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The Pursuit of Responsible Use of Medicines:

Sharing and Learning from Country Experiences

Technical Report prepared for the Ministers Summit

on

The benefits of responsible use of medicines:
Setting policies for better and cost-effective health care

World Health Organization

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Acronyms and abbreviations

3TC	Lamivudine
ACT	Artemisinin-based combination therapy
AIDS	acquired immunodeficiency syndrome
ART	antiretroviral treatment
ASU	Antibiotics Smart Use
AZT	Zidovudine
BHU	basic health units
EDP	Essential Drugs Programme
EDT	electronic dispensing tool
EGPAF	Elizabeth Glaser Pediatric AIDS Foundation
FPB	Popular Pharmacy Programme
FPB-E	Popular Pharmacy Programme Expansion
Fiocruz	Oswaldo Cruz Foundation
GOI	Government of India
HIV	human immunodeficiency virus
INCB	International Narcotics Control Board
INN	international nonproprietary name
MoHSS	Ministry of Health and Social Services
MTC	Mobile Telecommunications Limited
NDPSA	Narcotic Drugs and Psychotropic Substances Act
NGO	nongovernmental organization
NID	National Immunization Day
NMCP	National Malaria Control Programme
NPSP	National Polio Surveillance Project
NVP	nevirapine
OPV	oral polio vaccine
OTC	over the counter
P. falciparum/vivax	*Plasmodium falciparum/vivax*
PMTCT	prevention of mother-to-child-transmission
RDT	rapid diagnostic test
RDU	rational drug use
RMI	Recognized Medical Institution
sdNVP	single-dose nevirapine
SNID	sub-national immunization day
SOP	Standard Operating Procedure
SUS	Unified Health System
SUZY	Scaling UP Zinc for Young Children
TB	tuberculosis
UNAIDS	Joint United Nations Programme on HIV/AIDS
UNICEF	United Nations Children's Fund
USAID	United States Agency for International Development
vs	versus
WHA	World Health Assembly
WHO	World Health Organization

Summary of recommendations

Strategic recommendation 1: Develop and mandate a List of Essential Medicines at the national level to inform reimbursement decisions and ensure access to essential medicines.

A list of medicines to be used in public health-care facilities and/or provided to patients free of charge is a powerful tool in the development of a national medicines policy, aimed at ensuring access to these medicines. Furthermore, identifying these medicines by international non-proprietary name provides the basis for efficient procurement and institutionalization of the concept of generics and increases their use. If a full medicines assessment and prioritization effort cannot be done at the national level because of resource constraints, the World Health Organization Model List of Essential Medicines can be used to develop a national essential medicines list.

***Tactical recommendation 1.1**: A list of essential medicines should be identified at the national level to regulate access to medicines in public health-care facilities and to ensure a broader, more efficient use of these medicines.*

***Tactical recommendation 1.2**: Partial to full reimbursement should be granted at the national level to medicines included in the essential medicines list in order to increase access and promote their use in the health-care system.*

Strategic recommendation 2: Invest to ensure national medicines procurement and supply systems are efficient and reliable to support the responsible use of medicines.

A robust health-care system needs to be able to support the responsible use of medicines by assuring that essential medicines are procured efficiently through centralized tenders, delivered effectively to health providers and patients without stockouts, and routinely checked to assure quality. The reliability and effectiveness of the system is necessary for the right medicine to be available to the right patient at the right time; the efficiency of medicines procurement is of the essence to ensure public spending provides the best value for money.

***Tactical recommendation 2.1**: Establish centralized, tender-based procurement of essential medicines. Funds for medicines provided by international aid organizations should preferably be used through the same system, and comply with national priorities.*

***Tactical recommendation 2.2**: Establish routine quality testing procedures to verify that medicines procured through the national tendering system are of assured quality. Results of quality tests should inform the selection of medicine suppliers.*

***Tactical recommendation 2.3**: Establish a routine performance feedback system to ensure that suppliers who cannot deliver medicines of assured quality in time are informed, and excluded from future tenders.*

<u>Strategic recommendation 3</u>: Promote a shift in focus to early screening and accurate diagnosis to guide/inform medicines prescription and avoid overuse, underuse and misuse of medicines.

Medicines prescribed on the basis of an inaccurate diagnosis are a waste of resources, and a late diagnosis can adversely affect the health outcomes of an otherwise effective treatment. The consequences of a late or inaccurate diagnosis range from unnecessary side effects to hospitalization and inefficient use of resources. Early screening of at-risk patients, and diagnostics, are powerful tools in the pursuit of a responsible use of medicines. While diagnostics do have a cost, the potential benefits (both in health and savings) are considerable and outweigh the initial investment.

***Tactical recommendation 3.1**: Promote focus on accurate diagnosis, with the aid of diagnostics where possible, in order to guide the appropriate prescription of medicines.*

***Tactical recommendation 3.2**: Mandate early screening in at-risk segments of the population to ensure patients are diagnosed in time to maximize the benefits of treatment.*

<u>Strategic recommendation 4</u>: Facilitate the implementation of evidence-based treatment guidelines; where they exist, remove regulatory or administrative barriers and directly target all key stakeholders: prescribers, dispensers and patients.

The underuse, overuse and misuse of medicines can have adverse consequences on health outcomes and expenditure, and are often due to a lack of stakeholder awareness or engagement. Evidence-based treatment guidelines can be effective in avoiding this, and governments should facilitate their implementation by realigning regulatory/ administrative incentives to improve medicine use and to promote a culture in which prescribers, dispensers and patients value and advocate the responsible use of medicines.

***Tactical recommendation 4.1**: Sensitize and promote the engagement of prescribers, dispensers and patients through multi-stakeholder workshops, determining educational requirements for health-care professionals, and public information campaigns.*

***Tactical recommendation 4.2**: Reassess regulatory requirements on the dispensing of selected medicines to ensure their wider availability and accessibility. Regulations should permit over-the-counter availability of medicines of appropriate risk–benefit.*

***Tactical recommendation 4.3**: Reduce redundant paperwork and the administrative burden of prescribing/dispensing particular essential medicines to ensure appropriate patient access.*

<u>Strategic recommendation 5</u>: Promote initiatives that put patients at the centre of treatment in order to maximize adherence to therapy.

Poor adherence can impair the efficacy and safety of medicines, reduce the full benefits of treatment, and lead to unnecessary adverse events and hospitalization. Governments should take the lead in promoting, through national health policy, comprehensive initiatives to improve adherence to medicine treatment. To achieve this complex goal, community-based interventions should be explored to bring health-care professionals and the treatment as close as possible to patients and their lifestyles.

Tactical recommendation 5.1*: Promote the creation of, and provide technical support to community-based initiatives aimed at improving patient engagement and adherence to treatment.*

Tactical recommendation 5.2*: Facilitate health-care professionals in providing closer therapy support to patients, to motivate their health-seeking behaviour.*

Strategic recommendation 6: Monitor medicine use, from purchase to health outcome, to evaluate the real-world efficacy of treatment and guide evidence-based policy-making.

Policy-making aimed at improving the responsible use of medicines is only effective if it is monitored. Records of medicine expenditure provide a good picture of medicine use. Ultimately, patient use and health outcomes should be longitudinally monitored to evaluate adherence and the real-world effectiveness of medicines. The value of monitoring to improve resource allocation has been repeatedly demonstrated in hospitals; such monitoring should become routine in health-care institutions at all levels.

Tactical recommendation 6.1*: Institute a system of centralized monitoring of the purchase of medicines to inform budgeting and ensure optimal funding allocation to essential medicines.*

Tactical recommendation 6.2*: Collect data on medicine use at the national level to identify and evaluate prescribing trends and expenditure.*

Tactical recommendation 6.3*: Design a system to measure patient use of medicines, preferably at the point of dispensing, to assess patient adherence to therapy.*

Tactical recommendation 6.4*: Design a system to collect and aggregate information on patient health outcomes to measure real-world efficacy and safety of medicine use.*

Strategic recommendation 7: Ensure sustained, top-down commitment of national authorities and promote active, bottom-up engagement of prescribers, patients and dispensers to the principles and policies fostering the responsible use of medicines.

Government commitment is essential for a more responsible use of medicines. Commitment should be manifested by providing resources to upscale effective interventions to achieve their full potential, sustained support to successful interventions for as long as needed to ensure sustained results, and by directly engaging national and regional stakeholders to promote top-down commitment coupled with bottom-up engagement of prescribers, dispensers and patients.

