

THE WORLD MEDICINES SITUATION 2011

RATIONAL USE OF MEDICINES

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SUMMARY

- Irrational use of medicines is an extremely serious global problem that is wasteful and harmful. In developing and transitional countries, in primary care less than 40% of patients in the public sector and 30% of patients in the private sector are treated in accordance with standard treatment guidelines.
- Antibiotics are misused and over-used in all regions. In Europe, some countries are using three times the amount of antibiotics per head of population compared to other countries with similar disease profiles. In developing and transitional countries, while only 70% of pneumonia cases receive an appropriate antibiotic, about half of all acute viral upper respiratory tract infection and viral diarrhoea cases receive antibiotics inappropriately.
- Patient adherence to treatment regimes is about 50% worldwide and lower in developing and transitional countries, where up to 50% of all dispensing events are inadequate (in terms of instructing patients and/or labelling dispensed medicines).
- Harmful consequences of irrational use of medicines include unnecessary adverse medicines events, rapidly increasing antimicrobial resistance (due to over-use of antibiotics) and the spread of blood-borne infections such as HIV and hepatitis B/C (due to unsterile injections) all of which cause serious morbidity and mortality and cost billions of dollars per year.
- Effective interventions to improve use of medicines are generally multi-faceted. They include provider and consumer education with supervision, group process strategies (such as peer review and self-monitoring), community case management (where community members are trained to treat childhood illness in their communities and provided with medicines and supervision to do it) and essential medicines programmes with an essential medicine supply element. Printed materials alone have little effect and for guidelines to be effective they need to be accompanied by reminders, educational outreach and feedback.
- Less than half of all countries are implementing many of the basic policies needed to ensure appropriate use of medicines, such as regular monitoring of use, regular updating of clinical guidelines and having a medicine information centre for prescribers or drug (medicine) and therapeutics committees in most of their hospitals or regions.
- The second International Conference on Improving Use of Medicines in 2004 and World Health Assembly Resolution WHA60.16 in 2007 recognized the difficulty of promoting rational use of medicines in fragmented health systems. They recommend a cross-cutting health system approach and the establishment of national programmes to promote rational use of medicines, which would require much more investment than governments and donors have so far been willing to give.

1.1

INTRODUCTION

What is rational use?

Medicine use is rational (appropriate, proper, correct) when patients receive the appropriate medicines, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost both to them and the community (1). Irrational (inappropriate, improper, incorrect) use of medicines is when one or more of these conditions is not met. Worldwide, it is estimated that over half of all medicines are prescribed, dispensed or sold inappropriately (2,3). Moreover, it has been estimated that half of all patients fail to take their medication as prescribed or dispensed (4). Irrational use may take many different forms, for example, polypharmacy, over-use of antibiotics and injections, failure to prescribe in accordance with clinical guidelines and inappropriate self-medication. However, despite the global problem of inappropriate use, few countries are monitoring medicines use or taking sufficient action to correct the situation (5).

Consequences of irrational use

Irrational use is wasteful and can be harmful for both the individual and the population. Adverse medicines events cause significant morbidity and mortality and rank among the top 10 causes of death in the United States of America (6,7). They have been estimated to cost £466 million annually in the United Kingdom of Great Britain and Northern Ireland and up to US\$ 5.6 million per hospital per year in the USA (8-10). Antimicrobial resistance is dramatically increasing worldwide in response to antibiotic use, much of it inappropriate overuse (and is causing significant morbidity and mortality (3). It has been estimated that antimicrobial resistance costs annually US\$ 4000-5000 million in the USA and €9000 million in Europe (11,12). The use of unsterile injections is associated with the spread of bloodborne infections, such as hepatitis B and C and HIV/AIDS (13). Although evidence-based medicine has gained importance the use of both diagnostic and treatment guidelines is sub-optimal and could be greatly improved.

Inappropriate antibiotic use

Overuse and misuse of antibiotics is a particularly serious global problem. Established and newly emerging infectious diseases are increasingly threatening the health of populations. If antibiotics become ineffective, these diseases will lead to increased morbidity, health-care use and eventually premature mortality (14-16). Furthermore, antibiotics are required for other treatments (taken for granted in developed countries), such as surgery and cancer chemotherapy, which would become unavailable with the disappearance of effective antibiotics. Unfortunately, while resistance to older antibiotics is increasing, the development of new generations of antibiotic medicines is stalling (17). Therefore, efficient use of existing antibiotics is needed to ensure the availability in the long term of effective treatment of bacterial infections. Efficient use includes both restrictive and appropriate use. However inappropriate and incorrect use of antibiotics occurs in both developing and developed countries. Doctors prescribe antibiotics to patients who do not need them, while patients do not adhere to their treatment causing the risk of antibiotic resistance (18). Two thirds of all antibiotics are sold without prescription, through unregulated private sectors. Even in those European countries where over-the-counter delivery of antibiotics is not allowed, patients use antibiotics without prescription (19). Low adherence levels by patients are common, many patients taking antibiotics in under-dose or for shortened duration – 3 instead of 5 days (20,21).

Irrational use of medicines is both wasteful and harmful.

This chapter covers irrational use of medicines in both developing and developed countries, with a focus on developing and transitional countries. Since there is very little information on medicines use for chronic diseases or on the use of over-the-counter (OTC) medicines in developing countries, the chapter will focus mainly on use of prescription-only medicines in acute disease, particularly antibiotics, although mention will be made of treatment of chronic diseases, especially in terms of adherence to medication.

1.2

PRESENT SITUATION AND TRENDS

Monitoring the use of medicines is essential to ensuring that they are properly used. This section covers the assessment of medicines use, including the disparity in the amount of data available in developed and developing countries, and methods which can help in assessments of medicines use. Patterns and trends are also examined, with discussion of the findings from WHO's database of studies on the use of medicines in primary care in developing and transitional countries. In addition, antibiotic use and patients' adherence to treatment are covered. The section on targeted interventions to increase rational use concludes that multi-faceted interventions improving both education and managerial systems have tended to be more effective than those that employ one strategy.

1.2.1

Assessing (measuring) medicines use

It is essential to have reliable data on how medicines are used in order to:

- assess the accessibility, quality and cost-effectiveness of care
- monitor trends in consumption
- provide a benchmark for comparison with similar countries, regions, facilities
- compare medicines use against evidence-based guidelines
- increase awareness of stakeholders about medicine use
- identify problematic areas to develop targeted intervention strategies.

In many developed countries, medicines use is routinely monitored, often through insurance data and electronic medical records. Data generated in this way have been effective in improving use through feedback to prescribers and policy-makers. However, in developing countries, electronic medical records and insurance data are often absent and such monitoring of use not undertaken, nor are interventions to improve use widely implemented.

There are several well-established, but quite different, methods which can be used to assess medicines use. Aggregate methods, such as the Anatomical Therapeutic Classification (ATC)/Defined Daily Dose (DDD) methodology (developed by WHO's Collaborating Centre for Drug Statistics in Oslo, Norway: <http://www.whocc.no>), can be used to compare consumption among institutions, regions and countries. However, judgements about the appropriateness of use can only be made indirectly, either by comparison with consumption elsewhere, morbidity data and/or adherence to evidence-based guidelines.

Rapid appraisal of prescriptions, using standard methods and indicators, can usefully identify general prescribing problems and quality of care. The WHO/INRUD (International Network for the Rational Use of Drugs) indicators can be used to identify general prescribing and quality of care problems at primary care facilities (22). The WHO/IMCI (Integrated Management of Childhood Illness) indicators can be used to assess the quality of treatment in children (23). Focused medicines use evaluation through examination of medical records and prescriptions, and linking diagnosis to treatment, can be used to identify medicines use problems in depth, especially in hospitals. The ATC/DDD methodology has been used

Standard methods and indicators can identify prescribing problems and quality of care.

extensively in developed countries, while the WHO/INRUD and WHO/IMCI methodologies have been used much more in developing and transitional countries.

1.2.2

Patterns and trends in medicines use

Medicines use in developing and transitional countries

WHO has created a database of studies on the use of medicines in primary care (generally for acute conditions) in developing and transitional countries. The database consists of systematically extracted quantitative information on medicines use measured in these studies, plus details on study setting and methodology extracted from articles and reports published or produced during the period 1990–2006. Details of the methodology, the methodological limitations and analysis are reported elsewhere (3) but some of the major results are reported here. Six hundred and seventy-nine studies from 97 countries were identified, 71% had been undertaken in the public sector, 26% in the private-for-profit sector and 3% in the private-not-for-profit sector.

