = -9</math></p> <p>After Education: Hanoi <math>\Delta I - \Delta C = -21</math> Bangkok <math>\Delta I - \Delta C = -3</math></p> <p>After peer review: Hanoi <math>\Delta I - \Delta C = -24</math> Bangkok <math>\Delta I - \Delta C = -4</math></p>

	Region	Study design	Target group	Target condition	Sample size	Intervention	Outcome measure	Change
				ARI, STDs	I: 34 pharmacies in Hanoi, C:34 in Hanoi		Antibiotics Asking no questions and giving no advice	After regulatory: Hanoi $\Delta I - \Delta C = 0$ Bangkok $\Delta I - \Delta C = -2$  After Education: Hanoi $\Delta I - \Delta C = -26$ Bangkok $\Delta I - \Delta C = 0$  After peer review: Hanoi $\Delta I - \Delta C = -30$ Bangkok $\Delta I - \Delta C = -9$
							ARI: antibiotics dispensed	After regulatory: $\Delta I: 48 \rightarrow 35 = -13$ $\Delta C: 42 \rightarrow 30 = -12$  After Education: $\Delta I: 48 \rightarrow 15 = -33$ $\Delta C: 42 \rightarrow 32 = -10$

	Region	Study design	Target group	Target condition	Sample size	Intervention	Outcome measure	Change
							STD: correct syndromic treatment	After peer review: $\Delta I: 48 \rightarrow 30 = -18$ $\Delta C: 42 \rightarrow 43 = +1$  After regulatory: $\Delta I: 3 \rightarrow 10 = +7$ $\Delta C: 3 \rightarrow 10 = +7$  After Education: $\Delta I: 3 \rightarrow 22 = +19$ $\Delta C: 3 \rightarrow 14 = +11$  After peer review: $\Delta I: 3 \rightarrow 29 = +26$ $\Delta C: 3 \rightarrow 19 = +16$
Darbooy et al.	Asia	Pre and post with control	Households	Not specific	I: 300 households C: 300 households	Training sessions by general practitioners in primary care centres, distribution of booklet	Percentage of illnesses treated with self-medication  Intention to reuse medicines main reason for home storages  Average number of drugs stored at	$\Delta I: 19.3 \rightarrow 10 = -9.3$ $\Delta C: 16.3 \rightarrow 17 = +0.7$  $\Delta I: 58 \rightarrow 32 = -26$ $\Delta C: 60 \rightarrow 55 = -5$  $\Delta I: 7.3 \rightarrow 4.1 = -3.2$ $\Delta C: 4.3 \rightarrow 4.0 = -0.3$

	Region	Study design	Target group	Target condition	Sample size	Intervention	Outcome measure	Change
							home  Antibiotics as % of home stock Expired drugs as % of home stock  Able to explain indication correctly	  $\Delta I: 21 \rightarrow 14 = -7$ $\Delta C: 18 \rightarrow 19 = +1$ $\Delta I: 27 \rightarrow 8 = -19$ $\Delta C: 21 \rightarrow 19 = -2$  $\Delta I: 62 \rightarrow 80 = +18$ $\Delta C: 65 \rightarrow 68 = +3$
Dwiprahasto and Kristin	Asia	Pre and post	Doctors and paramedics	ARI, diarrhoea, muscle ache	I: 122 primary health care centres C: 40 primary health care centres	Interactive, systematic problem-based training	% of ARI patients receiving antibiotics  % of diarrhoea patients receiving antibiotics  Use of injection for muscle ache  Use of injection for ARI  Use of injection for	$\Delta I: 92.3 \rightarrow 32.7 = -59.6$ $\Delta C: 94.3 \rightarrow 92.5 = -1.8$  $\Delta I: 90.3 \rightarrow 25.9 = -64.4$ $\Delta C: 87.9 \rightarrow 87.2 = -0.7$  $\Delta I: 84.5 \rightarrow 46.9 = -37.6$ $\Delta C: 79.6 \rightarrow 65.4 = -14.2$  $\Delta I: \text{adult } 67.4 \rightarrow 14.9 = -52.5$ $\Delta I: \text{child } 38.5 \rightarrow 0 = -38.5$  $\Delta I: \text{adult}$

	Region	Study design	Target group	Target condition	Sample size	Intervention	Outcome measure	Change
							diarrhoea	52.8→22.6= -30.2 ΔI: child 27.6→0= -27.6
							Medication error	ΔI:73→29.1= 43.9
							Cost saved vs cost of training per health centre	729.8 vs 326.75
Hidayati and Munawaroh	Asia	RCT	Paramedics	ARI in children under 5	I: 12 health centres C: 12 health centres	2 hour small group discussion on STGs, followed by self-assessment discussions (SA1 and SA2), feedback seminar (FBS).	Items per encounter	4 months after SA2 ΔI: 4.1→ 3.1= -0.9 ΔC: 3.8→ 4.0= +0.2 After FBS ΔI: 4.1→ 3.0= -1.1 ΔC: 3.8→ 3.3 = -0.5
							% patients receiving antibiotics	4 months after SA2 ΔI: 63→22= -41 ΔC: 67→ 67= 0 After FBS ΔI: 63→ 21 = -42 ΔC: 67→ 44 = -23
							% patients prescribed	4 months after SA2 ΔI: 79→23= -56