Tactical recommendation 7.1*: National authorities should provide sustained, top-down policy and financial commitment to initiatives fostering a responsible use of medicines.*

Tactical recommendation 7.2*: Build consensus on medicine use among national and local stakeholders by stimulating the active engagement of prescribers, dispensers and patients.*

Chapter I – The case for better use of medicines

Background and rationale for the report

In the last decades, medicines have had an unprecedented positive effect on health, leading to reduced mortality and disease burden, and consequently to an improved quality of life. At the same time, there is ample evidence that a large 'missed potential' exists because of the way in which medicines are used: the right medicine does not always reach the right patient; approximately 50% of all patients fail to take their medicine correctly (1); and in many cases, the capability of the system is not sufficient to support the optimal use of medicines. There is much to be gained by using medicines more responsibly, primarily in terms of health gains; conversely, lost value has significant cost implications.

Given the importance of medicine use, the Ministry of Health of the Netherlands, in the context of the International Pharmaceutical Federation World Centennial Congress of Pharmacy and Pharmaceutical Sciences, is organizing a Ministers Summit in October 2012 with the theme 'The benefits of responsible use of medicines'. The purpose of this Summit is to explore solutions to improve patient outcomes and support sustainable and cost-effective health care.

From analyses conducted for the Summit, significant health-care costs can be avoided by using available medicines in a more appropriate way. For example, estimates that focus uniquely on reducing direct health-care costs such as hospitalization do not take into account other, indirect and avoidable costs to society, including loss of productivity.

This World Health Organization (WHO) report is one of two commissioned by the Ministry of Health of the Netherlands to fuel discussions at the Summit; the other is from the IMS Institute for Healthcare Informatics. While WHO uses case histories to glean policy lessons from experiences in low- and middle-income countries, the IMS Institute focuses on cost quantification, case studies, and supporting evidence from low-, middle- and high-income countries. A briefing paper further describes the context of the Summit, summarizes the findings of both reports, and identifies a potential way forward for improved use of medicines.

What is meant by the responsible use of medicines?

The term 'responsible use of medicines' implies that the activities, capabilities and existing resources of health system stakeholders are aligned to ensure patients receive the right medicines at the right time, use them appropriately, and benefit from them. This incorporates the importance of stakeholder responsibility and recognizes the challenge of finite resources. Conversely, suboptimal use is the opposite of what is meant by responsible use throughout this report.

This description complements and is not intended to substitute the WHO definition of rational medicine 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. Irrational (inappropriate, improper, incorrect) use of medicines is when one or more of these conditions is not met."* (2)

The framework for the Summit

The focus of the Summit is on how to recapture the lost value of medicines due to suboptimal use. The value of medicines can be assured if they are:

1. matched to the right patient at the right time
2. taken appropriately by the patient
3. used with the right capabilities.

Figure 1 illustrates these values within the broader context of universal access to medicines, and although the Summit framework does not explicitly cover topics such as innovation policies, pricing, or financing challenges, they are described in World Health Assembly resolution WHA 58.33[1].

Table 1. The value of medicines

Value of medicines is lost if these …	Requirement	
… are not developed	Drug innovation should align with health care needs and address pharmacotherapeutic gaps.	Addressed where relevant, but not in scope
… are not available/ affordable	General availability , affordability and access to medical care and medicines are a precondition for responsible use.	
… are not matched to the right patient at the right time	When patients present themselves to health care professionals, a medicine has to prescribed and dispensed that ideally fits treatment requirements, including appropriate timing.	Focus for the summit
… are not appropriately taken by the patient	When a medicine has been dispensed or sold to a patient, he/she has to be supported and empowered to use the medicine in such a way to ensure it improves his/her well-being.	
… are not used with the right capabilities in place	Health system capabilities such as human capital and data analytics should optimally support the prescriber, dispenser and patient to enable evaluation of interventions at the patient and system level.	

Source: Ministry of Health, the Netherlands

[1] https://apps.who.int/gb/ebwha/pdf_files/.../WHA58_33-en.pdf

The medicines challenge in the broader health system

Health systems aim to bring high-quality health care to their citizens at an acceptable cost. The decisions of health system leaders to optimize scarce resources are often made in light of political and economic interests. In some countries, high debt and fiscal deficits have placed health-care reform high on policy agendas, with medicines as a specific priority. In other countries, health technology assessments have been introduced to assist with implementation of universal health-care coverage.

Use of medicines is a critical factor in health system efficiency. On the one hand, medicine spending accounts for up to a fifth of all health spending, or even more in some countries. On the other, medicines contribute indirectly to efficient health systems as they can avert more costly interventions for severe conditions (e.g. vaccines and statins). However, medicines are often overused (e.g. antibiotics) or underused (e.g. non-adherence), resulting in avoidable adverse events and poor health outcomes.

Revisiting medicine use in light of health-care costs is timely

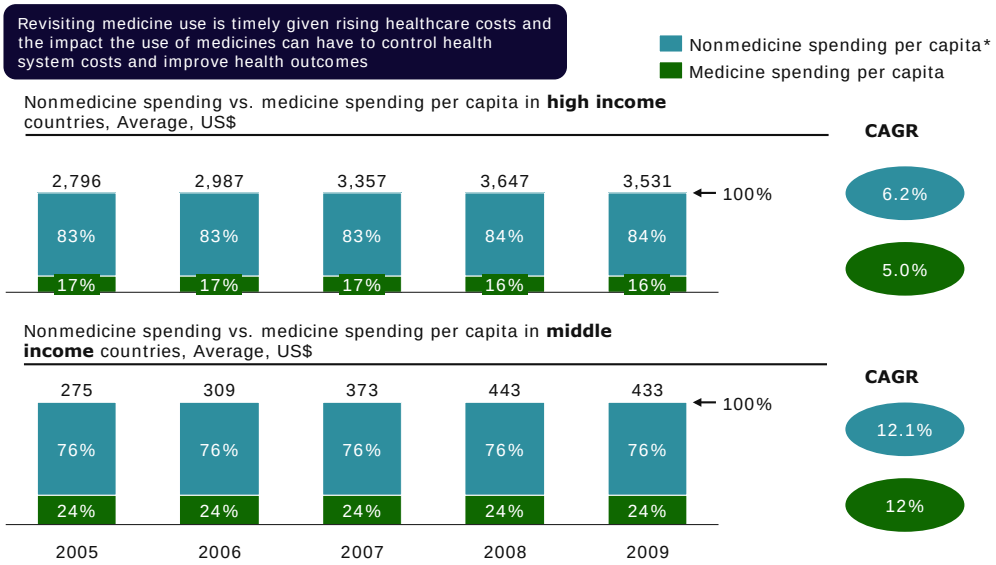
Total health expenditure is rising more rapidly than income across high-, middle- and low-income countries. Across high- and middle-income countries of the Organisation for Economic Co-operation and Development, health spending per capita has surpassed economic growth since 2000 (Figure 1). There is little reason to think this might change as emerging markets accumulate wealth and access to health-care increases. However, the growth rate of the medicines market will slow down: while global spending on medicines is predicted to near US$1 trillion by 2015, this is 3–6% lower (in 2012 – 2017) than the annual growth rate of 6.1% over the last 5 years (in 2007-2012) (3).

A closer look at health spending over the last decade reveals this trend. The rise in health spending combined with the inherent link between medicine use and overall health care (both costs and outcomes), it is extremely important to examine whether medicine use can be improved for the benefit of the entire health system.

This is particularly relevant as medicine access increases in low-income countries and the trend of the last 10 years continues (Figure 2). In fact, emerging markets are expected to surpass the EU 5 (France, Germany, United Kingdom, Italy and Spain) in terms of global medicines spending, and will account for 30% of global spending in 2016 (vs. 13% for the EU 5) (3).

