

Review article:

Intervention research in rational use of drugs: a review

AMANDA LE GRAND,¹ HANS V HOGERZEIL² AND FLORA M HAAIJER-RUSKAMP³

¹Consultant in public health, Nairobi, Kenya, ²Action Programme On Essential Drugs, World Health Organisation, Geneva, Switzerland and ³WHO Collaborating Centre for Teaching and Training, Department of Clinical Pharmacology, University of Groningen, The Netherlands

Many studies have been done to document drug use patterns, and indicate that overprescribing, multi-drug prescribing, misuse of drugs, use of unnecessary expensive drugs and overuse of antibiotics and injections are the most common problems of irrational drug use by prescribers as well as consumers. Improving drug use would have important financial and public health benefits. Many efforts have been undertaken to improve drug use, but few evaluations have been done in this field. This article provides an overview of 50 intervention studies to improve drug use in developing countries. It highlights what type of interventions exist and what is known about their impact.

It reveals that commonly used interventions, such as an essential drug list and standard treatment guidelines, have rarely been systematically evaluated so far. The majority of intervention studies are focused on prescribers in a public health setting, while irrational use of drugs is also widespread in the private sector. Furthermore, the magnitude of inappropriate drug use at community level is often overlooked and few interventions address drug use from a consumer's perspective. More research on different types of intervention strategies in various health care settings is needed to draw conclusions on the effectiveness of a specific intervention strategy. Also more research is needed on socio-cultural factors influencing the impact of drug use interventions, particularly from a user perspective. To enhance evaluative research, more technical support will be needed for researchers in developing countries. The design of available studies from developing countries is generally weak, only six of the 50 studies included in this overview were randomized controlled studies. In order to provide technical support and coordination of future intervention research the establishment of an international resource centre for drug use intervention research is recommended.

Introduction

Rational drug use is well recognized as an important part of health policy. The term *rational drug use* is in this overview limited to the medical therapeutic view accepted at the WHO conference of 1985 in Nairobi: rational use of drugs requires that patients receive medications appropriate to their clinical needs, in doses that meet their own requirements, for an adequate period of time, and at the lowest cost to them and their community.¹ The consumers' perspective of rational may well differ from the definition given. What is rational in a medical sense may not be rational for the consumer and vice versa. For the consumer, the rationality of using a drug is based on the (re)interpretation of its value for daily life, influenced by cultural perceptions and economic conditions. People may only buy a few antibiotic capsules because they can not afford more. Or they may spend money on analgesics to relieve their misery, while good food and rest would have been better for their health.

For understanding actual drug use (i.e. taking the drug), both perspectives need to be considered. In health care policy,

faced with deciding how to spend the limited resources available, the first priority is to promote the use of drugs according to their potential benefit for the health of the population. It is our view that the medical perspective is crucial to this effect, because pharmaceuticals are based on a rational scientific model.

Although limited to the medical therapeutic perspective for rational drug use, the overview will look at the situation for prescribers as well as consumers. The emphasis is, however, on interventions to improve drug prescribing, due to the simple fact that comparatively few interventions targeting drug use among consumers exist.²

Efforts to promote rational drug use have been mainly targeted at the formal health care services. This started back in the 1970s, when WHO introduced the concept of essential drugs. The principle of the concept is that a limited number of drugs would lead to a better supply of drugs, better prescribing and lower costs for health care. The model essential drug list includes about 250 drugs, which is generally considered sufficient to treat the majority of diseases. Despite the

introduction of an essential drug list in currently some 110 countries, drug consumption increased dramatically worldwide. During 1975–1985 the annual increase was 9%,³ and in recent years continued to be around 6–8% per year. Despite the abundance of drugs on the market, approximately half of the world population still lacks access to the most needed drugs.⁴ Shortages of essential drugs often occur due to inadequate selection of drugs, improper storage, irrational prescribing and non-adherence by patients.⁵ Irrational drug use is a major public health problem worldwide, with far reaching economic consequences.

Patterns of drug prescribing and use in developing countries have been studied extensively, but to date no published overview exists of the impact of interventions to change drug use practices in developing countries. This article provides an overview of different types of intervention studies in developing countries, with the aim to gain insight into the volume and methodological quality of these studies and to identify areas which need to be strengthened in future. The inventory was made in collaboration with the International Network for Rational Use of Drugs (INRUD) in preparation for the International Conference on Improving Use of Medicines (ICIUM) in 1997. On the basis of the inventory, INRUD developed a paper for ICIUM, focusing on a quantitative analysis of measuring the effects of different intervention strategies.⁶ This paper aims to complement the INRUD paper by providing a more general, qualitative overview.

First the context of drug use is described, identifying the main problems in drug use and their financial and public health consequences. Then there follows an overview of different intervention materials and approaches, and what is known about their impact on improving drug prescribing and use. Finally some recommendations are made for future research and action.

Methods

The term drug use in this overview denotes both prescribing and use, unless indicated differently. In order to prevent confusion, the term ‘inappropriate’ is preferred when referring to drug use by consumers, and ‘irrational’ when referring to prescribers.