Figures 1.1, 1.2 and 1.3 show medicines use over time, by region and by health facility ownership in developing and transitional countries. The figures show that use has remained sub-optimal in all regions of the world over the last 20 years, that it appears not to be improving, and that it is worse in the private sector as compared to the public sector. Figure 1.1 shows that while use of generic and essential medicines may have increased slightly over the past 20 years, overall use of medicines has increased and compliance with guidelines has remained low. Figure 1.2 shows that medicines use is similarly poor in all regions, and Figure 1.3 shows that use of generic and essential medicines and compliance with guidelines are better in the public sector compared to the private sector. Better treatment of acute diarrhoea (greater use of oral rehydration solution and less use of antibiotics and antidiarrhoeals) and acute respiratory tract infection (greater use of *appropriate* antibiotics for pneumonia and less inappropriate use of antibiotics for upper respiratory tract infection) is also seen in the public as compared to the private sector. In addition it can be seen that the use of antibiotics, often inappropriate as in their use for acute upper respiratory tract infection and acute diarrhoea, is increasing.

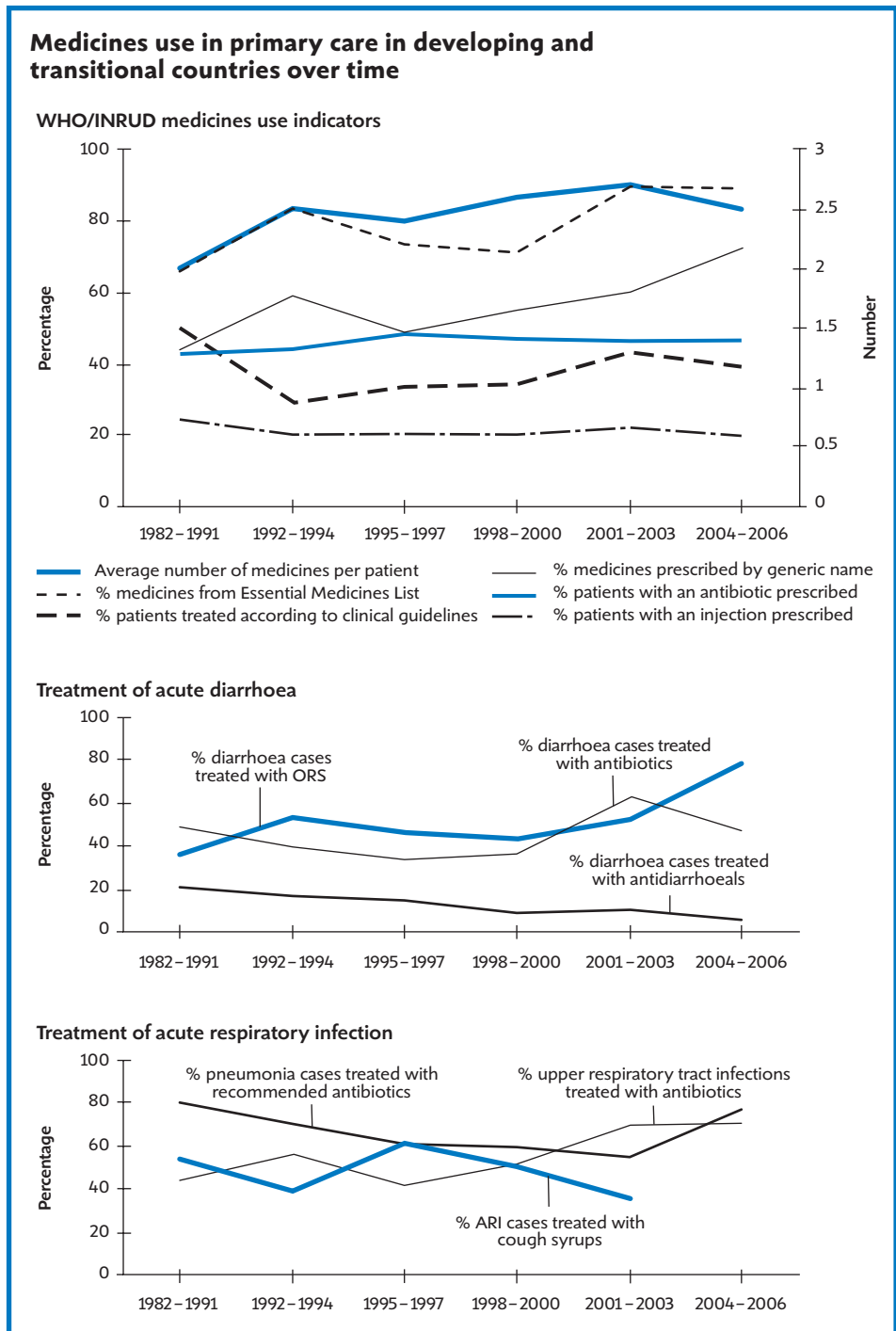
The dispensing process greatly influences how medicines are used. Data from the WHO database show that about 80% of all prescribed medicines are dispensed but often by unqualified personnel. The WHO database further shows that, on average, dispensing time is 1 minute, only half of patients are told how to take their medicines, about one third of patients do not know how to take their medicines immediately on leaving the facility, and that 20–50% of medicines dispensed are not labelled. In such circumstances it is not surprising that patient adherence to medicines is poor (see section on adherence below).

Medicines use in developed countries: studies on antibiotics

The problem of irrational use of antibiotics is also widespread in the rich developed nations. Figure 1.4 shows data from the European Surveillance of Antibiotic Consumption (ESAC) project comparing outpatient antibiotic consumption in 25 countries in 2003. It can be seen that there is large variation in antibiotic use across European countries. The number of DDDs per 1000 inhabitants is around 30 in Greece and France, while the Netherlands uses less than half this volume. Also, the types of antibiotic used vary across countries. In Greece, for example, the share of macrolides is much higher than in the Netherlands. Outpatient systemic antibiotic use in the USA is similar to that in southern European countries (24). Another European study showed that antimicrobial medicine self-medication prevalence

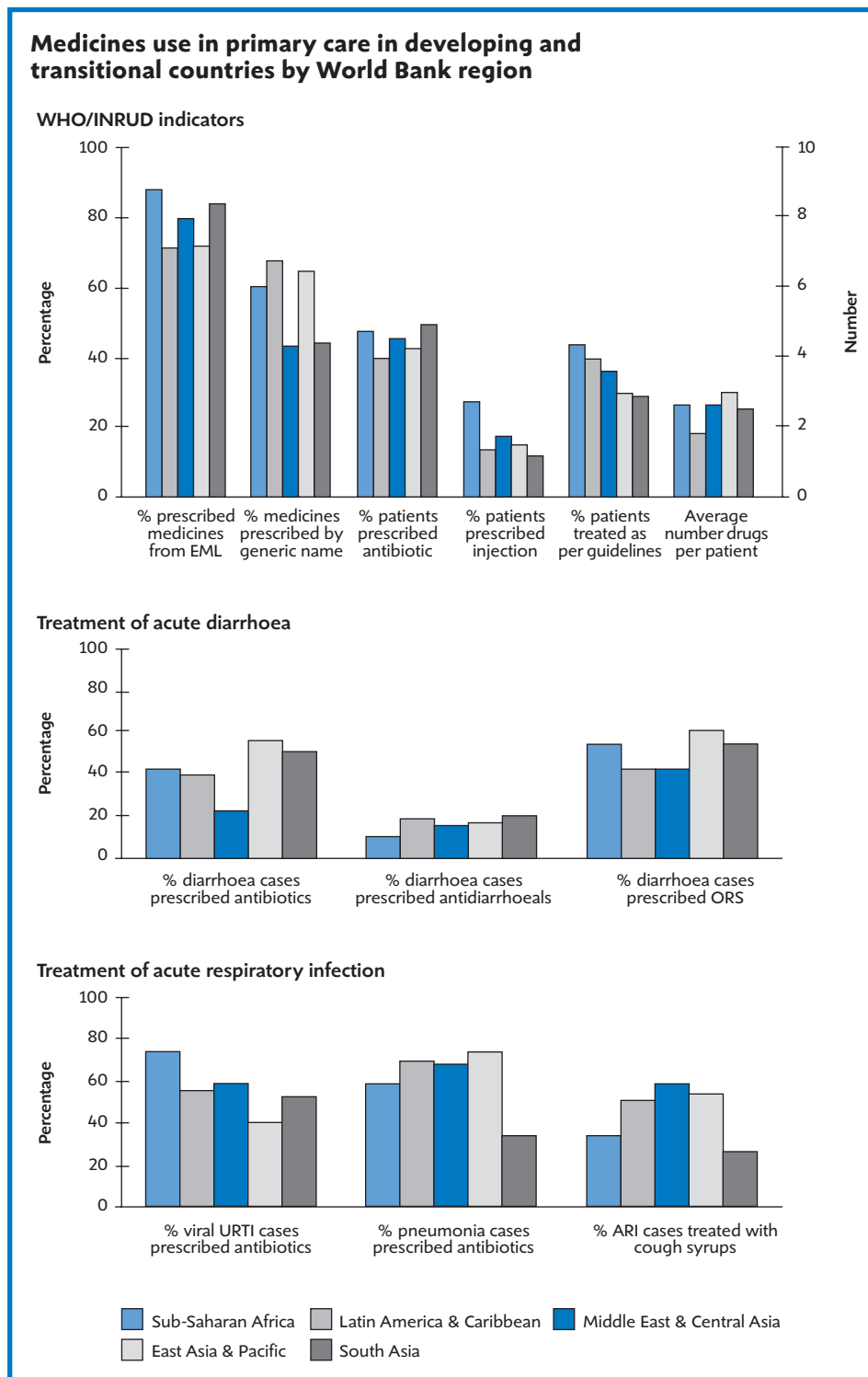
Antibiotics are misused and over-used in rich developed countries with wide variation in types and volume.