Figure 1. Total health vs medicine expenditure in high- and middle-income countries

Across middle and high income countries, medicine spending is less than a third of total health spending while growth rates are comparable



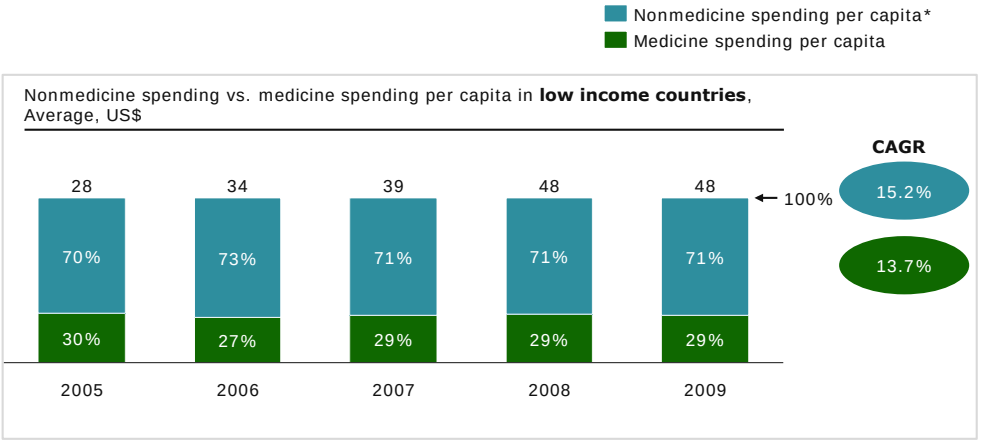
*Nonmedicine spending is calculated by subtracting pharmaceutical expenditure from total health expenditure per capita

Sources: IMS Institute for Healthcare Informatics, 2012; World Bank; WHO (latest available data for a subset of countries representing over 50% Of each income group based on World Bank income groupings)

CAGR, compound annual growth rate

Figure 2. Total health vs medicine expenditure in low-income countries

In low income countries, although medicine spending is a larger share of total health spending nonmedicine spending has been outpacing medicine spending



*Nonmedicine spending is calculated by subtracting pharmaceutical expenditure from total health expenditure per capita

Sources: IMS Institute for Healthcare Informatics, 2012; World Bank; WHO (latest available data for a subset of countries representing over 50% Of each income group based on World Bank income groupings)

A range of factors drives these trends: demographic shifts, changes in disease epidemiology, innovation, and health system components such as stakeholder incentive alignment.

Health system leaders are confronting new challenges in light of an ageing population, increasing noncommunicable disease burden, and rapidly evolving science and technology. These challenges also present opportunities. Today, countries have much greater access to information and evidence for decision-making and can learn from one another on a range of issues, from innovative payment schemes to human resource changes. At the core of the discussion is the patient, seen as a partner in the treatment of the disease or condition. This approach allows the patient to participate in the selection of, and therefore the best use of medicines.

These dynamics offer an ideal opportunity for all health-care stakeholders, particularly ministers of health, to exploit the full value of medicines for maximum health outcomes.

Chapter II – Structure of the report

The aim of this report

As noted above, the 'responsible use of medicines' means that patients receive the right medicines at the right time, use them appropriately, and benefit from them. This technical report illustrates sound examples of national-level policies implemented to promote the responsible use of medicines. Each case study is accompanied by strategic and tactical recommendations could be implemented by ministers of health in other countries and regions of the world.

Scope of the report

Great emphasis is placed on medicine prescribers, dispensers and patients as key stakeholders. This 'downstream' focus on the delivery of medicines recognizes that a functioning delivery system is a prerequisite to being able to implement the recommendations of this report. Here, 'dispensers' are not limited to pharmacists: although qualified pharmacists are best positioned to guide medicine management by supporting physicians in their prescription choices, and patients in their health-seeking behaviour, policy-makers should not underestimate the role "authorized non-pharmacist medicines distributors" play in the use of medicines in the short term. The adequate training and supply of qualified health-care professionals, and pharmacists in particular, is essential in the pursuit of a more responsible use of medicines and should be a priority in health-care systems strengthening.

Beyond human resources, the capabilities that need to be in place in a health-care system to ensure the successful implementation of the recommendations of this report range from a reliable and resilient supply system to robust quality controls and appropriate health-care financing. Although these capabilities are not taken for granted in this analysis, they fall at the margin of the 'downstream' delivery and stakeholder focus. Other fundamental challenges within the health-care system are high out-of-pocket spending and the fragmentation of care delivery.

It is not necessary for the Ministry of Health to own every step of the process. Good regulation of the market along with public–private partnerships and private contributions underpin the attainment of responsible use of medicines. On the other hand, unregulated, profit-driven health-care provision, from individuals or institutions, can severely jeopardize public health policy efforts. The importance placed by this report on universal health coverage under strong government stewardship is in line with the 2005 Fifty-eighth World Health Assembly resolution WHA 58.33, which promotes sustainable health financing, universal coverage and social health insurance for the highest attainable standard of health.

Structure and methodology

The following chapters of this report consider in turn the key areas of: the right medicines (Chapter III) matched to the right patient at the right time (Chapter IV) taken appropriately by the patient (Chapter V) with the right support capabilities (Chapter VI). Chapter VII centres on the benefits of broad, sustained stakeholder commitment to a more responsible use of medicines. Through 11 exemplary country case studies, policy options are explored for each of these key areas, highlighting the benefits of each intervention. The case studies selected by WHO for this analysis largely showcase national policies that have been implemented over a period of 3–5 years in developing countries, although examples from developed countries and longer-term policies are also illustrated where appropriate.

Each case study highlights how stakeholders have been engaged to secure the successful implementation of the national policy. Prescribers need to understand the benefits of responsible use, and practice it to avoid inappropriate use of medicines. Furthermore, dispensers need to be engaged to ensure that only prescribed/appropriate medicines are issued/dispensed to the patient. Finally, patients need to be sensitized to the value of adherence and proactive health-seeking behaviour. Although case studies illustrated in this report touch on the issue of an appropriate supply chain of medicines, the scope precludes a more extensive evaluation of this issue.

Policy recommendations

The recommendations of this report aim to guide national policy-making at two levels: high-level strategic recommendations designed to create the policy framework for a responsible use of medicines; and more concrete, point-of-implementation recommendations. Strategic recommendations are listed at the beginning of each chapter, while tactical recommendations are linked to the relevant case study.

The seven strategic recommendations of this report are the backbone of a multi-stakeholder policy roadmap that, if implemented, will ensure a more responsible use of medicines.

Chapter III – Implementing a list of prioritized medicines

Strategic recommendation 1: Develop and mandate a List of Essential Medicines at the national level to inform reimbursement decisions and ensure access to essential medicines.

The WHO concept of essential medicines was established over 35 years ago and has developed since then into a powerful tool to promote health equity on a global scale. Essential medicines are those that satisfy the priority health-care needs of the population and are selected with due regard to public health relevance, evidence of efficacy and safety, and whenever possible cost-effectiveness. Furthermore, essential medicines must be available at all times in adequate quantities, in the appropriate dosage forms, with assured quality and adequate information, and at a price the individual and the community can afford.

The latest WHO Model List of Essential Medicines is publicly available and comprises over 350 medicines. The list is regularly updated and is used today by many governments in developing countries as the basis (through their National Essential Medicines Lists) for procurement, supply and use of medicines for the health-care system. Although healthcare professionals in high income countries might not be familiar with the term WHO Model List of Essential Medicines, the vast majority of developed countries use lists of prioritized medicines that emulate this WHO Model List.

This chapter addresses the role of governments in identifying, procuring and supplying a list of prioritized medicines at the national level, with particular emphasis on developing countries. The identification and promotion of a limited list of priority medicines stimulates evidence-based medical practice and optimizes the efficiency of expenditure on medicines. Moreover, government commitment to providing access to, and reimbursing essential medicines naturally decreases the use of obsolete or suboptimal medicines, and can improve the health outcomes of treatment and avoid unnecessary expenditure on medicines of unproven efficacy. Therefore, governments should commit to prioritizing essential medicines, fostering and implementing targeted access and reimbursement policies.

National medicine policy should be based on the concept of essential medicines. The case histories in this Chapter illustrate how the governments of two countries obtained remarkable results by prioritizing access to medicines and reimbursement: Oman improved medicine use by limiting access in public health-care facilities to a specified list of priority (later termed "essential") medicines. Similarly, Brazil strived to increase access to priority medicines (which were a part of Essential Medicines) by establishing a nationwide pharmacy programme that provided these medicines for selected indications at low or no cost.

CASE STUDY 1 – Essential medicines list (OMAN)

Tactical recommendation 1.1: A list of essential medicines should be identified at the national level to regulate access to medicines in public health-care facilities and to ensure a broader, more efficient use of these medicines.