The summary of major problems in drug use and their public health consequences is based on two reviews of drug use in developing countries.^{7,8} Intervention studies to improve drug use were identified by searching the above-mentioned reviews, the INRUD database⁹ and available grey literature. Only studies which contained some quantitative or qualitative data on the effects of the intervention were included. The total number of studies encountered during the inventory was rather small, therefore some studies in which the evaluative component was limited were also included. The following issues are addressed in this overview: volume of intervention studies, study design used, content of the messages, target groups addressed, and type of intervention strategies evaluated (see Table 1). Before presenting the overview, the context of drug use is described: the most common drug use problems among consumers and prescribers, the causes of irrational and

inappropriate drug use, and their main public health and economic consequences.

Scope of the problem

Main drug use problems

Overuse of drugs and injections occurs as a consequence of overprescribing as well overconsumption. It concerns particularly the use and prescription of antibiotics, anti-diarrhoeals, painkillers, injections and cough and cold preparations.^{8,10,11,12} In many developing countries, the volume of sales of these drugs far exceeds the incidence of the disease they are supposed to treat.³ Injections have long had a special connotation as particularly powerful and fast acting medicines. Already 25 years ago, so-called ‘injection doctors’ existed,¹³ and still today, injections are widely overused by prescribers and consumers.^{14,15,16,17} In some instances the power attributed to injections by prescribers and consumers go hand in hand; the high use has also been shown to be caused by a mismatch between prescribers’ and consumers’ expectations.¹⁸

Multi-drug use or polypharmacy: The number of drugs per prescription is often more than needed, with an average of 2.4 up to ten drugs, while generally one or two drugs would have sufficed.^{19,20,21,22} Multi-drug use is also common among consumers who purchase their drugs from the private or informal sector. In Thailand, for example, *Yachud* is sold in almost every informal drug outlet: a locally prepared formula which contains several drugs of different form and colour.²³

Incorrect drug use involves the wrong drug for a specific condition (e.g. antibiotics or anti-diarrhoeals for childhood diarrhoea^{24,25}), drugs of doubtful efficacy (e.g. antimotility agents for diarrhoea), drugs of uncertain safety status (e.g. dypyrone) or use of drugs in the wrong dosage (which is often the case with antibiotics, ORS and antimalarials).^{26,27} Incorrect drug use occurs in the sense of incorrect prescribing as well as inappropriate use by consumers.

Causes of drug use problems

Problems in drug use may be distinguished at three levels: community, health care and national level.

Community level

Correct prescribing does not guarantee that drugs are used properly. Non-adherence to doctors’ prescriptions is very common.^{28,29} An example of non-adherence is for instance: a patient who uses a prescribed course of antibiotics in an under-therapeutic dose. There are many reasons for non-adherence, including among others: inadequate drug information, inadequate labelling, lack of money, and cultural perceptions on drugs.

In many countries up to 60–80% of health problems are self-medicated. Self-medication often results in inappropriate drug use.^{23,24,30,31} Some examples of drug misuse in self-medication are: the use of antibiotics and anti-diarrhoeals for

children with non-severe diarrhoea, the use of (expensive) cough and cold remedies for children with a minor cold, or the use of analgesics for slight fever.²⁴ Similar to non-adherence, self-medication is also influenced by many socio-cultural factors, such as people's own perceptions and preferences for certain pharmaceuticals.^{32,33} A study in the Philippines, for example, found that for the treatment of diarrhoea, antidiarrhoeals are preferred because they are believed to harden the stool. ORS, in contrast, is said to 'clean the intestines' and it is thus not believed to be effective in treating diarrhoea.³⁴

Health care level

In many developing countries objective information on drugs is scarce. Health workers receive limited basic training or continuing education on drugs. Knowledge, however, is only part of the problem. In many developing countries, ownership of health facilities by medical societies or practitioners creates conflict of interests, which may explain the overuse of drugs in therapy.³⁵ Prescribing and dispensing patterns are influenced by socio-cultural factors such as patient demand, the prescriber's attitude to risk, previous prescribing experiences and drug promotion.^{36,37} Misleading advertisements for pharmaceuticals and pressure from pharmaceutical sales men for certain drugs are common practice. Many drug advertisements in journals for medical and paramedical personnel in French-speaking African countries were found to contain incorrect or inadequate information.³⁸

National level

At the national level, the weakness or absence of national drug policies has been found to be an important obstacle for implementing interventions to improve drug use.³⁹ A drug policy can only be effective if mechanisms for implementation are in place, such as adequate monitoring of national drug regulation, a good distribution system, regular supervision, and adequate storage facilities.

Public health and economic consequences

The health consequences of inappropriate drug use have not been well quantified, but some evidence exists of the negative impact of inappropriate drug use on people's health. The review by Hardon and le Grand reports the following medical effects for inappropriate use of drugs:⁸

- *adverse, possibly lethal effects*, e.g. due to antibiotic misuse^{40,41} or inappropriate use of drugs in self-medication.⁴²
- *limited efficacy*, e.g. in the case of under-therapeutic dosage of antibiotics, tuberculosis or leprosy drugs.
- *antibiotic resistance*, due to widespread overuse of antibiotics as well as their use in under-therapeutic dosage.^{43,44}
- *drug dependence*, e.g. due to daily use of painkillers, was already described in 1978,⁴⁵ and still exists today;²³ and of tranquilizers.
- *risk of infection, due to improper use of injections*: injection related disorders are, among others, abscesses, polio, hepatitis and AIDS.^{46,47}

Besides public health consequences, inappropriate drug use may also have a far reaching impact on household as well as national health budgets. The use of expensive brand-name products while cheaper generic drugs are available, combination preparations, and multi-drug prescribing are evident examples of the waste of scarce financial resources. It has been estimated that savings by improving drug prescribing could be up to 50–70% of national or programme expenditures for drugs.^{5,48,49,50} No data are available on savings that could be made at the household level by improving drug use among consumers.