FIGURE 1.1



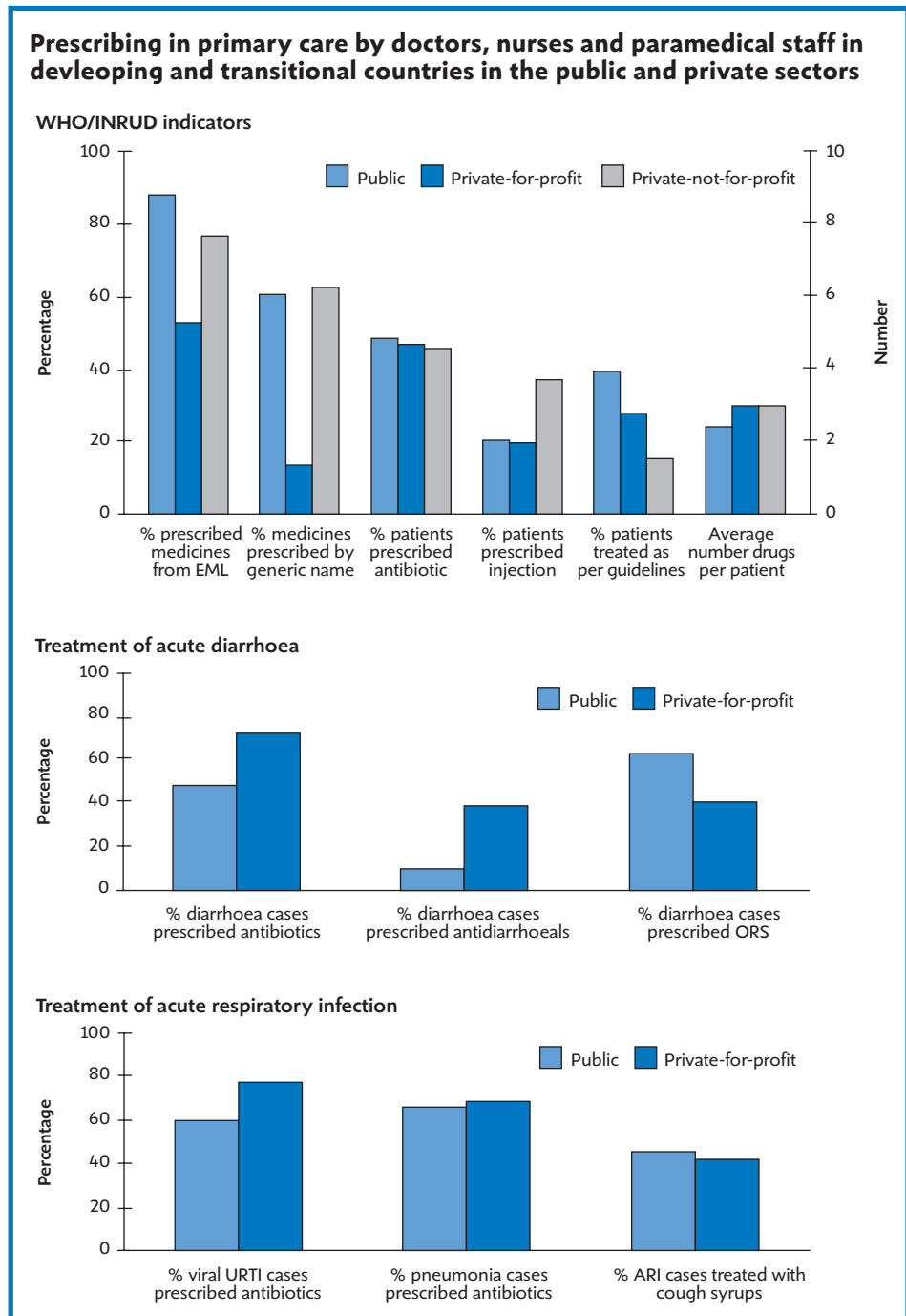
Source: WHO/EMP database 2009.

FIGURE 1.2



Source: WHO/EMP database 2009.

FIGURE 1.3



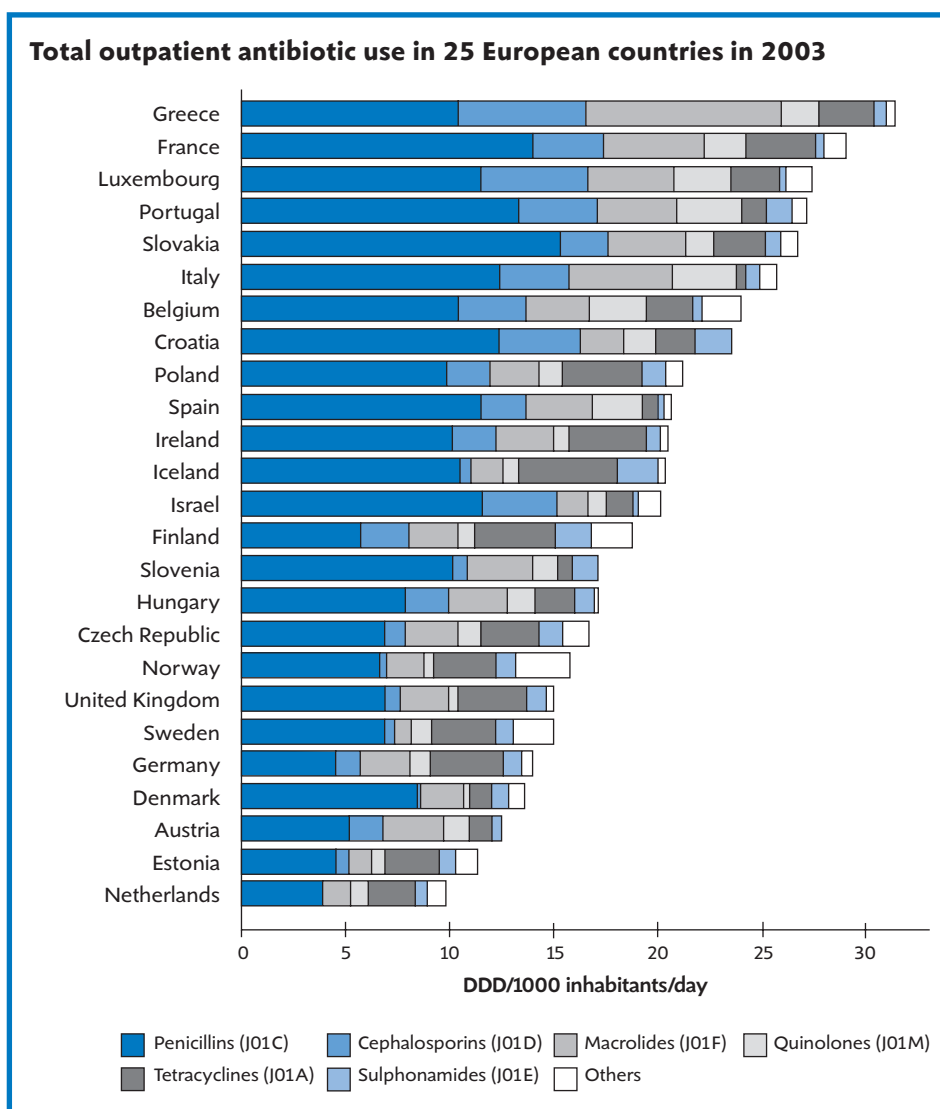
Source: WHO/EMP database 2009.

The medicine (drug) use indicators used in figures 1.1, 1.2 and 1.3 include: % medicines prescribed that belong to the EML; % medicines prescribed by generic name; % patients prescribed one or more antibiotics; % patients prescribed one or more injections; % patients treated in accordance with clinical guidelines; average number of medicines prescribed per patient; % viral upper respiratory tract infection cases treated with antibiotics; % pneumonia cases treated with appropriate antibiotics; % respiratory tract infection cases treated with cough syrups, antitussives or expectorants; % acute diarrhoea cases treated with oral rehydration solution; % acute diarrhoea cases treated with antibiotics; % acute diarrhoea cases treated with antidiarrhoeals.

varies widely among different European regions, with the highest rates in eastern and southern countries, and the lowest in northern and western (25).