	Region	Study design	Target group	Target condition	Sample size	Intervention	Outcome measure	Change
							antihistamine	$\Delta C: 75 \rightarrow 64 = -11$ After FBS $\Delta I: 79 \rightarrow 18 = -61$ $\Delta C: 75 \rightarrow 60 = -15$ 4 months after SA2
							% patients prescribed corticosteroid	$\Delta I: 21 \rightarrow 5 = -16$ $\Delta C: 22 \rightarrow 24 = +2$ After FBS $\Delta I: 21 \rightarrow 2 = -19$ $\Delta C: 21 \rightarrow 13 = -8$
							% patients prescribed phenobarbitol	4 months after SA2 $\Delta I: 3.1 \rightarrow 0.3 = -2.8$ $\Delta C: 1.1 \rightarrow 0 = -1.1$ After FBS $\Delta I: 3.1 \rightarrow 0 = -3.1$ $\Delta C: 1.1 \rightarrow 0.1 = -1.0$
							Average drug cost/ encounter	4 months after SA2 $\Delta I: 1163 \rightarrow 749 = -414$ $\Delta C: 1283 \rightarrow 1151 = -132$ After FBS $\Delta I: 1163 \rightarrow 621 = -542$ $\Delta C: 1283 \rightarrow 1016 = -267$
Holloway et	Asia	Pre and post	Primary	Not specific	2	Fee per drug unit (e.g.	Items per	

	Region	Study design	Target group	Target condition	Sample size	Intervention	Outcome measure	Change
al.		with control, allowing two comparisons at different time points	health care centres		districts, each with 10-12 health centres	<p>tablet or capsule) vs fee per drug item</p> <p>Comparison 1: Intervention group changed from fee per item to fee per unit, control continued with fee per item</p> <p>Comparison 2: Intervention group changed from fee per item to fee per drug unit, control continued with fee per drug unit</p>	<p>prescription</p> <p>Comparison 1</p> <p>Comparison 2</p> <p>% patients with antibiotics</p> <p>Comparison 1</p> <p>Comparison 2</p> <p>% patients with injection.</p> <p>Comparison 1</p> <p>Comparison 2</p> <p>% patients with vitamins, tonics</p> <p>Comparison 1</p>	<p><math>\Delta I: 2.1 \rightarrow 2.2 = +0.1</math></p> <p><math>\Delta C: 1.8 \rightarrow 1.9 = 0</math> (ns)</p> <p><math>\Delta I: 1.9 \rightarrow 1.8 = -0.1</math></p> <p><math>\Delta C: 2.2 \rightarrow 2.4 = +0.2</math> (ns)</p> <p><math>\Delta I: 54.4 \rightarrow 55.2 = +0.8</math></p> <p><math>\Delta C: 54.6 \rightarrow 53.4 = -1.2</math> (ns)</p> <p><math>\Delta I: 53.4 \rightarrow 52.4 = -1.0</math></p> <p><math>\Delta C: 55.2 \rightarrow 62.6 = +7.4</math> (ns)</p> <p><math>\Delta I: 17.6 \rightarrow 5.4 = -12.1</math></p> <p><math>\Delta C: 15.3 \rightarrow 10.9 = -4.4</math> (signif)</p> <p><math>\Delta I: 10.9 \rightarrow 7.2 = -3.8</math></p> <p><math>\Delta C: 5.4 \rightarrow 5.3 = -0.1</math> (signif)</p>

	Region	Study design	Target group	Target condition	Sample size	Intervention	Outcome measure	Change
							Comparison 2	$\Delta I: 15.8 \rightarrow 14.8 = -1.0$ $\Delta C: 8.4 \rightarrow 10.7 = +2.3$ (ns) $\Delta I: 10.7 \rightarrow 9.0 = -1.7$ $\Delta C: 14.8 \rightarrow 22.0 = 7.2$ (ns)
							Av number units per drug item Comparison 1	
							Comparison 2	$\Delta I: 14.4 \rightarrow 12.6 = -1.8$ $\Delta C: 15.7 \rightarrow 14.4 = -1.3$ (signif)
							% antibiotics prescribed in underdose Comparison 1	$\Delta I: 14.4 \rightarrow 13.7 = -0.7$ $\Delta C: 12.6 \rightarrow 12.8 = +0.2$ (signif)
							Comparison 2	$\Delta I: 15.8 \rightarrow 26.6 = +10.8$ $\Delta C: 11.4 \rightarrow 14.8 = +3.4$ (signif)
							Average cost per Rx Comparison 1	$\Delta I: 14.8 \rightarrow 19.8 = +5.0$ $\Delta C: 26.6 \rightarrow 26.9 = +0.3$ (signif)
							Comparison 1	$\Delta I: 23.7 \rightarrow 30.5 = +6.8$