Interventions to improve drug use

Four types of intervention strategies to improve drug use can be distinguished (adapted from Quick et al. 1991⁵¹): educational, managerial, financial, and regulatory. Educational interventions are the most commonly used, both for prescribers and consumers. In the sections below, existing examples of intervention strategies will be discussed. First an overview is given of interventions targeted at prescribers (A), and then those targeted at consumers and/or patients (B). The section on educational strategies for prescribers is divided into two subsections: educational materials to promote rational prescribing of drugs (1), and different ways of using these materials (2).

A. Interventions targeted at prescribers

1. Educational materials

The most commonly used educational materials for prescribers are standard treatment guidelines, flow charts, newsletters, bulletins and simple forms of printed information, such as leaflets.

Standard treatment guidelines or clinical guidelines

Many developing countries have standard treatment guidelines (STGs), but evaluations of their use are few and most studies mentioned below used a before/after study design without a control. In Kenya, the introduction of an STG for malaria (before/after study design) resulted in a sharp drop in unnecessary quinine use.⁵² The use of STGs for acute respiratory infections in Fiji resulted in a 50% reduction in antibiotic use.⁵³ In Uganda, the introduction of a national STG did not result in any significant change for most INRUD indicators, such as the number of drugs per prescription, number of antibiotics, or number of injections, despite intensive training and supervision. However, more cases were treated according to the national STGs, particularly cases of malaria. The STGs had most effect among untrained health workers.⁵⁴

In Indonesia and Kenya, a randomized controlled study of the introduction of an STG for treatment of diarrhoea by pharmacists and drug sellers showed significant short-term improvements.⁵⁵

Guidelines used in crash courses without proper follow-up had little impact on health workers' prescribing habits.^{39,56}

Table 1. Overview of intervention strategies

| Materials | Approaches | Content of message | Target groups studied | Country of study | Study design | Ref. |
|---|--|---|--|--|---|--|
| A. Prescribers | | | | | | |
| 1. Educational materials | | | | | | |
| Standard treatment guidelines/or manuals | face-to-face introduction training course | malaria ARI/antibiotics general anti-diarrhoeals/ORS | health workers prescribers (un)trained health workers drug sellers/pharmacists rural health workers | Kenya Fiji Uganda Indonesia and Kenya Zambia | b/a ¹ b/a b/a r/c ² and b/a b/a control | 52 53 54 55 56 |
| Bulletin/newsletters | involvement of h/staff in development | general antibiotics | prescribers | Sri Lanka | random by group/control | 59 |
| Flow charts | use in training training | common illnesses common illnesses common illnesses | rural health workers health workers health workers PHC workers | Kenya Benin Pakistan Indonesia | b/a b/a b/a controlled | 60 8 114 61 |
| Diagnostic counselling cards | | diarrhoea | | | | |
| Printed information (letter, circular) | outreach training course | antibiotics problem drugs | prescribers consumers | Costa Rica developing countries | b/a | 65 67 |
| 2. Educational approaches | | | | | | |
| Any of the above materials | | | | | | |
| As above | Face-to-face education (interactive training) | diarrhoea diarrhoea | pharmacists and drug sellers prescribers | Kenya and Indonesia Indonesia | b/a and controlled r/c | 55# 68 |
| As above | Peer review and feedback | injections rhinopharyngitis | prescribers | Mexico Mexico | b/a + control b/a + control | 71 72 |
| As above | Formal seminar/workshop | diarrhoea STG STG | prescribers health workers rural health workers | Indonesia Kenya Zambia | r/c b/a b/a + control | 68 69 56# ³ |
| As above | Focus group discussions | diarrhoea injections diarrhoea | pharmacists prescribers | Thailand Indonesia Indonesia | b/a b/a + control r/c | 70 18 68# |
| As above | In-service training/supervision | STG diagnosis STG STG STG | medical assistants dispensers/nurses health workers medical students medical students health workers PHC workers | Ghana Zimbabwe Uganda Uganda International Mali Zimbabwe | quasi exp. - r/c r/c r/c - - | 76 77 78 80 81 85 1,75 |
| Modules | Participation of health staff in development of STG | essential drugs problem drugs | | | | |
| Any above | Drug Information Centres | drug use | health professionals | Pakistan | - | 90 |
| 3. Managerial strategies | | | | | | |
| Essential drug list | training/campaign training/campaign | essential drugs essential drugs | prescribers dispensers prescriptions rural health workers | Yemen Sudan Ethiopia Kenya Benin/Guinea Yemen | r/c - retrospective b/a - - | 92 93 94 69# 97# 92# |
| KIT distribution system | training and STG training part of EDP | essential drugs | prescribers/health workers | | | |