There is a clear correlation between outpatient antibiotic use and penicillin-resistant *pneumococci*, emphasizing the importance of restrictive antibiotic prescribing policies (26). Nevertheless, even in the Netherlands, a country with low antibiotic use, overprescribing exists as was shown in a national survey among general practitioners (GPs). Six diseases for which national guidelines advised against prescribing of antibiotics were included. The percentage of consultations in which GPs prescribed an antibiotic for these diseases ranged from 6% (asthma in children < 12 years) to 67.2% (sinusitis) (27). Figure 1.5 shows the impact of antibiotic consumption on antimicrobial resistance with regard to *Streptococcus pneumoniae*. It can be clearly seen that those countries with higher consumption also have higher resistance.

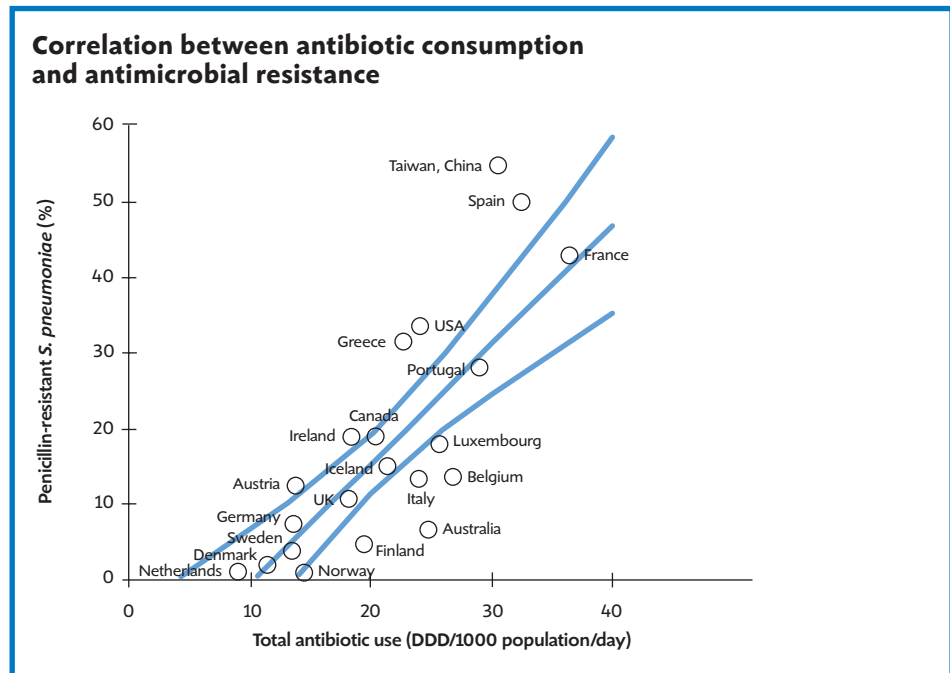
FIGURE 1.4



Source: Ferech, M. et al. *J. Antimicrob. Chemother.* 2006, 58:401-407; doi:10.1093/jac/dkl188.

FIGURE 1. 5

Countries with higher consumption have higher rate of antimicrobial resistance.



Source: Albrich, Monnet and Harbarth. *Emerg. Infect. Dis.*, 2004, 10(3):514–7.

Patient adherence to treatment: antibiotics and chronic medication

An important aspect of rational use is whether or not patients adhere to their treatment. Many studies show that patients often are not adherent. With regard to antibiotics, a patient survey in 11 countries across the world showed that 22.3% of patients who received antibiotic medication for acute community infections admitted not finishing the therapy. However, adherence rates varied widely across countries. The Asian countries, China and Japan, had the highest admitted non-adherence rates and the two European countries, Italy and the Netherlands, the lowest (18).

Patient adherence to treatment regimes is about 50% worldwide.

The problem of non-adherence is not only relevant for acute complaints, but even more so for chronic diseases. Due to the increasing number of patients suffering from diseases such as diabetes, cardiovascular disease, mental health problems, epilepsy, and chronic obstructive pulmonary disease (COPD) adherence to medication is becoming increasingly important. Overviews that quantify the extent of adherence abound, beginning in 1979 with the classic work of Haynes et al., *Compliance in Health Care*, (28). DiMatteo compiled 50 years of adherence research from 1948 to 1998. She calculated adherence rates in a meta-analysis of 569 studies and found an average non-adherence rate of 24.8% (29). She concluded that adherence is highest in patients with HIV-disease, arthritis, gastrointestinal disorders and cancer, and lowest in patients with pulmonary disease, diabetes mellitus and sleep-disorders. Consistent adherence among patients with chronic conditions is disappointingly low, dropping most dramatically after the first six months of therapy (30). For WHO, Sabaté undertook an overview of adherence for various medical conditions and concluded that it is a complicated problem affected by factors at different levels: social and economic factors, therapy-related factors, patient-related factors, condition-related factors and health system factors (4). Sabaté estimates that adherence to long-term therapies in the general population is around 50%, but lower in developing countries than in western society.

1.2.3 Targeted interventions to improve use of medicines

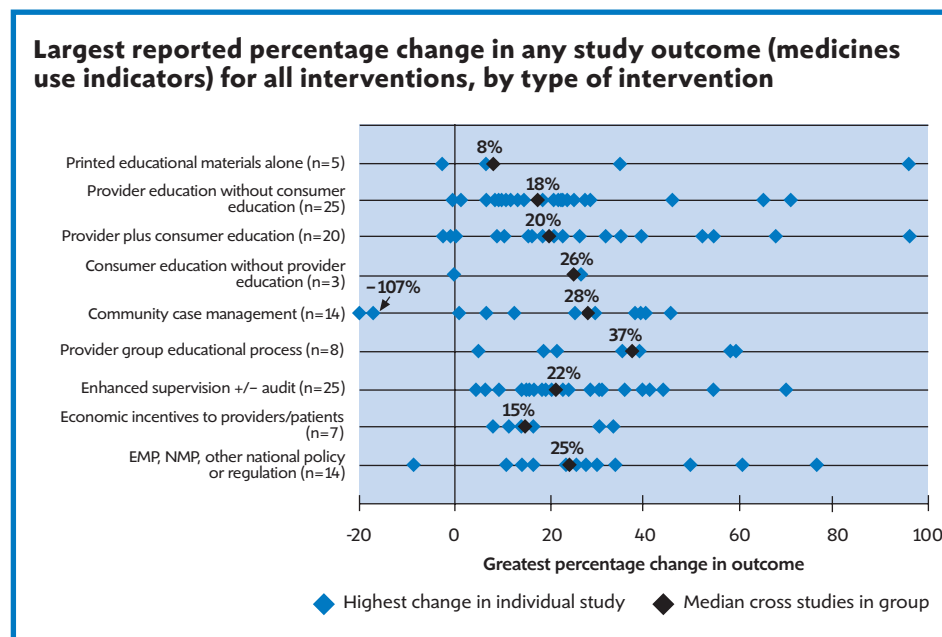
Both in developing and developed countries numerous interventions studies have been performed to improve the rational use of medicines. The WHO *Fact Book on Medicines Use in Primary Care in Developing and Transitional Countries* summarized such studies for developing countries (3).

1.2.3.1 Targeted interventions in developing and transitional countries

The WHO database of studies on the use of medicines in primary care in developing and transitional countries also contains information on 386 interventions (from 313 studies). Only 121 interventions (from 81 studies) were adequately evaluated (using randomized controlled trial, pre-post with control or time series study design) for their impact on medicines use. Two methods were used to summarize the effects of different types of intervention across studies which used various outcome measures, mostly INRUD and IMCI indicators. Firstly, the largest reported improvement in a key medicines use outcome that was targeted by the individual authors was compared across studies and the results are shown in Figure 1.6. Secondly, a composite indicator of improvement for each study was estimated by calculating the median effect across all outcomes measures reported in the main category of outcomes targeted by the authors. A comparison across studies was then conducted using this composite indicator and the results are shown in Figure 1.7. The second method provides a much more conservative estimate of effect than the first (3).