	Region	Study design	Target group	Target condition	Sample size	Intervention	Outcome measure	Change
							Comparison 2	$\Delta C: 26.0 \rightarrow 30.8 = +4.8$ (ns) $\Delta I: 30.8 \rightarrow 28.2 = -2.6$ $\Delta C: 30.5 \rightarrow 33.5 = +3.0$ (ns)
Kafle et al.	Asia	Pre and post comparing two interventions and control	Paramedics at primary health care facilities	Diarrhoea in children under 5  ARI in children under 5  Scabies  Undiagnosed fever	80 health posts (number in each group not specified)	I1. Small group training  I2. Small group training followed by peer-group discussion using self-assessment	ORS alone in diarrhoea  Co-trimoxazole and paracetamol in pneumonia  Paracetamol alone in non- pneumonia ARI  Benzylbenzoate alone in scabies  Paracetamol alone in undiagnosed fever	I1: ns I2: significant  I1: ns I2: significant  I1: ns I2: significant  I1: ns I2: significant
Kounnavong et al.	Asia	RCT	Provincial hospitals	Malaria, diarrhoea, pneumonia	24 depts. at 8 hospitals (I:12 depts.	Monthly audit sessions involving feedback on indicator scores	Treatment indicator scores  All three diseases	$\Delta I: 6.48 \rightarrow 7.94 = +1.46$ $\Delta C: 6.16 \rightarrow 7.38 = +1.22$

	Region	Study design	Target group	Target condition	Sample size	Intervention	Outcome measure	Change
					C:12 depts)		Malaria Diarrhoea Pneumonia	$\Delta I: 6.44 \rightarrow 8.66 = +2.22$ $\Delta C: 6.75 \rightarrow 7.9 = +1.15$ $\Delta I: 5.91 \rightarrow 7.73 = +1.82$ $\Delta C: 5.4 \rightarrow 6.9 = +1.5$ $\Delta I: 7.1 \rightarrow 7.3 = +0.2$ $\Delta C: 6.4 \rightarrow 7.5 = +1.1$
Pérez et al.	Latin America	Time series	Tertiary hospital for private and institutionalized patients	Parenteral use	10 clinical services at one hospital	Structured antibiotic order form, educational campaign	Weekly rate of: Aminoglycosides in dose intervals <24 hours Cephradin and cephalothin in dose interval >6 hours Ceftazidime and cefotazime in dose interval > 8 hour Any antibiotic prescribed > one hour before or after incision in surgery	- 47% No significant change -7.3% -20%
Reyes et al.	Latin America	Pre and post with control	Primary care physicians	ARI, hypertension, type 2	8 clinics, 194 physicians	Formulation of guidelines, training of clinical tutors,	ARI: Approp. Rx of antibiotics	$\Delta I: 28.6 \rightarrow 61.3 = +32.7$ $\Delta C: 33.3 \rightarrow 30.5 = -2.8$

	Region	Study design	Target group	Target condition	Sample size	Intervention	Outcome measure	Change
				diabetes		interactive workshops, individual tutorials, roundtable peer review sessions	Education to patient Approp. case-management Diabetes: Approp. Rx Approp. case-management Hypertension: Approp. Rx Diet recommendations Approp. case management	$\Delta I: 9.1 \rightarrow 62.9 = +53.8$ $\Delta C: 21.9 \rightarrow 33.3 = +11.4$ $\Delta I = +37.7$ (other data not specified) $\Delta I: 47.5 \rightarrow 76.5 = +29$ $\Delta C: 51.0 \rightarrow 66.7 = +15.7$ $\Delta I: 21.2 \rightarrow 48.1 = +26.9$ $\Delta C: 13.5 \rightarrow 28.1 = +14.6$ $\Delta I: 36.4 \rightarrow 61.6 = +25.2$ $\Delta C: 43.6 \rightarrow 56.0 = +12.4$ $\Delta I: 70.5 \rightarrow 91.9 = +21.4$ $\Delta C: 60.6 \rightarrow 66.7 = +6.1$ $\Delta I: 12.8 \rightarrow 36.5 = +23.7$ $\Delta C: 10.6 \rightarrow 16.7 = +6.1$
Saniel et al.	Asia	Pre and post comparing	Private physicians	UTI	I1:2 clusters	I1: interactive case-oriented sessions with	Non-pregnant patients:	

	Region	Study design	Target group	Target condition	Sample size	Intervention	Outcome measure	Change
		two interventions			of physicians n=47 I2: 2 clusters of physicians n=58	expert panel (ICD) I2: problem-based lecture discussion (LD)  Both followed by feedback and discussions of practice data (FD)	% prescribed approp. antibiotic regimen  Pregnant patients: % prescribed approp. antibiotic regimen	After ICD/LD $\Delta I1: 0 \rightarrow 18 = +18$ $\Delta I2: 0 \rightarrow 3 = +3$ After FD $\Delta I1: 0 \rightarrow 26 = +26$ $\Delta I2: 0 \rightarrow 22 = +22$  After ICD/LD $\Delta I1: 23 \rightarrow 26 = +3$ $\Delta I2: 15 \rightarrow 36 = +21$ After FD $\Delta I1: 23 \rightarrow 49 = +26$ $\Delta I2: 15 \rightarrow 35 = +20$
Shrestha et al.	Asia	RCT	Primary health care centres	Lung conditions	I: 19 health facilities C: 21 health facilities	Training in PAL guidelines	Number of medicines prescribed  Correct prescriptions for lung disease  % items EDL  % encounters where antibiotic prescribed	- 0.193  + 50%  Not significant