Table 1. Continued

| Materials | Approaches | Content of message | Target groups studied | Country of study | Study design | Ref. |
|---|---|--|---|--|---|---|
| Structured order forms (prescribing) | | antibiotics | physicians | – | – | 98 |
| Structured order forms (stock control) | In service training | antibiotics drug management drug management drug management leprosy | physicians dispensers dispensers dispensers prescribers and consumers patients | Thailand Zimbabwe Zimbabwe Tanzania Zanziba India Zimbabwe | contr/retrospective b/a b/a b/a r/b/a – – | 99 100 101 102 103 104 105 106 |
| Pre-packaging Labelling | | | | | | |
| 4. Financial strategies | | | | | | |
| Cost sharing | | essential drugs | consumers consumers consumers | Ghana Nepal Benin/Guinea | – – – | 107 108 97# |
| 5. Regulatory strategies | | | | | | |
| Banning unsafe drugs | | unessential/unsafe drugs | drug sales/retail outlets | Pakistan | survey | 110# |
| B. Consumers/patients | | | | | | |
| 1. Educational strategies | | | | | | |
| Patient education | Visual aids/advanced organizers | antibiotics | patients | Cameroon | b/a control | 111 |
| Public education | Public education campaign (posters, slides, radio, leaflets) | diarrhoea malaria RDU RDU RDU + hygiene overuse of drugs/herbs overuse of drugs/herbs vitamins/appetite stimulants | consumers pregnant women healthworkers/consumers healthworkers/consumers healthworkers/consumers patients/prescribers patients/healthworkers consumers | Peru Malawi Uganda Pakistan Philippines | b/a + control comparative comparative comparative comparative | 113 112 78# 114# 34 |
| | Non-drug therapy herbal medicine | | | Thailand Philippines Peru | control control control | 23 34# 113# |
| 2. Managerial strategies | | | | | | |
| Pre-packaging | | leprosy malaria | prescribers and consumers patients | India China | – cohort | 104# 118 |
| 3. Financial strategies | | essential drugs | consumers | | | |

¹ b/a = study design in which data are collected before and after the intervention.

² r/c = study design using a randomly selected control group.

³ References marked with # have been mentioned earlier in the table.

Bulletins/newsletters

Drug bulletins are supposed to be an ongoing source of objective drug information for prescribers. Bulletins are generally targeted at prescribers.⁵⁷ In Africa few countries have a drug bulletin and production is often irregular.⁵⁸ In Sri Lanka, a controlled study on the use of a newsletter on antibiotic prescribing showed some improvement, but the difference was not significant.⁵⁹

Flow charts/diagnostic cards

Flow charts aim to give guidance to health workers regarding the diagnostic path they should follow to define the most rational treatment. Flow charts are usually focused on one illness or group of illnesses, such as diarrhoea, malaria, sexually transmitted diseases, or mental disorders.

Studies in Benin and Kenya (before/after study design) showed that involvement of health workers in the development of flow charts increased their use.^{8,60} In Indonesia, diagnostic counselling cards were used to improve diagnosis and treatment of diarrhoea among PHC workers, with significant improvement in performance. In this study, a control group was used.⁶¹

Simple forms of printed information

Few studies are available on the impact of printed information, such as letters, 'dear doctor' circulars and leaflets, in developing countries. Several studies from industrialized countries^{62,63,64} and one study from Costa Rica⁶⁵ show that printed information alone has little influence on prescribers' behaviour and any influence is usually of short duration. Irrational prescribing is, however, seldom a question of knowledge alone.⁶⁶ It has already been noted before that many socio-cultural factors may influence prescribing practices, which are not being addressed by a leaflet with clinical information.

The 'Problem Drugs Pack' of HAI deserves special mention. It includes leaflets on specific problem drug categories, among others: antidiarrhoeals, antibiotics, analgesics, cough and cold preparations, growth stimulants and psychotropics.⁶⁷ An informal evaluation of the use of the Problem Drugs Pack indicated that the response received from people using the Problem Drugs Pack is generally very positive, but no details were available on how and for which target group the Problem Pack was used.

2. Approaches to introduce educational materials

Main methods to introduce educational materials for prescribers are: face-to-face communication (individual or small group), seminar/workshop (large group), in-service training, feedback or peer review and focus group discussions. The distinction between these methods is not always clear, neither in practice, nor in literature. The classification of approaches in this overview is based on how the approaches were described in the studies.

Face-to-face education

In Indonesia, a randomized controlled study found that face-to-face education was effective in shifting prescribers' practices towards the recommended norm, but small group face-to-face education did not have more impact than a large seminar.⁶⁸ Interactional face-to-face education for the introduction of STGs in Kenya and Indonesia had significant short-term improvements in a controlled study.⁵⁵

Seminar or workshop

Formal training seminars to improve health workers' knowledge in Kenya resulted in marked improvements, but frequent refresher courses and more supervision were recommended to further improve and sustain the results.⁶⁹ A two-day training seminar to introduce STGs in Zambia had only little effect and the authors wondered 'whether the activities were worth the effort'.⁵⁶ Similarly, a training programme on diarrhoeal diseases for pharmacists and drug sellers in Thailand found no significant impact.⁷⁰ Sufficient follow-up is generally lacking, thus reducing the impact of this type of intervention.⁸

Focus group discussion/participatory training approach

Two controlled studies showed good impact with the interactional and participatory approach: interactional group discussions to reduce the use of injections in Indonesia were found to be very effective, with a significant change in injection use in the intervention group.¹⁸ The participatory training approach was also noted to be an important condition for the success of diagnostic counselling cards in Indonesia.⁶⁸