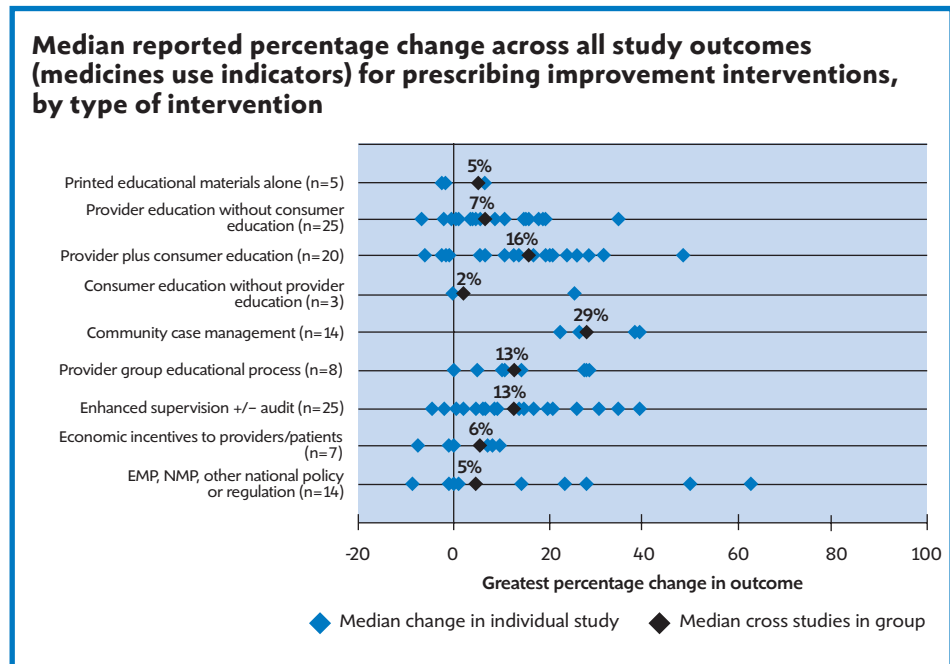
Most of the interventions were educational in nature. It was found that the multi-faceted interventions, involving both educational and managerial components, were more effective than those employing only one strategy. Interventions characterized by provider and consumer education, enhanced health worker supervision and group process educational strategies (such as self monitoring and peer review) were particularly effective. The use of printed materials and national medicine policies alone had limited impact.

FIGURE 1.6



Source: WHO/EMP/MAR/2009.3 (Reference 3).

FIGURE 1.7



Source: WHO/EMP/MAR/2009.3 (Reference 3).

Further analysis (3) showed that the median largest effect size and the median reported percentage change across all study outcomes were respectively:

Effective interventions to improve use of medicines are generally multi-faceted. Printed materials alone have little effect.

- 22% and 14% more where there was provider and consumer education with supervision compared to provider and consumer education without supervision, and
- 12% and 10% more where there was an essential medicines programme (with a medicines supply component) compared to a national medicine policy.

Many of these intervention studies and other experiences from developing countries were presented at the first and second international conferences for improving the use of medicines held in Chiang Mai, Thailand, in 1997 and 2004 (ICIUM 1997 and 2004: <http://www.icium.org>). The 2004 conference found that while many successful interventions had been undertaken, global progress remains confined primarily to demonstration projects and that few large scale national projects that could achieve public health impact had been implemented. Three major recommendations were made:

- Countries should implement national medicines programmes to coordinate long-term interventions on multiple levels of the health-care system to improve medicines use in the public and private sectors.
- Successful multi-faceted interventions should be scaled up to national level in a sustainable way, with in-built monitoring systems using valid indicators to monitor the long-term impacts.
- Interventions should address medicines use in the community, particularly focusing on education of children in schools, and provider education in pharmacies and medicine shops in the informal sector, regulation of medicine promotional activities, and involvement of civil society, such as community representatives and professional bodies.

1.2.3.2

Targeted interventions in developed countries

Many types of interventions to improve rational use of medicines have been undertaken in developed countries. In this section we will focus on three subjects: 1) the improvement of guideline adherence by health care professionals, 2) the improvement of patient adherence to medication, and 3) public education.

Guideline adherence by providers

Clinical guidelines that give recommendations about appropriate health care aim to improve the quality of care. A wide variety of guidelines has been developed in the last decades for hospitals and physicians. For both acute and chronic diseases, the implementation of guidelines is a complex process and the effects in terms of cost-effectiveness and long-term outcomes in patients are not well-studied (31-34). Research suggests that the implementation of guidelines is enhanced by higher quality of evidence supporting the recommendations, better compatibility of the recommendation with existing values; less complexity of the decision-making needed; more concrete description of the desired performance; and fewer new skills and organizational changes needed to follow the recommendations (33). Also, the baseline level of adherence to recommended practice seems important: in a review on the effect of audit and feedback in improving professional practice, published in 2006, Jamtvedt et al. conclude that effects of these interventions are likely to be greater when baseline adherence is low (35).

In 2004, Grimshaw et al. conducted a review to evaluate several implementation strategies (32). They conclude the following:

- Reminders: the results of intervention studies suggest that reminders are potentially effective and are likely to result in moderate improvements in process of care.
- Educational outreach is often a component of a multifaceted intervention. Combinations of educational materials and educational outreach appeared to be relatively ineffective. As such, educational outreach may result in modest improvements in process of care, which needs to be offset against the resources required to achieve this change and practical considerations.
- Educational materials and audit and feedback showed modest effects. The addition of educational materials to other interventions did not seem to increase the effectiveness of those interventions.
- Multifaceted interventions do not appear to be more effective than single interventions and the effects of multifaceted interventions do not appear to increase with the number of interventions.

However, other review studies in developed countries state that a combination of strategies to improve the implementation of guidelines is usually most effective (31,36). Differences in review findings may relate to whether the review focused on developed or developing countries. In developed countries a single intervention may be as effective as multiple ones due to existing health infrastructure. However, in developing countries, multiple intervention packages often include building infrastructure, such as supervisory systems, which are likely to increase impact.

Improving patient adherence: limited success

There have been many interventions to improve patient adherence to medication in developed countries. These are diverse in approach and intensity. A number of systematic reviews

A combination of strategies to improve implementation of guidelines is usually most effective.

have addressed their effectiveness (for example, Haynes et al. (2008), Bosch-Capblanch et al. (2007), Vermeire et al. (2005), (37-39). Van Dulmen et al. (2007) performed a meta review, including 38 review studies – representing over 1300 original studies – on interventions targeted at improving adherence (40). They conclude that effective adherence interventions include technical solutions such as simplifications of dosage and packaging. However, generally interventions on adherence have had varied and rather limited success. Effective interventions for long-term treatment are usually complex including combinations of solutions. But even the most effective interventions do not induce large improvements in both adherence and treatment outcomes (37). Haynes et al. state that “important innovations are more likely to occur if investigators join across clinical disciplines to tackle the problem, and take into account the resistance that many patients have to taking medicines..., perhaps including patients in the development of new interventions” (37). An international expert forum on patient adherence confirmed that interdisciplinary solutions and patient involvement are crucial for the development of interventions, as is the need for interventions that are simple to implement in daily clinical practice (41).

Public education campaigns: an example

Many European countries have undertaken public education campaigns in recent years to reduce inappropriate overuse of antibiotics. While some of these campaigns have had limited success, others have been very effective (see Boxes 1.1 and 1.2) (42). Box 1.1 shows information on a French programme directed towards antibiotic use.

BOX 1.1

Public information campaign in France

In 2002, the French National Health Insurance launched a long-term nationwide campaign to decrease antibiotic use in the community by 25%. The campaign targets the use of antibiotics in young children and is repeated every winter, because of the higher level of prescribing during this season.

With the central theme “Antibiotics are not automatic”, the public education campaign is directed at the parents of young children. It highlights issues such as higher consumption rates are linked to higher resistance levels, that antibiotics do not cure viral respiratory infections or even shorten duration of illness, and that it is important to fully respect the treatment duration and dosage prescribed. Information appeared in national media outlets, (prime-time television and radio and newspaper advertisements, and a web site, and in physicians’ offices, including putting booklets, handouts and posters in their waiting rooms). The total number of antibiotic prescriptions per 100 inhabitants decreased by 26.5% over five years (compared to the two years before the campaign was launched), with the greatest decrease observed in children aged 6–15 years (35.8%). In this way the French national campaign has succeeded in reducing unnecessary use of antibiotics.

Source: Sabuncu E et al. Significant reduction of antibiotic use in the community after a nationwide campaign in France. 2002–2007, *PLoS Med*, 2009; 6(6):e1000084.