Executive summary

- In order to ensure the quality, safety and effectiveness of essential medicines at an affordable price in Oman, the Sultanate enacted a national medicines intervention in 2000 focusing on the prioritization of medicines prescribed through the public health channel.
- The Central Drug Committee was strengthened in its role of selecting the medicines available for use in public sector facilities through the Ministry of Health Approved Drug List. This strengthening was based on a sharper focus on evidence-based medical needs and cost-effectiveness of the medicines.
- The more responsible approach to medicines use is calculated to have saved 10–20% of the forecasted medicine expenditure every year between 2003 and 2009 with no evident negative impact on the burden of disease in Oman.

Background

The Sultanate of Oman has experienced a remarkable improvement in the quality and availability of health care in the last 40 years. Through sustained commitment and investment, Oman has progressed from limited health-care provision in the 1970s to the present comprehensive universal health-care model which has been internationally acclaimed for its performance and cost effectiveness (4).

Initially, Oman had no clear national policy to ensure the availability of safe and effective medicines to its population, nor a functioning health-care infrastructure, since health-care providers were limited and predominantly trained outside the country (5). Due to this diverse background and training, the quality of care provided as well as the medicines prescribed were inconsistent. Thus, ensuring that appropriate medicines were made available and then used properly was a problem.

In order to ensure the quality, safety and effectiveness of essential medicines at an affordable price in Oman, the Sultanate enacted a national medicine intervention in 2000 focusing on the prioritization of essential medicines prescribed through the public channel (6).

Intervention

Following a WHO assessment in 1996 (7), the Central Drug Committee was strengthened in 2000 in its role of selecting the medicines available for use in public sector facilities through the Ministry of Health Approved Drug List (7). This strengthening was based on a sharper focus on evidence-based medical needs and cost-effectiveness of the medicines. Furthermore, all medicines were to be included in the Approved Drug List by international

non-proprietary name (INN) in order to encourage generic prescription. A system for the regular update of the Approved Drug List was established to take into account the feedback of prescribers and other sources of information related to the appropriate procurement of medicines. These concerted efforts culminated in 2003 in the publication of the Oman National Formulary for Ministry of Health Institutions (5).

This intervention was enacted in the context of increased and sustained focus of the Sultanate on the development of a comprehensive health-care system in which patients are treated free of charge, mainly through the public sector and by an appropriate number of trained professionals. Separate policies were enacted to ensure the appropriate supply of medicines to the treating centres and the appropriate quality monitoring of the medicines distributed (5).

In order to ensure the cooperation and support of all key stakeholders in this national effort, the Sultanate engaged physicians, pharmacists and patients separately (5). In 2002 Oman sponsored a series of courses promoting rational drug use (RDU), which consisted of an intensive two-week curriculum encompassing all aspects of how to improve the use of medicines. These courses were designed to train key prescribers on the importance of the new National Drug Policy and the impending Oman National Formulary, to allow them in turn to influence their peers on responsible prescribing. Furthermore, since 2001 the rational use of medicines became a requirement in the final examination of Medical Officer General Practitioners.

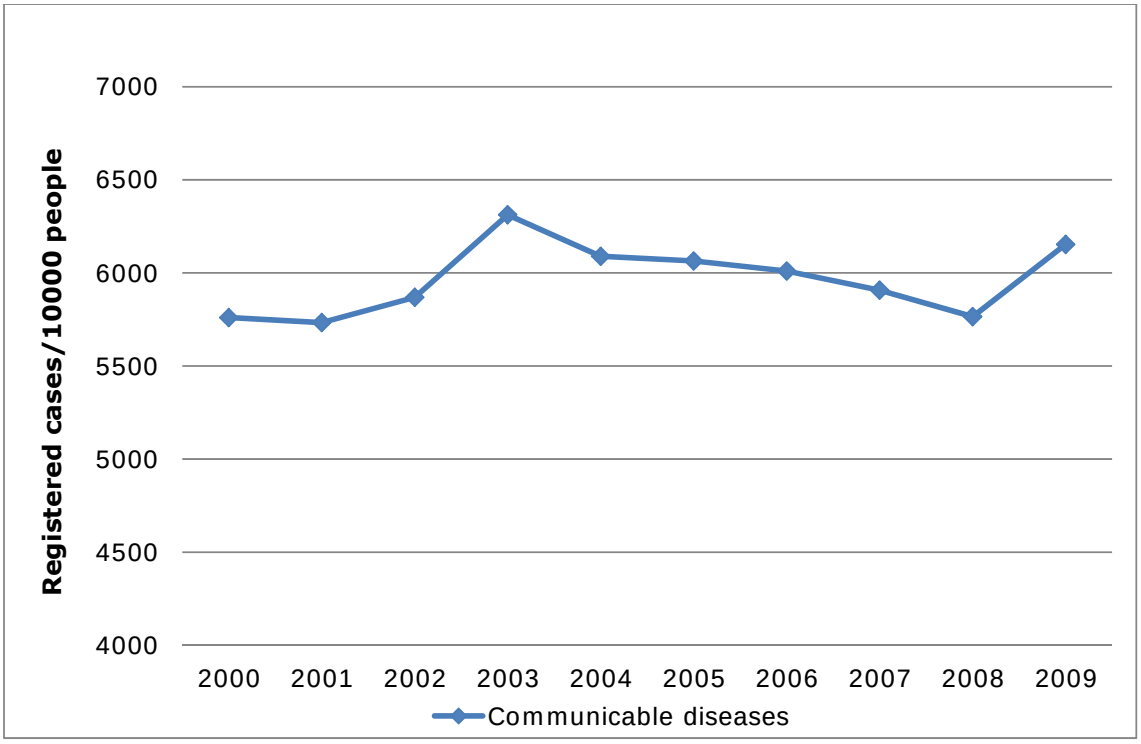
Renewed attention was also placed on the training of pharmacists. A training manual was developed to provide them with practical examples and suggestions in order to support prescribers to be more responsible in the use of medicines. This manual was published in 2004 and its implementation followed up through a series of workshops throughout the country. The recommendations were specifically tailored to the needs and nuances of the health-care situation in Oman.

A public education campaign was launched in 2011 to sensitize the general public to the benefits of a more responsible use of medicines in their homes with the title 'My health lies in the appropriate use of medicines'. The campaign consisted of a series of mass media advertisements and public events to raise awareness of the benefits of the new national medicines policy. The first phase of the public education campaign has been concluded, and a Ministry of Health report on the success of the initiative is currently being compiled.

Health outcomes

Figure 3 shows that a more responsible use of medicines had no negative effect on the burden of disease, since outpatient morbidity for communicable diseases (the proxy indicator for morbidity preventable by medicines) did not significantly change after 2003 (8).