Peer review and feedback

Two controlled studies in Mexico showed that peer review and feedback of prescribing patterns are also strategies which have yielded more positive results than other interventions: the active participation of the prescribers in a peer review committee to discuss prescribing practices for diarrhoea was very effective in the short as well as long term.⁷¹ A similar strategy to improve prescribing patterns for rhinopharyngitis was also successful and affordable.⁷²

Reviewing patient records to assess whether prescribing practices deviate from clinical guidelines is commonly used in developed countries. Also here, feedback with discussion was found to be more effective than feedback without comments.^{73,74} Feedback and peer review are particularly important for the adherence of prescribers to STGs.⁷⁵

In-service training/supervision

In Ghana, in-service training improved knowledge of prescribers, but it is not an effective means of changing prescribing if socio-cultural motivations of the prescriber are not addressed.⁷⁶ In Zimbabwe, on-the-job training of nurses using the ZEDAP (Zimbabwe Essential Drug Programme) dispensing modules had considerable impact on improving dispensing. However, the study was small and did not include

a control group.⁷⁷ In Uganda, reinforced supervision of health workers' prescribing practices resulted in a drop in the average number of drugs per prescription, and in the number of antibiotics and injections, while accuracy of prescribing improved.⁷⁸

The most cost-effective way to conduct training in rational drug use is probably through inclusion of a module on rational drug use in basic and post-basic medical education. A clinical pharmacology training manual, using problem-based teaching methods, was developed by WHO.⁷⁹ A multi-centre evaluation and a field trial (both randomized controlled studies) of the manual in Uganda showed significant improvements in prescribing practices.^{80,81}

The impact of face-to-face interventions is likely to depend on many aspects, such as duration of training, quality of education material used (if any), expertise of trainers, context in which training takes place, level of trainees, and whether there is any follow-up and supervision. It may also depend on the type of problem addressed, i.e. a disease, a drug or general prescribing problems, and on the extent to which it appeals to the trainees. Face-to-face interventions are relatively expensive due to the time and human resources required. They may, however, be worth the effort, as studies in industrialized countries have demonstrated that face-to-face interventions, focused on a particular problem, are one of the most effective strategies.^{82,83,84} Another indication of their cost-effectiveness is that they are intensively used by drug representatives.

Involving the target group in development of training materials

ZEDAP developed a set of treatment guidelines for health workers in close consultation with the target groups. Through workshops and peer review, hundreds of health workers were involved in the process. This contributed to a wide acceptance of the guidelines.^{1,75}

Another experience with modules developed to involve health staff in the process of developing an STG for rational prescribing was less successful.⁸⁵ An evaluation of such modules in Mali found that an eight-day training course was not sufficient to change prescribing habits and that continuing education and supervision on the job was required.

The need for involvement of prescribers in the development of guidelines and intensive follow up is also confirmed in studies done in Western countries.^{86,87,88,89}

Drug information centres

A number of countries have established a drug information centre. The importance of such centres in developing countries is stressed because of the general unavailability and scarcity of relevant drug information in those countries.⁹⁰ It would be interesting to know who are the major beneficiaries of these information centres.

3. Managerial strategies

Essential drug list

The concept of an essential drug list (EDL) has been widely adopted, but implementation is difficult as certain conditions should be met for the effective introduction of a national EDL. Successful implementation depends, among other things, on a good infrastructure and monitoring system. Countries with a strict and logical drug registration and regulation system have a more cost-effective drug prescription,⁹¹ but few developing countries have a fully comprehensive quality assurance system.³⁹ Few evaluations exist of the impact of an EDL.

A randomized controlled study in the former Democratic Republic of Yemen showed that after the introduction of an EDL, rational drug knowledge of prescribers increased significantly, as well as actual drug prescribing for three indicators.⁹² Likewise, in Sudan significant improvements were noted for the major indicators (use of essential drugs, injections and antibiotics) in all health facilities after introduction of the EDL.⁹³ In Ethiopia, the introduction of the EDL resulted in a significant decrease of non-essential drug prescribing.⁹⁴

Introduction of an essential drug list is most effective if accompanied by an introductory campaign and adequate follow-up.⁹⁵

Kit system distribution

One of the causes of irrational drug prescribing is inadequate drug supply, a common problem in many developing countries. In order to improve drug supply, essential drug kits have been introduced in a number of developing countries. These kits could at the same time serve to rationalize drug use, but this has not been well investigated. Results of one study covering five countries suggests some impact, notably in Democratic Yemen, but it was not clear whether this was due to the kit system alone, the training, or both.⁹⁶ In Benin and Guinea, providing drugs in prepackaged kits turned out to be too rigid a supply system for the local context where neither the epidemiology nor the health service utilization were well understood. Staff felt the list of essential drugs was too limited and continued to order and prescribe other drugs.⁹⁷

Pre-printed order forms

For the prescription of some drugs, particularly antibiotics, it is useful and cost-effective to have forms which structure and advise prescribers on the frequency and duration of the therapy.⁹⁸ A controlled retrospective study in Thailand on such order forms for antibiotics, however, found no effect.⁹⁹

Stock control

Poor drug stock management can lead indirectly to irrational drug use. When no overview exists of the available drugs in

stock, facilities may run out of essential drugs. Stock management is a serious problem in developing countries. This may be evident from the fact that during a rational drug use training project in Africa, four out of 12 intervention studies focused on stock control.^{100,101,102,103} Little can be said on the impact of such interventions as the studies were not randomized or controlled and little information was provided on the context in which the studies took place.