1.2.4

National policies to improve rational use of medicines

National policies, as well as interventions, can influence the rational use of medicines. WHO recommends that countries implement the following national policies to encourage or ensure more appropriate use of all medicines (2):

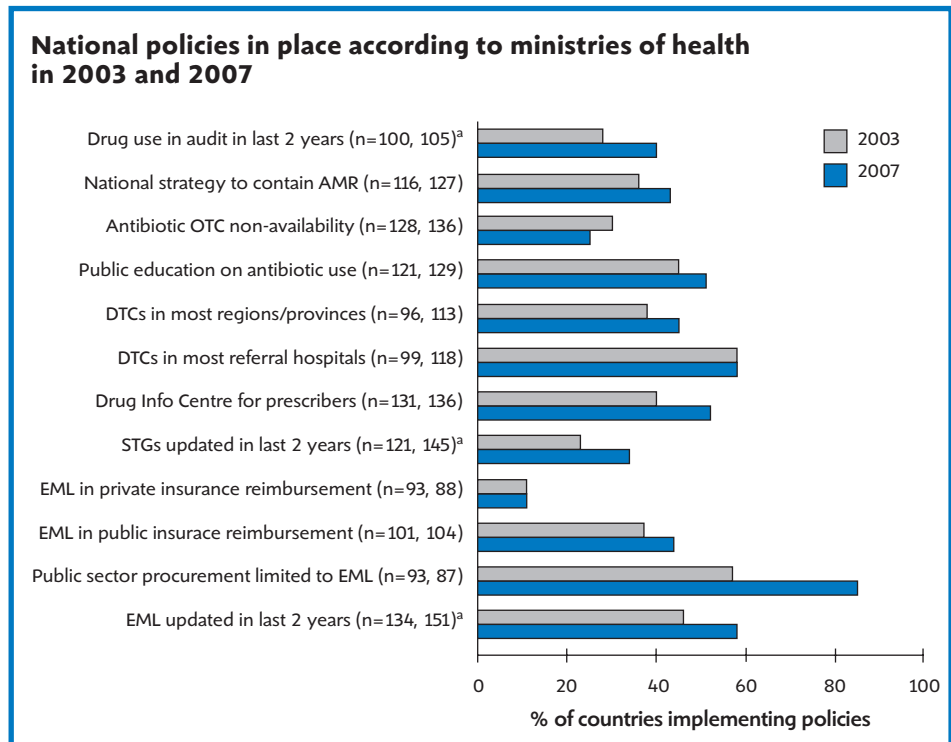
- establishing a mandated multidisciplinary national body to coordinate policies on medicines use and monitor their impact;

- formulating and using evidence-based clinical guidelines or standard treatment guidelines (STGs) for training, supervision and supporting critical decision-making about medicines;
- selecting, on the basis of treatments of choice, lists of essential medicines (EMLs) that are used in medicine procurement and insurance reimbursement;
- setting up drug (medicine) and therapeutics committees (DTCs) in districts and hospitals to improve the use of medicines;
- promoting problem-based training in pharmacotherapy in undergraduate curricula;
- making continuing in-service medical education a requirement of licensure;
- promoting systems of supervision, audit and feedback in institutional settings;
- providing independent information (including comparative data) about medicines;
- promoting public education about medicines;
- eliminating perverse financial incentives that lead to irrational prescribing;
- drawing up and enforcing appropriate regulation, including regulations to ensure that medicinal promotional activities are in keeping with the WHO Ethical Criteria for Medicinal Drug Promotion adopted in resolution WHA41.17 (see chapter on medicines promotion);
- reserving sufficient governmental expenditure to ensure equitable availability of medicines and health personnel.

WHO has also created a database on pharmaceutical policy based on a questionnaire that is sent to ministries of health once every four years. The last two such surveys were done in 2003 and 2007. Figures 1.8 and 1.9 show the results for 2003 and 2007 (5,43). Figure 1.8 shows that less than half of all countries are implementing many basic policies to encourage rational use of medicines, even though the proportion of countries implementing many policies has increased slightly from 2003 to 2007. Thus, for example, less than half of countries regularly monitor the use of medicines, update their STGs every two years, have a medicine information centre for prescribers, or have DTCs in the majority of their hospitals or regions.

Many countries allow OTC sales of antibiotics, some have run public education programmes on antibiotics but few have a national strategy to contain AMR, as is recommended by WHO (44). Although there appears to have been a big increase in the number of countries limiting public sector procurement exclusively to essential medicines still only a minority of countries are using the EML in insurance reimbursement. Figure 1.9 shows that the undergraduate training of doctors, nurses and paramedical staff has changed very little between 2003 and 2007. Only about 60–70% of countries stated that they trained their medical students on various aspects of prescribing and only about 50% required any form of continuing medical education. The basic training for nurses and paramedical staff, who often do the majority of prescribing, was even less, only about 40% of countries giving them any basic training on prescribing concepts, the EML, STGs or pharmacotherapy. The situation is probably even worse than described here because many policies that ministries of health state are in place are, in fact, poorly implemented. Furthermore, in both 2003 and 2007, about 27% of ministries of health mentioned that revenue from the sale of medicines is used to pay for or supplement health worker salaries and this is a serious incentive for over-prescribing. The existence of most policies tended to be higher in high-income compared to low-income countries (5).

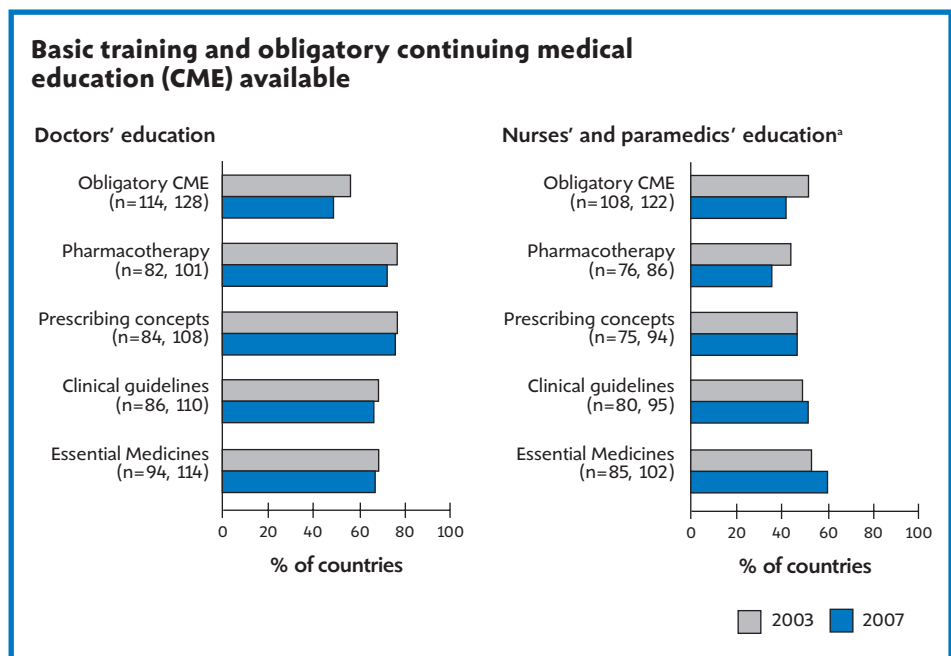
FIGURE 1.8



^a Over half of countries responding to this question did not give a date and were assumed not to have done a drug use audit or updated the EML/STG in the last 2 years; n = the number of countries responding to the question, the first number in 2003 and the second number in 2007.

Source: Level 1 pharmaceutical policy surveys 2003 and 2007.

FIGURE 1.9



^a For prescribing concepts in undergraduate education, an average was estimated across nurses and paramedics.

Source: Level 1 pharmaceutical policy surveys 2003 and 2007.

Austvoll-Dahlgren et al. undertook a review that evaluated policies to improve drug use or to save drug spending (or both) which were implemented by governments, non-government agencies and health insurance companies (45). They evaluated five policies that made patients financially contribute for their medicines while filling their prescription in the pharmacy. These five included: 1) caps, which means that patients receive reimbursement for this medicine up to a maximum amount and have to pay the rest themselves; 2) fixed co-payments, where patients pay a fixed amount per prescription or medicine; 3) tier co-payments, where co-payment depends, for example, on whether the prescribed medicine is a generic or not; 4) co-insurance, meaning that patients pay a proportion of the medicine's price and 5) ceilings, which means that patients pay a maximum amount (e.g. per year) and do not pay once they have reached this maximum. The review showed that cap and co-payment policies have the potential to decrease overall medicines use and the costs for health insurers. These decreases were also found for medicines that are important in treating chronic conditions, which made the authors warn against potential negative consequences. Thus there is a potential imbalance between quality and costs, which should be taken into account. In 2000, Australia tried to find such balance by formally adopting the National Medicines Policy with as its overall policy goal "to meet medication and related service needs, so that both optimal health outcomes and economic objectives are achieved" (46). For that purpose the National Prescribing Service was established (see Box 1.2).

Only a few studies have evaluated the impact of national policies on medicines use. One such study was done in the Republic of Korea, where a national policy, introduced in 2000, prohibiting dispensing by GPs, was associated with a reduction in antibiotic use from 80.3% to 72.8% of viral illness episodes and from 91.6% to 89.7% for bacterial illness episodes (47). Another study was done in Chile, where a new regulation in 2000 prohibiting the dispensing of antibiotics without prescription by private retail outlets was associated with a reduction in overall sales of antibiotics in the private sector – from 0.34 DDD/1000 inhabitant-days (US\$37,603,688) in 1996 to 0.25 DDD/1000 inhabitant-days (US\$32,141,856) in 2000 (48).