	Region	Study design	Target group	Target condition	Sample size	Intervention	Outcome measure	Change
							% encounters with injection.	Not significant  Not significant
Summers et al.	Africa	Pre and post with control	Primary health care nurses	URTI  Diarrhoea and vomiting (DV)	I: (11 clinics) C: (11 clinics)	Training programme on effective prescribing	URTI: Items per Rx  % non-drug treatment  % items generic  % items EDL  % Rx with antibiotics  % Rx with injection	$\Delta I: 2.40 \rightarrow 1.71 = -0.69$ $\Delta C: 2.12 \rightarrow 1.95 = -0.17$  $\Delta I: 0.0 \rightarrow 12.5 = +12.5$ $\Delta C: 6.1 \rightarrow 4.1 = -2.0$  $\Delta I: 49.0 \rightarrow 73.0 = +24.0$ $\Delta C: 55.9 \rightarrow 39.8 = -16.1$  $\Delta I: 83.1 \rightarrow 88.8 = +5.7$ $\Delta C: 87.7 \rightarrow 76.3 = -11.4$  $\Delta I: 69.6 \rightarrow 30.3 = -39.3$ $\Delta C: 54.6 \rightarrow 46.6 = -8.0$  $\Delta I: 2.1 \rightarrow 1.2 = -0.9$ $\Delta C: 0.3 \rightarrow 0.6 = +0.3(NS)$

	Region	Study design	Target group	Target condition	Sample size	Intervention	Outcome measure	Change
							% items STG	$\Delta I: 47.2 \rightarrow 60.6 = +13.4$ $\Delta C: 51.9 \rightarrow 35.6 = -16.3$
							DV Items per Rx	$\Delta I: 2.52 \rightarrow 1.61 = -0.91$ $\Delta C: 2.20 \rightarrow 1.99 = -0.21$
							% non-drug treatment	$\Delta I: 2.0 \rightarrow 21.2 = +19.2$ $\Delta C: 4.6 \rightarrow 0.0 = -4.6$
							% items generic	$\Delta I: 15.8 \rightarrow 33.2 = +17.4$ $\Delta C: 16.2 \rightarrow 15.3 = -0.9 (NS)$
							% items EDL	$\Delta I: 79.6 \rightarrow 85.5 = +5.9$ $\Delta C: 89.0 \rightarrow 88.7 = -0.3(NS)$
							% Rx with antibiotics	$\Delta I: 66.4 \rightarrow 44.0 = -22.4$ $\Delta C: 80.5 \rightarrow 67.5 = -13.0 (NS)$
							% Rx with Injection	$\Delta I: 2.8 \rightarrow 0.6 = -2.2$ $\Delta C: 1.9 \rightarrow 4.6 = +2.7 (NS)$
							% Rx with AD	$\Delta I: 8.0 \rightarrow 3.4 = -4.6$

	Region	Study design	Target group	Target condition	Sample size	Intervention	Outcome measure	Change
							% Rx with AM % Rx with no ORS % Rx only ORS % items STG	$\Delta C: 0.0 \rightarrow 0.0 = 0.0(\text{NS})$ $\Delta I: 28.1 \rightarrow 8.2 = -19.9$ $\Delta C: 11.2 \rightarrow 5.9 = -5.3(\text{NS})$ $\Delta I: 43.2 \rightarrow 28.0 = -15.2$ $\Delta C: 41.1 \rightarrow 47.6 = +6.5(\text{NS})$ $\Delta I: 3.1 \rightarrow 24.1 = +21.0$ $\Delta C: 5.0 \rightarrow 6.1 = +1.1$ $\Delta I: 31.2 \rightarrow 47.1 = +15.9(\text{NS})$ $\Delta C: 35.1 \rightarrow 35.8 = +0.7$
Sunartono	Asia	Time series	Health services in one district	Not specific	One province	Decentralization of drug procurement, and the responses made to it in one district	% patients receiving antibiotics Percentage of antibiotic prescriptions less than 5 days Number of health centres Generic prescribing Injection use	$50 \rightarrow 13 = -37$ $100 \rightarrow 25 = -75$ $33 \rightarrow 24 = -9$ $100 \rightarrow 96 = -4$ $2.6 \rightarrow 0.8 = -1.8$

	Region	Study design	Target group	Target condition	Sample size	Intervention	Outcome measure	Change
							Average drugs per encounter	2.75→3.0= +0.25
Suryawati	Asia	Time series	Not specific	Not specific	21 public hospitals 11 private hospitals, 32 public health centres, 38 private pharmacies, 36 private drug stores from 3 provinces	Currency crisis	% of prescriptions with antibiotic  Availability of essential medicines  Availability of generics  Prescription costs	Approx 46→ 54.5 = +8.5  94→>80= -14  94→>94  Maintained and then increased
Valera et al	Asia	Time series	Not specific	Not specific	18 tertiary hospitals	Expanded insurance coverage for drugs	Monthly percentage antibiotic costs	No change