Course-of-therapy packaging

Blister packs have been notably helpful for diseases which require long lasting treatment with many different drugs, such as leprosy and tuberculosis. In India, use of blister packs decreased the workload of PHC staff (up to 50% in leprosy treatment).¹⁰⁴

Effective package labelling

Clear labelling of drugs is known to be a problem, but no completed evaluative studies are known as yet on package labelling, hence two studies are mentioned here of which the results were not available. In Zimbabwe posters were developed to remind prescribers about appropriate drug labelling¹⁰⁵ and colour coding was introduced for labels for essential drugs.¹⁰⁶

4. Financial interventions

Many initiatives have been undertaken in the field of drug financing. The Bamako Initiative, in which essential drugs are sold at a slightly higher price to create a fund for improving primary health care services, is probably the most well known. Making people pay for drugs which used to be provided free of charge could reduce overconsumption of drugs. However, it could at the same time result in overprescribing; health staff selling drugs have an interest to sell as many drugs as possible, because this will increase the revenues of the facility. In Ghana, the implementation of a 'cash and carry' system resulted in many prescriptions containing injections and three or more drugs (56% and 89% respectively). These prescriptions yielded 120–200% profit to the health centre.¹⁰⁷ In Nepal, improved drug supply and cost-sharing resulted in more appropriate prescribing in terms of dosage, but it led also to more polypharmacy and excessive drug use.¹⁰⁸

A substantial number of evaluations have been done on the impact of user fees, but they are generally focused on *service* utilization rather than drug utilization. User fees often have an unwanted effect, that health services become beyond the reach of poorer people, who may turn to the informal sector to purchase (incomplete dosages of) drugs. Accountability is a common problem, at the health care level as well as the community level. It is beyond the scope of this paper to go into details on the Bamako Initiative and other drug financing regulations.

5. Regulatory strategies

Regulatory strategies involve, for example, banning unsafe drugs, and limiting the import of drugs on the market.

Countries with more strict and logical drug registration and regulation systems have more cost-effective drug prescription.⁹¹ Quite a few countries have taken regulatory action to restrict the use of certain drugs. A number of paediatric formulations of antidiarrhoeals were banned in Indonesia, Mexico, Pakistan, Peru and Sri Lanka.¹⁰⁹ Regulatory interventions are, however, not always successful. Banning unsafe drugs could result in the black marketing of banned drugs, and may lead to use of (other) irrational drugs. In Pakistan, deregistration of paediatric antimotility drugs was not successful because it failed to address the educational or patient-demand factors responsible for physicians' irrational prescribing practices in the case management of acute diarrhoea in children.¹¹⁰

B. Interventions targeted at consumers/patients

1. Educational interventions

Educational interventions for patients/consumers often involve a multi-fold approach, including a combination of different educational strategies and materials.

Methods to address the general public include posters, booklets, mass media, education in primary schools and innovative methods such as theatre, role plays, comics and videos.

Patient education

In Cameroon, visual aids and advanced organizers were found to cause considerable improvement in patient compliance to antibiotic treatment.¹¹¹

In Malawi, three alternative interventions to improve compliance of malaria chemo-prophylaxis among pregnant women were assessed: a new health education message adapted to local perceptions on malaria symptoms, a non-bitter tasting antimalarial, the existing health education message, and a combination of these three. Either a new message or a different medication was found to be more cost-effective than a combined strategy, as two interventions together would be redundant.¹¹²

Public education

A broad combination of strategies (poster display, exposition, slides, radio programmes, theatre, leaflets and demonstration marches) in Peru resulted in some change, but not always that desired, in treatment of diarrhoea.¹¹³

In Pakistan, community health workers (CHWs) received training in appropriate drug use in order to provide health education to mothers. Preliminary results of an evaluative study revealed that health education sessions resulted in considerable change in knowledge and practice among the mothers, while training of CHWs would need further improvement.¹¹⁴ In Uganda the impact of public health education through posters was not successful, as the messages were not correctly understood.⁷⁸

In several countries efforts have been undertaken to encourage the use of herbal medicine in public or private health

services to curb the ever-increasing consumption of pharmaceuticals. In Thailand, promoting herbal medicine had quite positive results in reducing the use of analgesics in the area covered by non-governmental health facilities, but less so in a government setting.²³ A community-based health programme in the Philippines successfully promoted herbal remedies for common health problems, resulting in a larger percentage of common illnesses being treated with herbs instead of pharmaceuticals. However, the use of non-essential pharmaceuticals continued.³⁴ The same was noted in another more recent study in the Philippines.¹¹⁵ In Peru, strategies to promote non-pharmacological treatment resulted in a reduction of the consumption of multi-vitamins and appetite stimulants.¹¹³ Reference to traditional medicine in relation to pharmaceutical use is important, as the concepts which apply to traditional medicine may influence the use of pharmaceuticals. People easily apply traditional concepts on pharmaceuticals, unaware of the potential risk of these drugs.¹¹⁶

WHO/DAP has recently completed an inventory and analysis of Information Education and Communication (IEC) methods on drug use for consumers. A general observation was that information on consumer education is difficult to access: few experiences are published and often educational interventions are not documented at all. Preliminary analysis of consumer education projects revealed that one quarter of the projects claimed to have measured reported changes in behaviour.¹¹⁷ Project evaluation was usually focused on the progress of the activities rather than on their impact.²