Figure 3. Outpatient morbidity, communicable diseases, 2000–2009

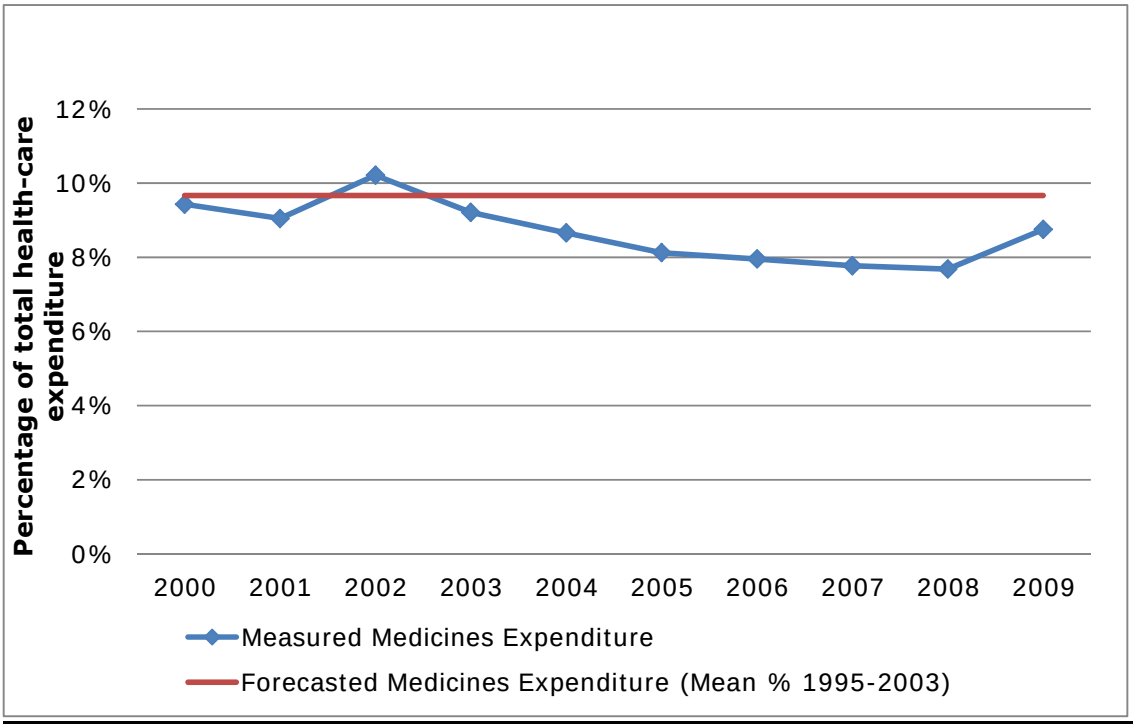


Source: Annual health reports, Ministry of Health of the Sultanate of Oman

Financial outcomes

The economic benefits of an increased focus on essential medicines are clear from expenditure on medicines after 2003, when the Oman National Formulary was published and most stakeholder engagement programmes were under way. Figure 4 shows a comparison of actual medicine expenditure as a percentage of total health-care expenditure between 2000 and 2009 with its forecasted value based on mean medicine expenditure between 1995 and 2003: a more responsible approach to the use of medicines consistently saved 10–20% of the forecasted medicines expenditure between 2003 and 2009 (8).

Figure 4. Measured vs forecasted medicines expenditure, 2000–2009



Success factors

The medicine policy reform, and implementation of the National Essential Medicines List in Oman went smoothly because of the predominantly public health-care system that had been built during the previous decades. The Oman National Formulary was updated and expanded in 2009. Uptake of essential medicines was not as great in the private sector; however, this represents less than 10% of total health-care services.

A further factor in the success of this intervention was the engagement of key stakeholders. Without a strong and sustained educational effort targeting physicians, prescribers and patients, the intervention may have been seen as a mere cost-cutting procedure.

Conclusions

The establishment of a well-developed and implemented essential medicines list has allowed the Sultanate to ensure the availability of safe and effective medicines, and at the same time secure significant economic benefits from better medicine expenditure control. Furthermore, it is clear that these gains were not made at the expense of an increased burden of disease. The experience in Oman shows how the prioritization of medicines at the national level can be instrumental in supporting a more responsible use of medicines.

CASE STUDY 2 – Popular pharmacy programme (BRAZIL)

Tactical recommendation 1.2: Partial to full reimbursement should be granted at the national level to medicines included in the essential medicines list in order to increase access and promote their use in the health-care system.

Executive summary

- In Brazil, equal access to medicines is a priority for the Government. However, a significant part of the population is not covered by the national health-care system.
- To improve access to essential medicines, the Brazilian Government introduced the Popular Pharmacy Programme Brazil (FPB-P) in 2004, creating Government-owned pharmacies throughout the country where patients could obtain 107 medicines at low cost.
- The programme was expanded in 2006 to the private sector (FPB-E), making more low-cost medicines available at more locations.
- For all medicines, the Government reimburses 90% of either the reference value or the pharmacy retail price of generic medicines.
- Since 2011, selected medicines for diabetes and hypertension have become available free of charge at the pharmacies participating in the FPB-E.
- As a result, access to, and use of essential medicines has increased.
- This implies that by prioritizing national reimbursement policies, a government can improve the affordability and accessibility of essential medicines.

Background

In Brazil, access to essential medicines became a constitutional right for its population of over 190 million and an obligation for the State in 1988. To ensure equal, universal and integral access to health care for all citizens, the Brazilian Government introduced the Unified Health System (SUS), covering all Brazilian citizens. However, 30% of the population – 57 million people – remained outside the reach of the public health-care system in 2008 for several reasons, including their residence in remote locations and/or far from pharmaceutical services. For these persons, health care and medicines had to be obtained through private insurance or through out-of-pocket payments, meaning that essential medicines were unaffordable and inaccessible for a substantial, and the poorest, part of the population (9).

Responsible use of medicines requires that the patient take them appropriately. Based on WHO strategies to minimize non-adherence, a holistic approach was adopted to enhance the private-sector reimbursement of essential medicines through a policy intervention: in 2004, the Brazilian Government initiated the *Programa Farmácia Popular do Brasil* (FPB-P, Brazilian Popular Pharmacy Programme). In 2006 the project was extended by a public–private sector initiative called *Aqui tem Farmácia Popular* (Here there is a Popular Pharmacy). This extension, also known as FPB-E, is a private-sector managed, co-paying system that offers

essential medicines at low prices for a number of conditions such as hypertension, diabetes, asthma and glaucoma among others.(9).

The overall objective of these two projects was to optimize the use of essential medicines for people in Brazil who had no access to SUS benefits, of who had private health-care insurance but no financial resources to purchase medicines (private health plans in Brazil rarely cover medicines). Brazil achieved this objective by increasing the availability and affordability of essential medicines through public–private partnerships, since patients clearly cannot adhere to treatment they cannot afford. Although socioeconomic policy interventions are not within the boundaries of this report, this case study is a good example of how the responsible use of medicines can be improved by facilitating access for the whole population, i.e. a holistic approach to minimize non-adherence (9).

Intervention

The two parts of the FPB can be described as drivers of the Brazilian health-care system to serve those not covered by the SUS. The initial, public sector project (FPB-P) was introduced in 2004 and extended to the private sector managed project (FPB-E) in 2006. The FPB-P is managed by the Brazilian Ministry of Health and the Oswaldo Cruz Foundation (Fiocruz), cooperating with non-profit organizations in the public and private sectors. For the introduction of the FPB-P in 2004, 27 new pharmacies – the Popular Pharmacies – were created to dispense medicines from a list of 107 items, comprising 96 medicines.[1]

Recent data show that the number of Government-owned Popular Pharmacies has reached 556, covering 440 municipalities (80%). All 107 medicines dispensed at these pharmacies are centrally purchased by auction bids from official public and private laboratories, and made available at the same price across the country. Prices are set at an affordable level, ranging from R$ 1-10 (=US$ 0.50-5.00) per single dose for incidental treatment medicines to R$ 0.01–0.50 (US$ 0.01–0.25) for single units for chronic treatment medicines, including antibiotics and hormonal preparations.

The extension of the project in 2006 is managed by the private sector and includes 20 373 registered retail pharmacies nationwide. This extension includes medicines for hypertension, diabetes, dyslipidaemia, asthma and rhinitis, glaucoma, Parkinson disease, osteoporosis, influenza H1N1 and contraceptives, as a subset of the medicine list of the initial programme. For all medicines, a reference value (RV) was established by the Government. When the pharmacy retail price is equal to or higher than the RV, the Government reimburses 90% of the RV; when the pharmacy retail price is lower than the RV, the Government reimburses 90% of the pharmacy retail price. The RVs of the FPB-E are based on generic medicines.

[1] The complete list of medicines available through the Popular Pharmacies can be consulted on the Brazilian Ministry of Health web site: http://portal.saude.gov.br/portal/arquivos/pdf/tabela_farmaciapopular_abril08.pdf.

The extension model was expanded in early 2011, making diabetic and antihypertensive medicines available for free to eligible patients at the enrolled pharmacies. Four conditions apply for this part of the programme:

1. The medicines are only dispensed monthly;
2. The medicines must be dispensed to the user of the medicines or a proxy who can justify obtaining the medicines;
3. The pharmacy must keep a record of the medical prescription;
4. The user must sign for the medicines.

The Ministry of Health buys the medicines from private and public industry which are then sold by the governmental pharmacies (FPB-P) and private retail stores (FPB-E) at the predefined prices.

In summary, the policy interventions undertaken by the Federal Government for the first part of the programme included the creation and management of Popular Pharmacies to deliver selected essential medicines. The policy interventions for the second part included registration of participating pharmacies and implementing a nationwide reimbursement policy for a defined list of generics.

Since the aim of the FPB project was to optimize pharmaceutical care and adherence to medicine treatment, the first stakeholders engaged were pharmacists. However, prescription practice had to be in line with the available medicines at the Popular Pharmacy and the participating private sector pharmacies. Therefore, although prescribers were not the principal stakeholders in this case study, their commitment to responsible prescribing of medicines was essential.