	Region	Study design	Target group	Target condition	Sample size	Intervention	Outcome measure	Change
							Monthly percent appropriate antibiotic type	Increased before coverage expanded
							Monthly percent cefuroxime prescriptions	Unchanged
							Monthly percent prescriptions reimbursable (i.e. on list of covered drugs)	Unchanged
Yudatining-sih et al.(a) (2 related studies)	Asia	RCT	Health centres	ARI	I: 6 health centres C:6 health centres	Feedback to reinforce MTP (ie both I and C had had MTP)	% patients receiving antibiotics	$\Delta I: 34 \rightarrow 11 = -23$ $\Delta C: 35 \rightarrow 40 = +5$
Yudatining-sih et al. (b)		Time series	Health centres	ARI	24 health centres (including 6	MTP plus repeated feedback	Number of drugs prescribed per pt	$\Delta I: 3.5 \rightarrow 3.2 = -0.3$ $\Delta C: 3.6 \rightarrow 3.7 = +0.1$
							% patients receiving antibiotics	$\Delta I: 50 \rightarrow 20$ (immed. after MTP) $\rightarrow 35$ (13 months after MTP) $\rightarrow 26\%$ (after feedback) $\rightarrow 13\%$ (month

	Region	Study design	Target group	Target condition	Sample size	Intervention	Outcome measure	Change
					from study 13)			48, after 3 sets of feedback)

**Summary table 2: evaluations of packages of interventions (antibiotic-related results only)**

Authors	Region	Study design	Target group	Target condition	Sample size	Intervention	Outcome measure	Change
Cars, Cars et al.	Europe	Time series and other designs	General	Not specific	National data	National programme to improve use and monitor resistance, involving local and regional activities	<p>National antibiotic sales DDD/1000inh/day</p> <p>Use of antibiotics in primary care, DDD/1000inh/day, under 7 years</p> <p>Use of macrolides, 0-6 years of age, primary care, DDD/1000inh/day</p>	<p>17.7→13.9= -3.8</p> <p>16→8.8= -7.2</p> <p>3.7→1= -2.7</p>

Authors	Region	Study design	Target group	Target condition	Sample size	Intervention	Outcome measure	Change
							Use of quinolones for uncomplicated UTI	21%→12%= -9%
Gunn and Suleiman	Middle East	Time series	General	Not specific	Various surveys: sample size not specified	Establishment of Directorate of Rational Drug Use	% of prescriptions containing an antibiotic  Consumption of 14 common antibiotics in primary health care: DDDs/1000/day	31→43→37 = +6  24.89→26.69→24.9= +0.01
Ofori-Adjei et al, Gyansa-Lutterodt et al	Africa	Time series (3 points)	General	Not specific	20, 40, 20 health facilities from 10 regions	National Drug Policy, STGs, training programme for clinical pharmacy and Drug and Therapeutic Committees	% prescriptions including an antibiotic	46.6→56.0→42.5
Pont et al. Mackson et al.	Oceania	Time series (data from a variety of	GPs	URTI	National data	National programme on prescribing of antibiotics, including	Prescriptions for antibiotics	23.08mill→ 21.44mill= -1.64mill

Authors	Region	Study design	Target group	Target condition	Sample size	Intervention	Outcome measure	Change
		sources)				academic detailing, clinical audit, case studies, small group discussions, printed publications, feedback of prescribing data	DDD/1000 popn/day Antibiotic Rxs per 100 URTI encounters No. of Rxs for broad spectrum penicillin Cephalosporin Rxs per 100 URTI encounters Appropriate use of amoxicillin	22.1→20.5= -1.6 42.1→33.1= -9.0 No change 9.5→5.7= -3.8 33→45= +12 (acute otitis media)
Qazi	Asia, Africa, Latin America	RCTs, Pre and post with control, dose-response designs,	Health workers treating children	Child health		Case management training	Percentage of children needing antibiotics and/or	IMCI areas: 65, 50, 70 Non-IMCI areas: 50, 36, 32

Authors	Region	Study design	Target group	Target condition	Sample size	Intervention	Outcome measure	Change
		comparison of intervention and non-intervention areas					antimalarials prescribed drug correctly  Caretaker of child prescribed oral antibiotics advised how to administer  Caretaker of child prescribed oral antibiotics knows how to administer	IMCI: 98% Non-IMCI area: 18%  IMCI: 68% Non-IMCI area: 46%
Suryawati and Santoso	Asia	Time series	Prescribers in hospitals	Various, defined by hospitals	6 hospitals in Indonesia, 13 in Cambodia 28 in Lao PDR	Monitoring-Training-Planning approach	% Use of antibiotics in normal delivery  % Use of antibiotics in traumatology ward	100→15 = -85  100→63= -37