2. Managerial strategies

Course of therapy packaging

In India, use of blister packs facilitated patient adherence to leprosy treatment.¹⁰⁴ In China, the use of antimalarial drug packaging resulted in a significant improvement in patient compliance. However, the study did not demonstrate whether compliance improved due to the use of blister packs.¹¹⁸

3. Financial interventions

Community revolving drug funds

Some financial interventions have been implemented at the community level, for example, the establishment of community revolving drug funds. A primary aim of such funds was to ensure regular availability of essential drugs at the community level, so that people did not have to rely on the informal market where non-essential drugs are usually provided. However, management of funds and accountability were some of the problems commonly encountered. No evaluations were available on the impact of community revolving funds on community drug use.

4. Regulatory strategies

Although regulatory strategies are not targeted at consumers, their success may depend on the extent to which consumer behaviour and demand is addressed. In Pakistan, deregistration of a paediatric antimotility drug failed because it did not

address the educational or patient-demand factors responsible for physicians' irrational prescribing.¹¹⁰

Limitations of the overview

Finding references of intervention research appeared difficult, for unpublished as well as published reports. Few of the published studies were indexed as 'intervention' or 'evaluation', and had to be searched on the many different keywords for intervention research (e.g. peer review, medical training, pharmacist education).

Categorizing studies was difficult, because of the wide terminology used for different intervention strategies, without a clear definition of what is understood by the terms used. One study may use the term seminar, another study may refer to training, while both actually discuss the same approach. Similarly, two studies may say they present the results of the evaluation of a manual, but they may not be comparable because each study has used different educational materials.

The combination of different intervention strategies in some studies also made it difficult to categorize studies according to the strategies used.

As noted before in the introduction, this overview has been limited to interventions which aim at improving drug use from the medical perspective. As a result, there has been an overemphasis on prescribers and irrational prescribing. However, existing interventions aiming at improving drug use from a medical as well as a consumer perspective are very few. The fact that inappropriate drug use is also common among consumers is not adequately reflected in the available studies to improve drug use.

Discussion and recommendations

Some major issues which came out of this overview are: the limited volume of intervention research, the poor quality of research design, a lack of reference to the context in which the study took place, and a bias of intervention research towards prescribers and higher levels of health care.

Volume of intervention research

This inventory does not pretend to be comprehensive, but serves the purpose of providing a general overview of what type of intervention strategies exist, and what impact they have. Despite its limitations, it still shows that the volume of intervention research in developing countries is rather limited compared with industrialized countries. Existing databases on drug use¹¹⁹ were found to include only 0% to 3% references of drug use intervention research. All published reviews of intervention research are from industrialized countries.^{87,88,120}

Methodological issues

The large majority of the studies included in this overview are quasi experimental, using a before/after study design, sometimes with a control group but usually not. Only six studies had

a randomly selected control group (see Table 1). The ICIUM review⁶ also found that only 36 (61%) of 59 intervention studies reviewed had a study design meeting minimum criteria. This weakness is not specific for intervention research, but is also encountered in, for example, descriptive drug use studies⁷ and health education interventions.¹²¹ It is also not specific for research in developing countries, as a review of intervention studies in developed countries also found that most evaluations were not properly done.¹²²

Context of research

A major weakness of intervention activities in developing countries is that they are rarely based on baseline data on existing drug prescribing and use.⁷ Knowing and understanding the context of the drug use situation is crucial in order to be able to evaluate the impact of an intervention. Several studies have stressed the need to first research local drug use practices among prescribers and consumers, before embarking on an intervention study. For effective interventions, insight is needed in the socio-cultural context in which inappropriate drugs use takes place, as well as the underlying factors of drug misuse.^{123,124} The context in which interventions take place has not been documented systematically. Only one study in the Philippines focused specifically on what socio-cultural and economic factors would influence drug use interventions. The interventions included, among others, training of community health workers, the establishment of village pharmacies and public education. The study found that involvement of the community in developing and planning the interventions, wide availability of non-essential drugs, and taking into account cultural concepts of diseases and drugs in health education, were all important factors of influence on the impact of the interventions.¹¹⁵ The large variation in results of intervention studies shows that much is still unknown about the mechanisms determining the success of an intervention. Many factors influence the impact of an intervention beyond the channel of dissemination, such as the content of the message, who is providing the message, the way in which the message is presented, and people's perceptions on pharmaceuticals and health. It is therefore important to evaluate and compare the impact of various strategies in different settings, in order to gain better insight into what socio-cultural and health care factors may influence drug use and prescribing.

Target groups and level of care

About half of the 50 intervention studies included in this overview were targeted at prescribers in a public health setting, while a large part of irrational drug use practice takes place in the private sector and at the community level. Published interventions targeted at the community level mainly aimed at improving case management of childhood diseases, such as pneumonia, acute respiratory diseases and diarrhoea. In those studies, improving drug use is generally a small component of a wide range of interventions to reduce mortality.¹²⁵ These studies stressed, however, the need to consider drug-use behaviour in a wider socio-cultural context.

A separate overview is needed of studies which concentrate on consumer perspectives on drug use. In the last decade a

number of descriptive studies have been done in this field.^{7,93} Such an overview may add to a better understanding of the mismatch between the medical therapeutic characteristics of drugs and their actual consumption.