1.3

FUTURE CHALLENGES AND PRIORITIES

Irrational use of medicines is a global public health crisis and the lack of investment to improve the situation is a major challenge for the future. In order to advocate for more investment, more research must to be done and informational needs addressed.

1.3.1

Unaddressed global public health crisis of irrational use of medicines

There is now substantial global evidence for continuing irrational use of medicines. Less than 40% of patients in the public sector and less than 30% in the private sector are treated in accordance with existing guidelines, and the situation is not improving in either developing or transitional countries. Likewise, in developed countries there is much evidence of irrational use of medicines. While much intervention research has been undertaken and effective interventions identified for improving the use of medicines, few of these interventions have been scaled up to national level. Furthermore, about half of all countries are not implementing many basic policies recommended by WHO to promote rational use of medicines. Many health system factors and stakeholders influence the use of medicines and due to these complex underlying factors, it has been recommended that countries develop a coordinated national approach to promoting rational use of medicines and containing antimicrobial resistance (ICIUM 2004, WHO 2001). Furthermore, WHO Member States endorsed such a coordinated approach in adopting Resolutions WHA 58.27 in 2005 and WHA60.16 in 2007 (49,50).

Countries should develop a coordinated national approach to promoting rational use of medicines and containing antimicrobial resistance.

BOX 1.2

Antibiotic programmes of the National Prescribing Service in Australia

Australia has an extensive National Medicines Policy (see also chapter on medicine policy). One of its main objectives is Quality Use of Medicines (QUM). In 1998, the National Prescribing Service (NPS) was established to undertake work in QUM. Its purpose is to support the best use of medicines to improve health and well-being. The NPS provides health professionals and consumers access to information and other supports for good prescribing and medicines use decisions. For health professionals this includes professional education activities (e.g. peer group meetings and meetings with QUM facilitators [academic detailing], case studies, clinical audits and pharmacy practice reviews) and access to a range of information resources (e.g. new medicines information [NPS Radar], therapeutic topic reviews [NPS News], a journal on drug and therapeutic issues [Australian Prescriber]) via a variety of channels (e.g. print, web, prescribing software). In addition, medical and pharmacy students use the National Prescribing Curriculum, a set of online learning modules modelled on the WHO manual, *Guide to Good Prescribing*. Consumers have access to a range of information resources (e.g. new medicines information [Medicines Update], factsheets on medicines [Consumer Medicines Information] and about managing your medicines [Medicines Talk], and on topics such as help with managing common colds. Mass media campaigns are run from time to time and work is undertaken with specific groups in the community (e.g. seniors).

The NPS ran seven antibiotic programmes for general practitioners (GPs) and pharmacists between 1999 and 2009. Key messages of these programmes were: “antibiotics are not indicated for most upper respiratory tract infections” and “when indicated amoxicillin is generally first line”, and they have been consistent with national clinical practice guidelines (*Therapeutic Guidelines*). At first GP participation was low but in 2005, 5000 GPs took part in the programme through academic detailing or clinical audits. All campaigns included prescribing feedback and newsletters. In addition, consumer campaigns have been run regularly since 2000 to make the public aware that antibiotics are not effective for coughs and colds. The campaigns involved promotion of key messages through local newsletters, radio, TV, storybooks and distribution of resources to all GPs and community pharmacies. The campaigns cost Aus\$1 million in 2007 and Aus\$500,000 in 2008. During this past decade of provider and consumer education campaigns, it was found that the number of prescriptions for those antibiotics commonly used for upper respiratory tract infections declined from 80 per 1000 consultations in 1996 to 50 per 1000 consultations in 2007. Furthermore, the number of prescriptions for all antibiotics fell from 15.5 per 100 encounters in 1999 to 13.25 per 100 encounters in 2007.

Source: National Prescribing Service, Australia: <http://www.nps.org.au> and personal communication from Lynn Weekes and Jonathan Dartnell of NPS.

A major reason for this failure to adopt a coordinated approach is that promoting rational use of medicines has not been “institutionalized” within health systems in many countries and so there is no structure to undertake the necessary monitoring and coordination of policy. While many rich nations have adapted their health systems to address this issue by setting up national systems for medicines selection, prescription monitoring and obligatory continuing medical education, few low- and middle-income countries have done this. Although such efforts in rich countries may seem to be piecemeal and not within a national programme, they are effective because they are implemented within an existing coordinated underlying national infrastructure, including strong health insurance systems. Such an infrastructure often non-existent in low- and middle-income countries where there may be a need for a different national model which is cost-effective (due to the inevitable resource limitations). A major challenge will be to adapt health systems to “institutionalize” promotion of the rational use of medicines and incorporate the necessary structures within their health systems.

1.3.2

Lack of investment in promoting rational use of medicines

At present there appears to be relatively little investment in promoting rational use of medicines. Restructuring health systems on the lines mentioned above and undertaking the necessary monitoring and implementation of interventions and policy will require significant extra investment. It could be argued that such investment would be paid back many times over by the savings from better use of medicines, particularly reduced misuse (46). However, these savings would take some time to achieve and thus might not be felt by the investing government, particularly in health systems where there is a very large private sector and most medicines are paid for out-of-pocket by patients and not by government.

In developed and some transitional countries, where a large proportion of the population is covered by health insurance, the health insurance agency may play a significant role in promoting rational use of medicines by only reimbursing prescriptions that comply with guidelines or that contain essential medicines. In some high- and middle-income countries insurance agencies are reimbursing medicines according to whether they are essential medicines, generic medicines or approved for a certain use. However, in many low-income countries, insurance coverage is low and there is insufficient infrastructure to establish health insurance in the short term. A major future challenge will be to persuade governments, donors, and the international community to invest sufficiently in promoting rational use of medicines.

An added challenge is that while governments are not investing in promoting more prudent use of medicines, the pharmaceutical industry is promoting increased use of its products. Globally, most prescribers receive most of their prescribing information from the pharmaceutical industry and in many countries this is the only information they receive. Unfortunately, information from the industry may be biased, and the huge imbalance in expenditure between industry and government with regard to providing prescribers with adequate information needs to be addressed urgently (see the chapter on medicine promotion).

1.3.3

Research and informational needs

Much is now known about medicines use in primary care and how to improve it (even if few governments have adopted proven interventions on a national scale). However, relatively little is known globally about medicines use outside of primary care facilities and how to promote rational use of medicines in these settings. Particular areas that need further research include:

- community use of medicines, including informal medicine sellers in the private sector;
- prescribing and dispensing in the private sector where financial incentives encourage over use of medicines and the use of more expensive medicines;
- hospital use, particularly with regard to antibiotic use in developing countries;
- establishing quality assurance mechanisms on prescribing, including monitoring systems, supervisory systems and DTCs;
- national policy implementation and monitoring;
- improving adherence in patients with chronic diseases, particularly since there will be a global increase in the number of patients who need chronic medication (see chapter 2).

Unlike the situation for medicines use in primary care, for which robust standardized indicators to assess use have been developed and utilized, equivalent indicators have yet to be developed for those areas requiring further research listed above (i.e. indicators to assess medicines use in hospitals, communities and the informal sector, indicators to assess patient adherence and indicators on the functionality of DTCs, and the degree of implementation of national policies). This makes monitoring progress difficult, if not impossible. Future areas of research should include the development of standardized indicators in each of the above areas. While the urgent need for indicator development may seem more obvious in some areas, such as hospital or community use or adherence to treatment, it equally applies to the areas of policy implementation, and functional supervisory systems and DTCs. Without the latter, progress in improving the rational use of medicines will remain extremely limited.

REFERENCES

1. *The rational use of drugs. Report of the Conference of Experts.* Geneva, World Health Organization, 1985.
2. *Promoting rational use of medicines: Core components.* WHO Policy Perspectives on Medicines, No.5. Geneva, World Health Organization, 2002. Available at: <http://apps.who.int/medicinedocs/pdf/h3011e/h3011e.pdf>
3. *Medicines use in primary care in developing and transitional countries: Fact book summarizing results from studies reported between 1990 and 2006.* Geneva, World Health Organization, 2009. Available at: http://www.who.int/medicines/publications/primary_care_8April09.pdf
4. Sabaté E. *Adherence to long-term therapies. Evidence for action.* Geneva, World Health Organization, 2003.
5. *Using indicators to measure country pharmaceutical situations: Fact book on WHO Level I and Level II monitoring indicators.* Geneva, World Health Organization, 2006. Available at: <http://apps.who.int/medicinedocs/index/assoc/s14101e/s14101e.pdf>
6. White TJ, Araekelian A, Rho JP. Counting the costs of drug related adverse events. *Pharmacoeconomics*, 1999, 15(5):445-458.
7. Lazarou J, Pomeranz BH, Corey PN. 1998. Incidence of adverse drug reactions in hospitalized patients: A meta-analysis of prospective studies. *Journal of the American Medical Association*, 279(15):120-125.
8. Hitchen L. Adverse drug reactions result in 250 000 UK admissions a year. *British Medical Journal*, 2006, 332:1109. Available at: <http://www.bmj.com/cgi/reprint/332/7550/1109>
9. Pirmohamed M et al. Adverse drug reactions as cause of admission to hospital: Prospective analysis of 18,820 patients. *British Medical Journal*, 2004, 329:15-19. Available at: <http://www.bmj.com/cgi/reprint/329/7456/15>
10. Reducing and preventing adverse drug events to decrease hospital costs. *Research in Action*, Issue 1, March 2001. Agency for Healthcare Research and Quality. Available at: <http://www.ahrq.gov/qual/aderia/aderia.htm>
11. Institute of Medicine. *Microbial threats to health: emergence, detection and response.* Washington, D.C., National Academies Press, 1998.