Health outcomes

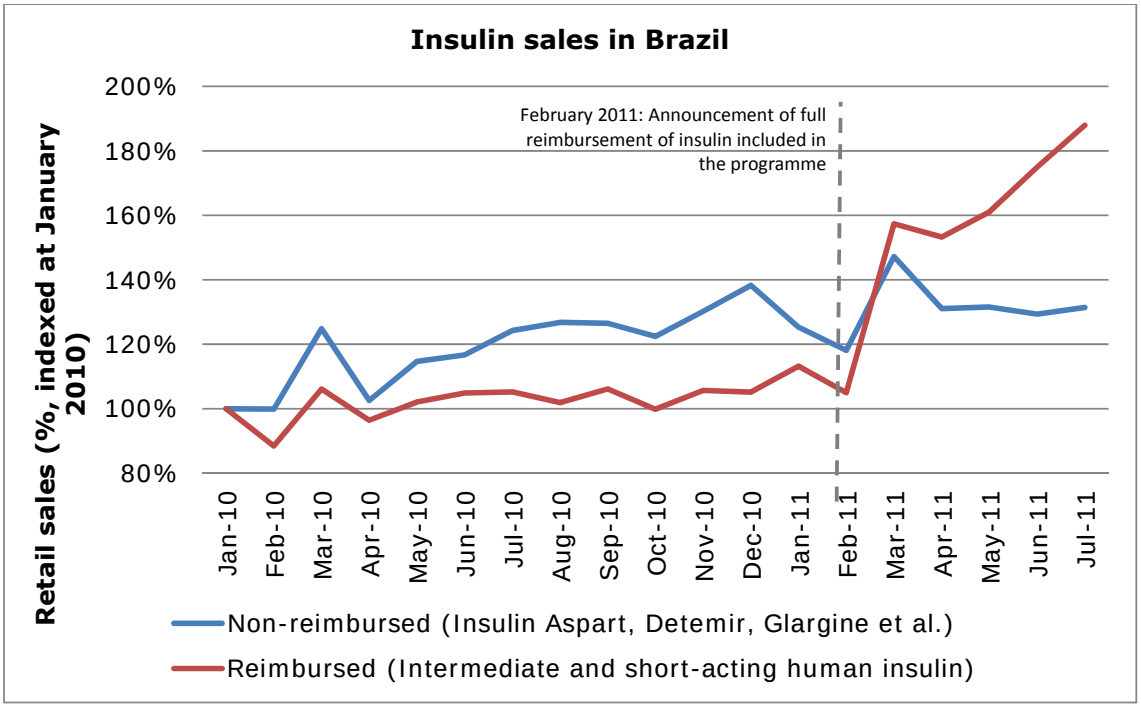
Although no mortality data were available, improved utilization of essential medicines for chronic conditions should lead to improved health outcomes, both on the individual and population scale. According to government data, the introduction of the FBP has allowed patients to continue taking their medicines without a break in treatment. Furthermore, the programme has decreased the financial burden on families (10).

Financial outcomes

The financial outcomes of the FPB can be derived from pharmaceutical sales data obtained from IMS Health Brazil. Data not included in this report show the example of insulin after it was made available free of charge, as part of the second expansion of the FPB in 2011. Consumption of insulin derivatives not covered in the private sector remained stable, whereas there was a two-fold increase in sales of insulin provided for free through the FBP-P. Figure 5 shows how increased access to insulin medicines in Brazil encouraged people who were not using them before 2011 to start using them when they became available free of charge. Data from IMS Health Brazil show that the volume of insulin provided free

accounted for 51% of the total market volume, while their cost accounted for only 26% of the total market costs of insulin in Brazil (9).

Figure 5. Insulin sales before and after extension of the Popular Pharmacy Programme in Brazil



Source: IMS Health Brazil

Success factors

The key success factor of this programme was the commitment of the Brazilian Government to improve access to essential medicines for all its citizens. Furthermore, the approach of engaging public and private sectors, including municipalities, a philanthropic organization and retail pharmacies, made possible the nationwide outreach of the programme. Expanding the programme to the private sector created a win-win situation: participating retail pharmacies could increase revenue; patients could afford their medicines; and the Government could maximize the impact on health of its reimbursement policy.

Conclusions

Brazil is a large, highly populated country, and so achieving nationwide results from a centrally managed project was a real challenge. As the case study shows, this challenge was successfully addressed through the introduction, evaluation and continuation of the FPB. The outcomes of this case study may serve as recommendations for other countries wishing to improve affordability of medicines and thereby adherence to treatment schedules and their health outcomes.

Chapter IV – Treating the right patient at the right time

Strategic recommendation 2: Invest to ensure national medicine procurement and supply systems are efficient and reliable to support the responsible use of medicines.

Strategic recommendation 3: Promote a shift in focus to early screening and accurate diagnosis to inform medicine prescription and thereby avoid overuse, underuse and misuse of medicines.

Strategic recommendation 4: Facilitate the implementation of evidence-based treatment guidelines; where they exist, remove regulatory or administrative barriers and directly target all key stakeholders: prescribers, dispensers and patients.

The efficient procurement and reliable supply of medicines of assured quality remain concerns in many developing and developed countries alike. Referring more specifically to essential medicines, a robust health-care system needs to support the responsible use of medicines by assuring that they are procured efficiently through tenders, delivered effectively to health-care providers and patients without stockouts, and checked routinely to assure quality. As seen in case study 3 on the medicines supply system reform in Bhutan, the reliability and effectiveness of the system is necessary to ensure the right medicine is available to the right patient at the right time. Therefore, the efficiency of medicines procurement is of the essence to ensure that funds spent provide the best value for money.

The availability of effective medicines alone, however, is not sufficient to guarantee that the patient receives the appropriate treatment for the maximum health outcome; the responsible use of medicines requires a correct and timely diagnosis, and prescription and dispensing of the right medicines in correct quantities. An accurate diagnosis is needed to avoid the misuse of medicines, and a late diagnosis can annihilate the health outcomes of an otherwise effective treatment. The consequences of the suboptimal use of medicines due to any of these causes can be dire, ranging from unnecessary suffering from side-effects to hospitalization due to complications and the waste of scarce resources.

As in the malaria case study 4 below, the impact of diagnostics is increasing as physicians rely on them to target therapy and avoid the misuse of medicines. The value of a correct diagnosis is evident, especially in instances where the disease progression is very rapid or the medicines are expensive. Furthermore, early screening of patient groups that are known to be at heightened risk of a specific disease can greatly increase the effectiveness of available therapy. Case study 5 on HIV antenatal screening best illustrates the value of such proactive, early screening in critical patient groups.

Diagnosis needs to be followed by the correct prescription and dispensing of the appropriate quantity of medicines: evidence-based treatment guidelines are fundamental in guiding prescription, and regulatory/administrative incentives play a significant role in determining

prescribing behaviour. The case studies on Antibiotics Smart Use in Thailand (see Case Study from Thailand); medical use of opioids in India (see Case Study from India) and zinc in diarrhoea treatment (see Case Study from Bangladesh) are examples of actions that can be taken to avoid underuse, overuse and misuse of medicines.

The six case studies included in this Chapter offer concrete, practical suggestions on how efficient supply management, correct and timely diagnosis, and evidence-based guidelines can be leveraged to promote the responsible use of medicines.

CASE STUDY 3 – Medicines supply reform (BHUTAN)

Tactical recommendation 2.1: Establish centralized, tender-based procurement of essential medicines. Funds for medicines provided by international aid organizations should preferably be used through the same system, and comply with national priorities.

Tactical recommendation 2.2: Establish routine quality testing procedures to verify that medicines procured through the national tendering system are of assured quality. Results of quality tests should inform the selection of medicines suppliers.

Tactical recommendation 2.3: Establish a routine performance feedback system to ensure that suppliers who cannot deliver medicines of assured quality in time are informed, and excluded from future tenders.