Authors	Region	Study design	Target group	Target condition	Sample size	Intervention	Outcome measure	Change
							% Use of antibiotics post caesarian section	100→36= -64
							% Use of antibiotics post scrotal hernia surgery	100→33= -67
							% Use of antibiotics in diarrhoea	83→26→13= -70
							% Use of antibiotics in diarrhoea in adult and paediatric OPDs	67→2 = -65
							% Use of antibiotics in ARI	94→45= -49
							% Use of	85→8= -77

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<b>Authors</b>	<b>Region</b>	<b>Study design</b>	<b>Target group</b>	<b>Target condition</b>	<b>Sample size</b>	<b>Intervention</b>	<b>Outcome measure</b>	<b>Change</b>
							antibiotics pre-scrotal hernia surgery	

**Summary table 3: other evaluations of interventions (antibiotic-related results only)**

Authors	Region	Study design	Target group	Target condition	Sample size	Intervention	Outcome measure	Change
Abu	Africa	Post-interventions study, intervention and control areas	Health care workers Mothers	Diarrhoea and ARI in children	All children in all health facilities in 8 villages- 4 int and 4 non-int	Primary health care strategy: including purchase and distribution of appropriate drugs, mobilization and education campaigns, capacity building for health workers	Appropriate prescribing	No clear quantitative data presented
Akter et al. (abstract only)	Asia	Pre and post with control	Doctors in paediatric hospital wards	Not specific	3466 paediatric patients (2171 pre and 1295 post)	Training programme	% appropriate antibiotics for pneumonia and diarrhoea  Antimicrobial expenditure	I: 16.4→56.8 = +40.4  -31.7%
Babar et al	Asia	Time series	Not applicable	Not applicable	56 drugs	Privatization of authority which procures and distributes medicines in public hospitals	Prices of antibiotics	**** abs?? Prices of 46/56 drugs increased, on average 67% 10/56 decreased, on average 33%

Authors	Region	Study design	Target group	Target condition	Sample size	Intervention	Outcome measure	Change
Cassimjee et al.	Africa	Pre and post, without control	Health facilities	Not specific	5 public health centres	Formation of DTCs, reports of measures taken, follow-up communication, repeat assessments	% of encounters with antibiotic prescribed at each health centre	55→43= -12 37→9= -28 6.7→17= +10.3
Cebotarenco et al.	Russia and the Newly Independent States	Pre and post with control (but post not yet analysed)	Children and parents	Cold and flu	I: 22 schools C: 21 schools	Peer education with outreach to parents		Data not yet available
Dung et al.	Asia	Pre and post with control	Physicians	ARI	I: 9 districts C: 9 districts	Local guideline development, peer review, supervision	Knowledge (correct answers)  % antibiotics in non-pneumonia  Correct antibiotics	I: 47.7→73.1= -25.4 C: 69.0→68.0= -1.0  I: 99.7→66.2= -33.5 C: 99.2→99.1= -0.1  I: 25.0: →56.9= +31.9 C: 36.6→35.2= -30.5
Gitau and Kiambuthi	Africa	Pre and post without control	Health care providers	ARI and Malaria	6 mission hospitals 2465 prescriptions	Education on drug management, appropriate prescribing. STGs issued	Use of antibiotics	2% decline

Authors	Region	Study design	Target group	Target condition	Sample size	Intervention	Outcome measure	Change
Gulaev et al. (presented by Lobyntsev)	Russia and the Newly Independent states	Time series – 2 separate studies	Doctors	1. Bronchitis and ARI  2. Surgical prophylaxis	1260 prescriptions pre and 1260 post  300 prescriptions pre and 300 post	Training	1. % antibiotic prescribing  2. % antibiotic prophylaxis  Antibiotic prescribing after surgery	51.8→24.0= -27.8 (ARI) 89.4→56.3= -33.1(Bronchitis)  I: 6.9→50.3= +43.4 (public) C: 90.3→63.4= -26.9 (private)  I: 96.4→67.0= -29.4 (public) C: 86.4→44.5= -41.9 (private)
Holloway and Gautam (a)	Asia	Post intervention with control	Health facilities	Not specific	I: 33 facilities C: 16 control facilities	Cost sharing drug supply scheme	% antibiotics prescribed in full dose  % patients prescribed antibiotics	I: 79 C: 45  I: 54 C: 28

Authors	Region	Study design	Target group	Target condition	Sample size	Intervention	Outcome measure	Change
							Cotrimoxazole availability	I: 93%, 91%, 95% C: 70%
Holloway and Gautam (b)	Asia	Comparison of intervention and control (i.e. post-only)	Private drug shops	Not specific	I: 16 shops C: 21 shops	NGO supported programme providing training, supervision and cost-price drugs	% customers sold antibiotics  %antibiotics sold in inadequate amount	I: 28 C: 23  I: 76 C: 86
Isah et al	Africa	Time series post intervention	General	Not specific	100 prescriptions per month at university teaching hospital	National Essential Drug Programme and National Drug Policy	% encounters where antibiotic prescribed	36.1→46.6= +10.5
Kandeke et al.	Africa	Pre and post without control		Not specific	5 hospital, pre and post	Training workshop on use of antimicrobials	Availability of key antibiotics  % admissions with at least one antibiotic  Average	95→85= -10  63→61= -2