12. *Resistance: a sensitive issue. The European roadmap to combat antimicrobial resistance.* Utrecht, The Strategic Council on Resistance in Europe, 2004.
13. Simonsen L et al. Unsafe injections in the developing world and transmission of bloodborne pathogens: a review. *Bulletin of the World Health Organization*, 1999; 77(10): 789-800. Available at:
http://www.who.int/injection_safety/toolbox/Simonsen.pdf
14. Livermore DM. Bacterial resistance: Origins, epidemiology, and impact. *Clinical Infectious Diseases*, 2003, 36(Suppl. 1):S11-S23.
15. Levy SB. Antibiotic resistance: The problem intensifies. *Adverse Drug Delivery Reviews*, 2005, 57:1446-1450.
16. Harbarth S, Samore MH. Antimicrobial resistance determinants and future control. *Emerging Infectious Diseases*, 2005, 11:794-801.
17. Kaplan W, Laing R. *Priority medicines for Europe and the world.* Geneva, World Health Organization, 2004. Available at: <http://hinfo.humaninfo.ro/gsdldata/collect/medicinedocs/index/assoc/s14208e/s14208e.pdf>
18. Pechère JC et al. Non-compliance with antibiotic therapy for acute community infections: a global survey. *International Journal of Antimicrobial Agents*, 2007, 29:245-253.
19. Grigoryan L. *Self-medication with antibiotics in Europe and its determinants.* Dissertation, Groningen University, 2007.
20. Lansang M et al. Purchase of antibiotics without prescription in Manila, the Philippines: Inappropriate choices and doses. *Journal of Clinical Epidemiology*, 1990, 43(1):61-67.
21. Van der Geest S, Hardon A. Self-medication in developing countries. *Journal of Social and Administrative Pharmacy*, 1990, 7(4):199-204.
22. *How to investigate drug use in health facilities: Selected drug use indicators.* Geneva, World Health Organization, 1993. Available at:
<http://apps.who.int/medicinedocs/pdf/s2289e/s2289e.pdf>
23. *Indicators for IMCI at first-level facilities and households (Rev 1).* Geneva, World Health Organization, 2001. Available at:
<http://www.paho.org/English/AD/DPC/CD/imci-indicators-7-01.pdf>
24. Goossens H et al. European Surveillance of Antimicrobial Consumption Project Group. Comparison of outpatient systemic antibacterial use in 2004 in the United States and 27 European countries. *Clinical Infectious Diseases*, 2007, 44:1091-1095.
25. Grigoryan L et al. Self-medication with antimicrobial drugs in Europe. *Emerging Infectious Diseases*, 2006, 12(3):452-459.
26. Goossens H. Antibiotic consumption and link to resistance. *Clinical Microbiology and Infection*, 2009, 15(Suppl. 3):S12-S15.
27. Van Roosmalen MS et al. Antibiotic prescribing in primary care: First choice and restrictive prescribing are two different traits. *Quality and Safety in Health Care*, 2007, 16(2):105-109.
28. Haynes RB, Taylor DW, Sackett DL. *Compliance in health care.* Baltimore, MD, The Johns Hopkins University Press, 1979.

29. DiMatteo MR. Variations in patients' adherence to medical recommendations: A quantitative review of 50 years of research. *Medical Care*, 2004, 42:200–209.
30. Myers LB, Midence K. *Adherence to treatment in medical conditions*. Amsterdam, Harwood Academic Publishers, 1998.
31. Francke AL et al. Factors influencing the implementation of clinical guidelines for health care professionals: A meta-review. *BMC Medical Informatics and Decision Making*, 2008, 8:38.
32. Grimshaw JM et al. Effectiveness and efficiency of guideline dissemination and implementation strategies. *Health Technology Assessment*, 2004, 8(6):iii–iv, 1–72.
33. Grol R, Grimshaw J. From best evidence to best practice: Effective implementation of change in patients' care. *Lancet*, 2003, 362:1225–1230.
34. Lu CY et al. Interventions designed to improve the quality and efficiency of medication use in managed care: A critical review of the literature – 2001–2007. *BMC Health Services Research*, 2008, 8:75.
35. Jamtvedt G et al. Audit and feedback: Effects on professional practice and health care outcomes. *Cochrane Database of Systematic Reviews*, 2006, 19(2):CD000259.
36. Wensing M, van der Weijden T, Grol R. Implementing guidelines and innovations in practice: which interventions are effective? *British Journal of General Practice*, 1998, 48:991–997.
37. Haynes RB et al. Review: Evidence on the effectiveness of interventions to improve patient adherence to prescribed medications is limited. *Evidence-based Nursing*, 2008, 11(4):109.
38. Bosch-Capblanch X et al. Contracts between patients and healthcare practitioners for improving patients' adherence to treatment, prevention and health promotion activities. *Cochrane Database of Systematic Reviews*, 2007, (2):CD004808.
39. Vermeire E et al. Interventions for improving adherence to treatment recommendations in people with type 2 diabetes mellitus. *Cochrane Database of Systematic Reviews*, 2005, (2):CD003638.
40. van Dulmen S et al. Patient adherence to medical treatment: A review of reviews. *BMC Health Services Research*, 2007, 7:55.
41. van Dulmen S et al. International Expert Forum on Patient Adherence. Furthering patient adherence. A position paper of the International Expert Forum on Patient Adherence based on an internet forum discussion. *BMC Health Services Research*, 2008, 8:47.
42. Huttner B et al. CHAMP Consortium. Characteristics and outcomes of public campaigns with the aim to improve outpatient antibiotic use in high income countries. *Lancet Infectious Diseases*, 2010; 10(1):17–31.
43. Country pharmaceutical situations. Fact book on WHO Level 1 indicators 2007. Geneva, World Health Organization, 2009. Available at:
<http://apps.who.int/medicinedocs/documents/s16874e/s16874e.pdf>
44. WHO global strategy for containment of antimicrobial resistance. Geneva, World Health Organization, 2001. Available at: http://www.who.int/csr/resources/publications/drugresist/en/EGlobal_Strat.pdf

45. Austvoll-Dahlgren A et al. Pharmaceutical policies: Effects of cap and co-payment on rational drug use. *Cochrane Database of Systematic Reviews*, 2008, 23(1):CD007017.
46. *National medicines policy 2000*. Canberra, Commonwealth Department of Health and Aged Care, 2000. Available at: <http://www.health.gov.au/internet/main/publishing.nsf/Content/nmp-objectives-policy>
47. Park S et al. Antibiotic use following a Korean national policy to prohibit medication dispensing by physicians. *Health Policy and Planning*, 2005, 20(5):302-309.
48. Bavestrello L, Cabello A, Casanova D. Impact of regulatory measures in the trends of community consumption of antibiotics in Chile. *Revista Médica Chile*, 2002, 130(11):1265-1272.
49. World Health Assembly Resolution 58.27. *Improving the containment of antimicrobial resistance*. Geneva, World Health Organization, 2005.
50. World Health Assembly Resolution 60.16. *Progress in the rational use of medicine*. Geneva, World Health Organization, 2007.

ABBREVIATIONS

AMR	Antimicrobial Resistance
ATC	Anatomical Therapeutic Classification
ARI	Acute Respiratory Tract Infection
CME	Continuing Medical Education
COPD	Chronic obstructive pulmonary disease
DDD	Defined Daily Dose
DTC	Drug (medicine) and Therapeutics Committee
EML	Essential Medicines List
ESAC	European Surveillance of Antibiotic Consumption
GPs	General Practitioners
HIV/AIDS	Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome
ICIUM	International Conference for Improving the Use of Medicines
INRUD	International Network for Rational Use of Medicines
IMCI	Integrated Management of Childhood Illness
NPS	National Prescribing Service
ORS	Oral Rehydration Solution
OTC	over-the-counter
QUM	Quality Use of Medicines
STG	Standard Treatment Guidelines
WHA	World Health Assembly
WHO	World Health Organization
URTI	Upper Respiratory Tract Infection
USA	United States of America