Executive summary

- An Essential Drugs Programme was initiated in Bhutan in 1986, which included the creation of an Essential Medicines List, new treatment guidelines and the monitoring of medicines use. One key aspect of the programme has been the focus on improving the procurement and delivery of medicines.
- The first key action undertaken by the Ministry of Health was to centralize the procurement of all medicines to be prescribed in public health-care facilities through a system based on supplier competition in yearly tendering, as opposed to single-manufacturer emergency purchase. The quality of medicines procured was monitored through a mix of random sample testing and staff reports of suspected poor quality.
- The availability of essential medicines in basic health units (BHU), the chief providers of primary health care services for a large portion of the population in remote areas, increased from 6% before the Essential Drugs Programme (EDP) to 66% in 1989.
- The increase in competition among suppliers resulted in a 6% drop in average medicine prices before inflation between 1985 (before EDP implementation) and 1990. Only 3% of randomly sampled essential medicines failed laboratory quality controls between 1988 and 1992; the failure rate of all procured products in the period 1988–1997 was 1.5%. The majority of recorded quality failures were minor.

Background

When the Government of Bhutan set out to improve the quality of its health-care system, it became evident that the procurement, storage and supply system for medicines was neither resilient nor reliable enough to support the responsible use of medicines. The overall availability of medicines was heavily influenced by decentralized direct procurement, a lack of Government or other control over accounting of donated supplies, and frequent stockouts due to a combination of short medicine shelf-life and poor transportation routes during the monsoon months.

An Essential Drugs Programme was initiated in 1986 in partnership with WHO and international health-care professionals, and has been run with increasing independence by local staff since the early 1990s. The programme includes interventions ranging from the creation of an Essential Medicines List to new treatment guidelines and the monitoring of medicines use. The programme has particularly focused on improving the procurement and delivery of supplies. Six-monthly drug consumption reports were introduced, along with annual indent forms for medical supplies other than drugs (11).

Intervention

In order to secure more reliable and efficient procurement, the first key action undertaken by the Ministry of Health was to centralize the procurement of all medicines to be prescribed in public health-care facilities. This centralization allowed economies of scale and laid the foundation for a procurement system based on supplier competition in yearly tendering, rather than emergency purchase from a single manufacturer. A new list of suppliers was drafted for national procurement purposes, including at least three manufacturers for each medicine in the essential list to ensure appropriate competition. The tender process was then opened to both local and international manufacturers. This centralization included the procurement of donated medicines (27% of the total medicine expenditure between 1987 and 1997) whose bid prices were compared with those proposed by manufacturers in the tender list. This policy was designed to obtain the best value for money in procurement, and focus donated funds solely on essential medicines (11).

Through the use of centralized tenders, it became possible to lay down more specific conditions on the medicines procured and the timeliness of their delivery. Purchase order terms were revised to specify that the medicines procured had to have a minimum of two years' shelf-life when received by ministerial facilities, splitting deliveries for products with shorter shelf-lives. Furthermore, given the narrow window of opportunity of medicine distribution throughout the country due to the constraints imposed by the monsoons, supply deadlines were firmly enforced. The enforcement of these conditions was particularly influential as late deliveries or those not meeting ministerial specifications would eventually result in exclusion from the national tender suppliers list.

The quality of medicines procured was ensured through a two-pronged approach. First, only manufacturers that had secured a WHO Good Manufacturing Practices Certificate (issued by the manufacturer's national authorities according to WHO Guidelines) were admitted to the tendering list. The quality of the medicines delivered was then assured

through a mix of random sample testing and staff reports of suspected poor quality. All failures in quality control tests were reported, which influenced supplier selection in subsequent tenders. Because Bhutan did not have a national institution in charge of verifying medicine quality through laboratory tests, two WHO collaborating centres (in Thailand and India) were identified to assess a limited number of medicine samples on an ongoing basis. The availability of these laboratories allowed a sharing of the quantity of medicines tested in any one centre, and the Ministry of Health to double-check test results (11).

Although these policies were essential to support the responsible use of medicines in the 'downstream' area of health-care delivery, the interventions focused on shifting the procurement power from manufacturers to the Ministry of Health. In order to broaden the key targets of the interventions beyond medicine manufacturers and suppliers to include prescribers and dispensers, the following activities were regularly conducted: workshops on good prescribing practices; good store and inventory management for all health workers, especially pharmacy technicians responsible for medical store in the hospitals; and training for prescribers on the rational use of drugs.

Health outcomes

Not all the positive results of the broad Essential Drugs Programme can be attributed to the interventions on procurement. However, key outcomes reflect the success of the policies implemented to support the responsible use of medicines via supply reforms. As it was not possible to carry out a robust comparison of key outcome indicators before and after implementation of the Essential Drugs Programme, the results are clearly limited.

The significant increase in access and price reductions were not obtained at the expense of quality. Only 3% of randomly sampled essential medicines failed laboratory quality controls between 1988 and 1992 (1.5% failure of all procured products in the period 1988–1997). The majority of recorded quality failures were minor, underlying the importance of supplier screening via WHO Certification (11).

Financial outcomes

The EDP showed an impressive impact on the availability of essential medicines in remote areas of Bhutan. BHUs, chief providers of primary health services for a large portion of the population in remote areas, increased from 6% to 66% in 1989. The essential medicines pertaining to BHUs and hospitals were available in over 80% of audits performed between 1990 and 1997. In addition, over 90% of 27 basic medicines were available in all health facilities throughout the year during the 1989 and 1997 audits. The wastage of medicines due to expiry also declined to an average 0.73% of the total medicines budget between 1993 and 1996 (11).

The increase in competition among suppliers resulted in a 6% drop in average medicine prices before inflation between 1985 (before EDP implementation) and 1990. This price reduction slowed in the following years, with inflation-adjusted average prices in 1997 being only 10% less than those of 1990. Due to strict adherence to the new procurement policies

aimed at fostering price competition, the average medicine prices paid in Bhutan in 1997 were 50% lower than average international prices (11).

The legislation for regulation of medicines was enforced only when the medical supply system was well instituted and fully functioning: in 2003, the Bhutan Medicines Act was passed by Parliament and effective enforcement of medicinal product registration was initiated in 2005. Today, only medicinal products that are registered with the Drug Regulatory Authority, independent of the Ministry of Health, are allowed in the country. The provisions are drafted to be more facilitative, to focus on the best practices of developed countries, and to ensure availability of the essential drugs needed in the country.

Success factors

The clear focus on quality and timeliness of delivery, coupled with yearly performance assessments shared with the supplier, placed pressure on all stakeholders to work to the best of their ability in order to remain on the national tendering list. The inclusion in tenders of three or more suppliers for each essential medicine ensured that both the cost and the quality of medicines procured were always controlled.

Conclusions

The reform of both medicine supply and delivery were fundamental in supporting the ministerial campaign for responsible use of essential medicines. This experience underlines the importance of ensuring robust and resilient supply systems to support prescribers, dispensers and patients in the 'downstream' delivery of health care.

CASE STUDY 4 – Malaria rapid diagnostic test (SENEGAL)

Tactical recommendation 3.1: Promote focus on accurate diagnosis, with the aid of diagnostics where necessary, in order to guide the appropriate prescription of medicines.

Executive summary

- Due to suboptimal availability and affordability of adequate diagnostics, febrile patients are often inappropriately treated with antimalarial artemisinin combination therapy (ACT) medicines.
- Rapid diagnostic tests (RDTs) are important tools in the accurate and specific diagnosis of, for example, *Plasmodium falciparum* malaria.
- In Senegal, the Government prioritized accurate diagnosis by introducing RDTs as the first-choice diagnostic for malaria-suspected patients.
- As a result, presumptive treatment based on clinical symptoms decreased and ACT medicines correctly targeted patients with confirmed malaria.
- This intervention is very likely to have contributed to the significant decrease in malaria that occurred.

Background

The parasitic disease malaria is a significant cause of death, mainly for children in sub-Saharan Africa under five years of age (12). To help countries to manage the burden of malaria, WHO has published treatment guidelines that encourage early diagnosis, built on solid scientific evidence. Prompt parasitological confirmation by microscopy or by RDT is recommended in all patients suspected of malaria before treatment is started (13). Treatment based solely on clinical suspicion should only be considered when a parasitological diagnosis is not accessible (i.e. within 2 hours of the patient presenting); symptomatic diagnosis has very poor specificity, as the first symptoms of the disease can also be attributed to minor viral infections (13).

Presumptive treatment of febrile illnesses without parasitological confirmation has led to overuse of medicines, which is one of the contributing factors to the development of resistance. Oral artemisinin-based monotherapy medicines also play a major role in the development of resistance. To avoid and delay the development of resistance, combination therapies are given (13). Therefore, prompt and accurate diagnosis of malaria is essential to provide the correct medical treatment for both confirmed malaria cases and the management of other febrile diseases.