Authors	Region	Study design	Target group	Target condition	Sample size	Intervention	Outcome measure	Change
							number antibiotics per hospitalization	1.6→1.5= -0.1
Karkee et al.	Asia	Pre and post with control, post data not yet available	Mothers, children, drug retailers, community leaders	ARI	800 children with ARI in last 2 weeks in I and C areas	Child-to-child school educational programme, mother and drug retailer education	% children under 5 with severe ARI treated according to guidelines  % people taking ARI for common cold	Post data not available
Kiambuthi	Africa	Pre and post without control	Mission hospitals	Not specific	3 hospitals	Training by outside team (complemented in one hospital by an internally organized CME programme)	% of prescriptions with antibiotic	48→67= -19 69→75= +6 61→30= -31(hospital with CME)
Kristiansson et al. (b)	Europe	Pre and post with control	Schoolchildren	Not specific	12 schools	Education/information for schoolchildren, and teachers' guidelines	Knowledge assessed by questionnaire	I: 6.9→8.8= +1.9 C: 6.9→6.9= 0
Lates and Shiyandja	Africa	Time series (1 pre and 2 post measurements)	General	Not specific	30 prescriptions from	National Drug Policy	% of prescriptions containing an	39→43→51= +12

Authors	Region	Study design	Target group	Target condition	Sample size	Intervention	Outcome measure	Change
					each of 44 public health facilities		antibiotic	
Lerner et al (a)	North America	Pre and post with control	Primary care physicians	URTI	I: 21 drs at 2 clinics, C: 9 drs at 2 clinics	Interactive, case-based educational programme on URIs	Antibiotic prescribing rates for URIs (all physicians)	$\Delta I: 49.9 \rightarrow 37.6 = -12.3$ $\Delta C: 45 \rightarrow 42.8 = -2.2$
Lerner et al (b)	North America	Pre and post without control	School children	Not specific	300 school children	Educational programme, including interactive tools	Knowledge tests (10 items)	15.1% improvement (raw data not provided)
Makhmudova	Russia and the Newly Independent states	Pre and post, but post only measured in intervention group	Doctors in outpatient depts	Not specific	23 out-patient depts. pre int, and 5 post intervention	Training workshops on rational drug use	% of patients receiving antibiotics	47 $\rightarrow$ 49.6 = +2.6
Munawaroh et al.	Asia	Pre and post with control	Paramedics in health centres  (doctors as resource people)	ARI	18 health care centres	Small group discussion and feedback meetings, compared with small group discussions only, or control	% of patients with ARI receiving antibiotics (paramedics)  % of patients	SGD+FB: 49.5 $\rightarrow$ 29.2 = -20.3 SGD: 75.1 $\rightarrow$ 53.9 = -21.2 C: 56.6 $\rightarrow$ 60.0 = +3.4  SGD+FB: 49.7 $\rightarrow$ 30.0 = -

Authors	Region	Study design	Target group	Target condition	Sample size	Intervention	Outcome measure	Change
							with ARI receiving antibiotics (doctors)	19.7 SGD: 63.6→54.7=-8.9 C: 58.6→57.3=-1.3
Nurgozhin	Russia and the Newly Independent states	Pre and during intervention, post data collection planned	Physicians from outpatient primary care facilities	ARI	29 out-patient primary care facilities	IMCI training sessions	% of patients with ARI prescribed antibiotics	42 →25.5= -16.5
Ofei et al.	Africa	Pre and post with control	House officers in teaching hospital	LRTI	2 teaching hospitals	Managerial and educational intervention designed by consultants in intervention hospital	Average number of antibiotics prescribed for LRTI  Non-guideline antibiotics prescribed for LRTI	I: 4.9→5.5→5→4.6= -0.3 C: 3.8→1.8→2→1.7= -2.1  I: 67→92→92→99= +32 C: 7→5→16→10= +3
Park et al.	Asia	Pre and post without control	Physicians	Not specific	50,999 cases	Prohibition on physician dispensing	% of bacterial illness where antibiotic prescribed	91.6→89.7 = -1.9

Authors	Region	Study design	Target group	Target condition	Sample size	Intervention	Outcome measure	Change
							% of viral illness where antibiotic prescribed	80.8→72.8 = -8.0
							Number of antibiotics prescribed for bacterial illness	1.7→1.6 = -0.1
							Number of antibiotics prescribed for bacterial illness	1.5→1.4 = -0.1
Prasad et al.	Asia	Pre and post, but not post data collected yet	Primary health care centres, health posts, and sub-health posts	Diarrhoea, pneumonia, non-pneumonia ARI, scabies in children	3 Primary health centres, 6 health posts in the district	Peer-group discussion		No data presented