Recommendations for future research

Use of sound study design

To adequately assess the impact of an intervention, control for existing trends or for effects of other influencing factors is essential. In principle, three study designs can be used. The most rigorous, the randomized controlled trial, can provide the best evidence. However, randomization is not feasible in all situations. A controlled before/after design can also provide adequate control. In this design, the drug use of the experimental group in which the intervention has taken place is compared with the drug use of a group where no intervention was done. When, for a variety of reasons, no control group can be found, a design using interrupted time series is also possible. In this approach, the drug use of the population where the intervention takes place is assessed at several intervals before and after the intervention.

When assessing the impact of interventions, different outcomes can be measured: knowledge and attitude, intended behaviour regarding drug use and actual behaviour. Measuring the latter is to be preferred. In general, interventions are aimed at improving actual behaviour. It is well known that improving knowledge is not directly translated into improving drug use.

Evaluation of use and impact of standard treatment guidelines

Evaluation of the impact of standard treatment guidelines (STGs) is an important area for future research. Many different STGs exist, focusing on specific drugs, illnesses, or prescribers (medical doctors, health workers, pharmacists, community health workers). Countries have been adapting the guidelines to their own essential drug list and prescribing practices, and many countries have used different approaches to introduce the guidelines. A review is needed of where and how the guidelines have been used, what factors are conducive or obstructive for their use and whether they had any impact on drug prescribing practices. A second step would be to conduct (multi-centre) studies to evaluate the effects of international treatment guidelines in different ways (such as face-to-face, feedback or peer review).

Evaluation of impact of drug bulletins

Bulletins are available in quite a few countries, but their use and impact has hardly been studied.

Impact of public education

Considering the large volume of self-medication and its far reaching consequences for public health, more research on interventions targeted at improving consumers' drug use are urgently needed. These intervention studies should address

inappropriate drug use practices, as well as the complexity of factors which may influence drug use among consumers.

Cost-effectiveness of interventions

Little information exists on the cost-effectiveness of different intervention strategies, such as face-to-face, interactional group discussions, and feedback for prescribers.

Impact of contextual factors

Little is known about what factors are beneficial or obstructive for the success of specific intervention strategies. Multi-country studies could reveal what conditions are conducive for specific interventions. Such research would also be helpful to develop typologies of countries; for example, countries with a strong essential drug programme, a dominant private sector, an important informal sector, a poor health care infrastructure, weak drug regulations, good quality of training for health workers, prevailing perceptions on drugs, etc.

Focus of study

Many interventions are focused on a particular disease (mainly diarrhoea, malaria, acute respiratory infections) or drug (antibiotics, antidiarrhoeals, and oral rehydration therapy). Interventions addressing other problem drugs, such as painkillers, vitamins, coughs and colds, or injections, are relatively little studied. More intervention research is needed on drugs which are not essential but widely prescribed and utilized.

Recommendations for future action

Intervention research is very dispersed, and often only available as grey literature. Therefore an international database bringing together all drug use intervention research would be of great help to facilitate researchers, health managers and policy-makers involved with drug use issues to find the relevant literature. The inventory and review papers made for the ICIUM conference are likely to provide a fairly accurate overview of what has been done in this field so far. These references are all available in the INRUD database, but further efforts will be required to maintain and update all references on intervention research. There is also a need for standardization of keywords for indexing intervention research.

Accessibility to the available information and knowledge on intervention research should be supported by careful methodological review. Data of reviewed studies should be made widely available through publications and the internet. Therefore an International Resource Network (IRENE) has been created with support from research groups from Asia, Africa, Europe and USA, sponsored by WHO. IRENE targets researchers, health managers and policy-makers in developing countries.

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Biographies

Amanda le Grand is a biologist specializing in medical anthropology. She has been working in the field of drug use research since 1987, and health systems research since 1992, for among others the Royal Tropical Institute, Amsterdam, and WHO. Currently she is a freelance consultant in public health, based in Nairobi.

Hans V Hogerzeil, Ph.D., is an international expert on the subject of promoting rational prescribing. He qualified from Leiden University and received a Ph.D. in public health in Nijmegen, the Netherlands. In 1996 he became a Fellow of the Royal College of Physicians in Edinburgh and in 1998 he received a honorary D.Sc. from the Robert Gordon University, Aberdeen. For 5 years he was a mission doctor in India and Ghana, and in 1985 he joined the WHO Action Programme of Essential Drugs. Currently he is responsible for all country support activities of the Action Programme, as well as coordinating WHO's work in promoting rational prescribing.

Professor Dr Flora M Haaijer-Ruskamp is an expert in drug utilization studies. Her research activities are focused on rational drug use, and effective strategies to improve this, in particular prescribing practices. At present she coordinates the development of a resource network of centres in Europe, the US and developing countries, where reports of intervention studies (unpublished as well as published) in developing countries are collected, reviewed and made accessible. Professor Haaijer works at the dept of Clinical Pharmacology, University of Groningen, where the WHO Collaborating Centre for Pharmacotherapy Teaching and Training is located.

Correspondence: Amanda le Grand, c/o J Wittenberg, National Museums of Kenya, PO Box 40658, Nairobi, Kenya. E-mail: amanda@ken.healthnet.org