Authors	Region	Study design	Target group	Target condition	Sample size	Intervention	Outcome measure	Change
Qing et al.	Asia	Pre and post with control but no post data presented for control	Surgeons and pharmacists in surgery depts. of large public sector hospital	Thyroid-ectomy, mastectomy, cholecyst-ectomy, and hysteromyo-mectomy plus appendect-omy	I: 1 hospital, C: 1 hospital	Staff involved in formulating guidelines, others trained on guidelines, monitoring of compliance	Average antibiotic cost per operation  Irrational prophylactic use (% cases)  Antibiotic use after 3 days of operation (% cases)  Incorrect administration route	I: 740→352→495 = -245 C: 1306→822= -484  I: 68.6→8.2→47.1= -21.5 C: 100→100=0  I: 52→2.5→20.4= -31.6  I: 6.1→4.0→3.9= -2.2
Ran and Tomson (abstract only)	Asia	Time series	Prescribers in village health stations	Not specific	441 health stations in rural area	Monthly subsidies to document prescribing behaviour	Antibiotics per prescription	0.78→0.35= -0.43
Sharma et al.	Asia	Pre and post with control	Physicians in medicine and paediatric depts.	URTI; diarrhoea, malaria, hypertension, asthma	2 tertiary care hospitals	Advocacy and dissemination of STGs, educational intervention to reinforce acceptance		No results about antibiotics presented

Authors	Region	Study design	Target group	Target condition	Sample size	Intervention	Outcome measure	Change
Sia et al (presented by Galang)	Asia	Pre and post with control	Drug sellers	ARI	I: 37 pharmacies C: 134 pharmacies	Interactive group discussion plus leaflets(IGD), or drugstore visit (DV)	Dispensing amoxicillin without prescription  Recommending antibiotics for flu symptoms	IGD: 91.8→70.6= -21.2 DV: 88.5→78.8= -9.7 C: 76.1→90.3= +14.2  IGD: 88.2 →72.9= -15.3 DV: 82.7→80.8= -1.9 C: 60.4→56= -4.4
Sisounthone et al.	Asia	Time series (4 points)	Hospital staff	Various, defined by hospitals	28 hospitals	Monitoring-Training-Planning	% patients receiving antibiotics	In four hospitals 60→45= -15  60→30= -30  46→20= -26  40→20= -20
Srun and Sokhan	Asia	Time series (4 points)	Hospital staff	Various, defined by hospitals	13 hospitals	Monitoring-Training-Planning	% patients receiving antibiotics  Normal delivery  Post-caesarean	  100 →15= -85  87→36= -51

Authors	Region	Study design	Target group	Target condition	Sample size	Intervention	Outcome measure	Change
							surgery Post-scrotal hernia surgery Traumatology ward Malaria	100→33= -67 100→63= -37 30→20= -10
Stålsby Lundborg et al.	Asia	Pre and post without control	Private pharmacies	Drug quality	366 samples in 1997, 300 in 1999	Inspection of pharmacies, provision of information, distribution of regulations, sanctions	% of sub-standard ampicillin % of sub-standard tetracycline	67→9= -58 38→12= -26
Suryawati et al.	Asia	Time series (post intervention)	Hospital staff	Various, defined by hospitals	6 hospitals	Monitoring-Training-Planning	% patients receiving antibiotics Teaching hospitals: Hernia surgery	Pre-surgery 100→100= 0 Post-surgery 100→15= -85

Authors	Region	Study design	Target group	Target condition	Sample size	Intervention	Outcome measure	Change
							Scrotal hernia surgery	85→8= -77
							Public Hospitals Acute diarrhoea	Internal OPD: 78→12= -66 Paed. OPD: 35→3= -32
							Caesarian section	Pre-surgery: 100→100= 0 Post-surgery: 100→0= -100
							Private hospitals ARI	95→45= -50
							Diarrhoea	21→3= -18
Th-Akib	Asia	Pre and post with control	High school children and women's associations	Not specific	I: 5 high schools and 5 women's associations C: 5	Poster competition: I: posters on rational antibiotic use C: posters on generic drugs	Knowledge of rational use of antibiotics	I: 6.7→8.0= +1.3 (high school) 5.8→8.6= +2.8 (women's association) C: 6.3→6.9= +0.3

Authors	Region	Study design	Target group	Target condition	Sample size	Intervention	Outcome measure	Change
					high schools and 5 women's associations			(high school) 6.0→8.4= +2.4 (women's association)
Toktobaeva and Karymbaeva	Russia and the Newly Independent States	Time series	General practitioners	Not specific	55 family group practitioners, 55 pharmacies	Clinical protocols, National EDL and National Formulary, new pharmacies in remote regions	% patients prescribed antibiotics	36→30→35.7= -0.3
Tumwikirize et al	Africa	Pre and post with control	Counter attendants at private pharmacies and drug shops	ARI in children under 5	191 drug outlets	Face-to-face education	% practices dispensing an antibiotic for  Mild ARI  Severe ARI	  I: 40.5→36.9= -3.6 C: 52.9→47.1= -5.8  I: 58.8→70.6= +11.8 C: 55.6→79= +23.4
Ziganshina et al	Russia	Time series (3 points)	Paediatricians	Uncomplicated acute URTI	7 out-patient clinics	Pharmacotherapy courses	Percentage of patients given antibiotics	65.7→35.2→31.3= -34.4