Following a parasitological confirmation, artemisinin-based combination therapy (ACT) is the evidence-based and cost-effective first-choice treatment for uncomplicated falciparum malaria recommended by the WHO malaria treatment guideline. Increasing accurate diagnoses reduces the frequency of false-positive results, which in turn reduces drug wastage, overuse and pressure towards resistance (13,14).

The decision on diagnostic testing by microscopy or RDT largely depends on the setting. In remote areas, for example, quality microscopy is not as available as in main hospitals. Thus, when an outpatient on-the-spot diagnosis is required, RDTs are the preferred diagnostic. RDTs are easy to use and effective in early diagnosis of malaria. Importantly, they deliver a rapid and point-of-care diagnosis without the delays associated with centralized laboratory diagnostics. Since their introduction in 1993, the accuracy, availability and affordability of quality products have progressively improved, although this remains suboptimal in many countries (12).

This case study shows the successful introduction of malaria RDTs in Senegal, a lower-middle-income country with a malaria incidence of more than 10% of the total population, depending on the area. The potentially fatal *P. falciparum* parasite is responsible for virtually all reported cases and the relatively benign *P. vivax* parasite is a small fraction. Before the introduction of RDTs in 2007, malaria diagnosis depended primarily on clinical assessment, with microscopy confirmation limited to the larger hospitals.

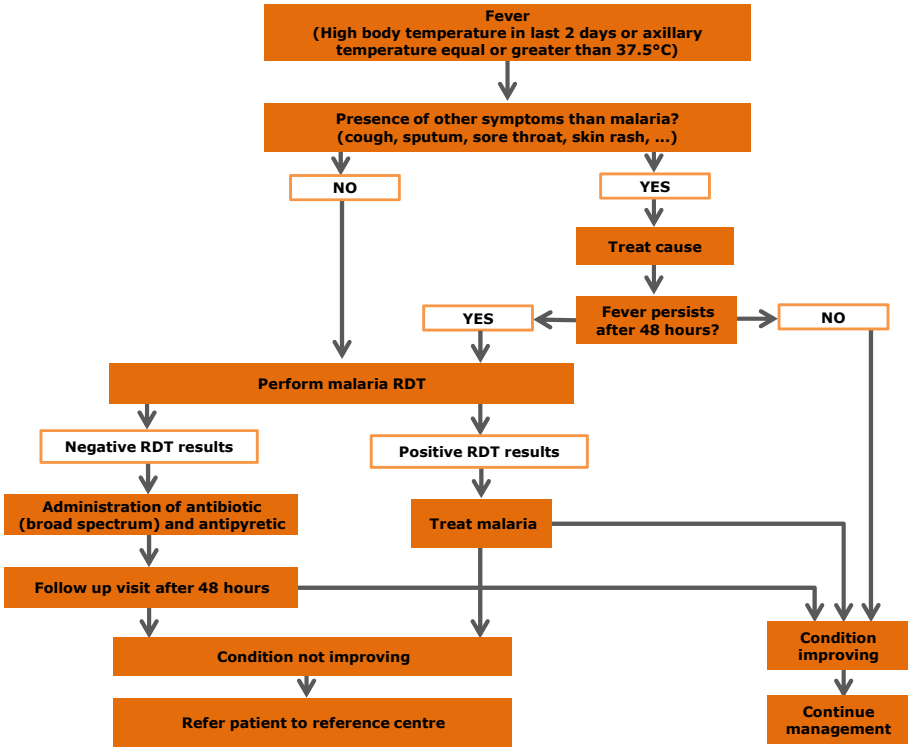
The impact of RDTs on treatment exposure and health outcomes is poorly documented in many countries. The results of the Senegal intervention, however, were carefully evaluated in the peer-reviewed academic journal *PloS-One* (14), providing a generalizable rationale for implementation of RDTs in malaria-endemic countries, in line with WHO guidelines (13).

Intervention

Since 1995, the National Malaria Control Programme (NMCP), affiliated to the Government, has been the overarching institute in Senegal responsible for the development and implementation of malaria policy. Over the years, the NMCP has attracted several grants to fund their projects from international organizations including the Global Fund to Fight AIDS, Tuberculosis and Malaria, the United Nations Children's Fund (UNICEF) and the World Bank. The programme sought to scale up the use of RDTs and decrease the overuse of ACTs, and hence increase effective and responsible use. This is integral to the mission of the NMCP and WHO to control and ultimately eliminate malaria.

The project started in September 2007 with incorporation of the use of RDTs in the national guidelines for the management of febrile illness. All presented cases with suspected malaria in the community were subjected to an RDT, restricting ACT to positive cases. Figure 6 shows the treatment algorithm to be followed when a case was presented at the community point of care (14,15). This guideline change reached all hospitals, public sector health centres and community health huts in 2008, making RDTs accessible to all patients presenting at health-care settings in Senegal with febrile disease. This shows that this intervention had good short-term feasibility.

Figure 6. Febrile illness case management algorithm recommended in Senegal, 2007



Source: Malaria case management algorithm of the Senegal NMCP, 2007

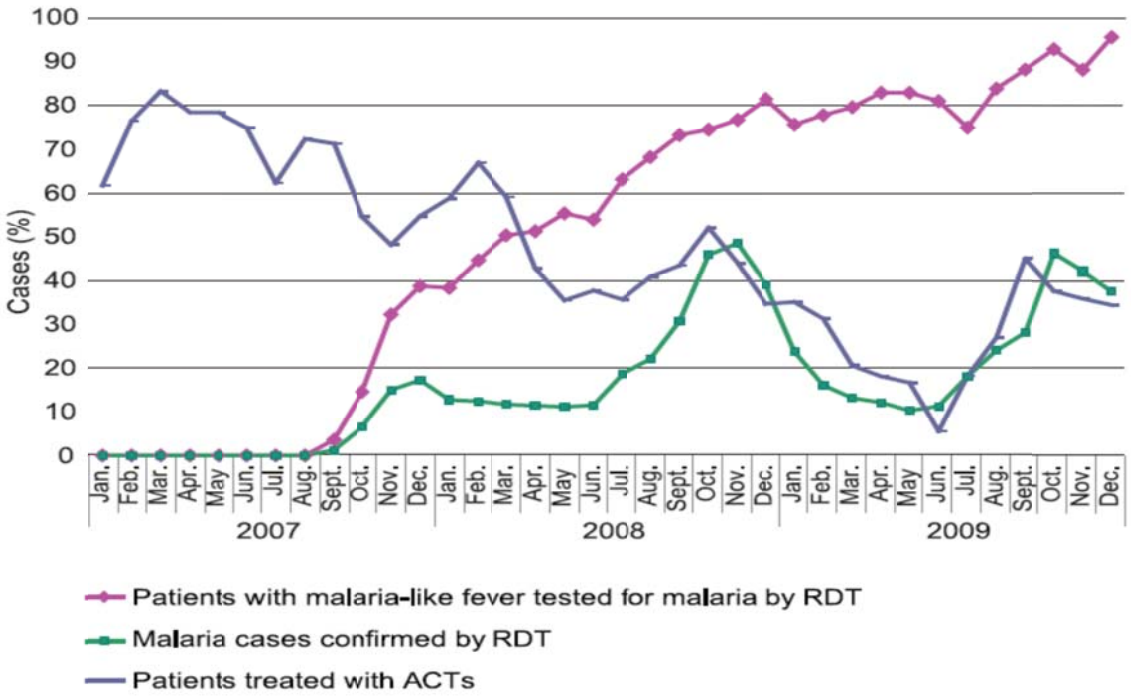
Stakeholder engagement was ensured by the wide scope of the project. Although it was a top-down policy (from national to community level), all malaria facilities were enrolled. To train health-care workers in the field, the project was piloted on a small scale in the capital Dakar. During this pilot period, educational materials were developed supported by WHO training manuals. The NMCP collaborated with the University of Cheikh Anta Diop (Dakar) to establish district and regional training teams to educate health-care workers in the management of the new treatment guideline. The University also actively contributed to community engagement by disseminating data to nongovernmental organizations (NGOs) and community organizations showing the reliability of the RDTs and the new treatment guideline. As a result, key opinion leaders advocated reliance on RDTs in the media.

Health outcomes

The primary results of the intervention can be seen in three major outcomes (Figure 7 & 8):

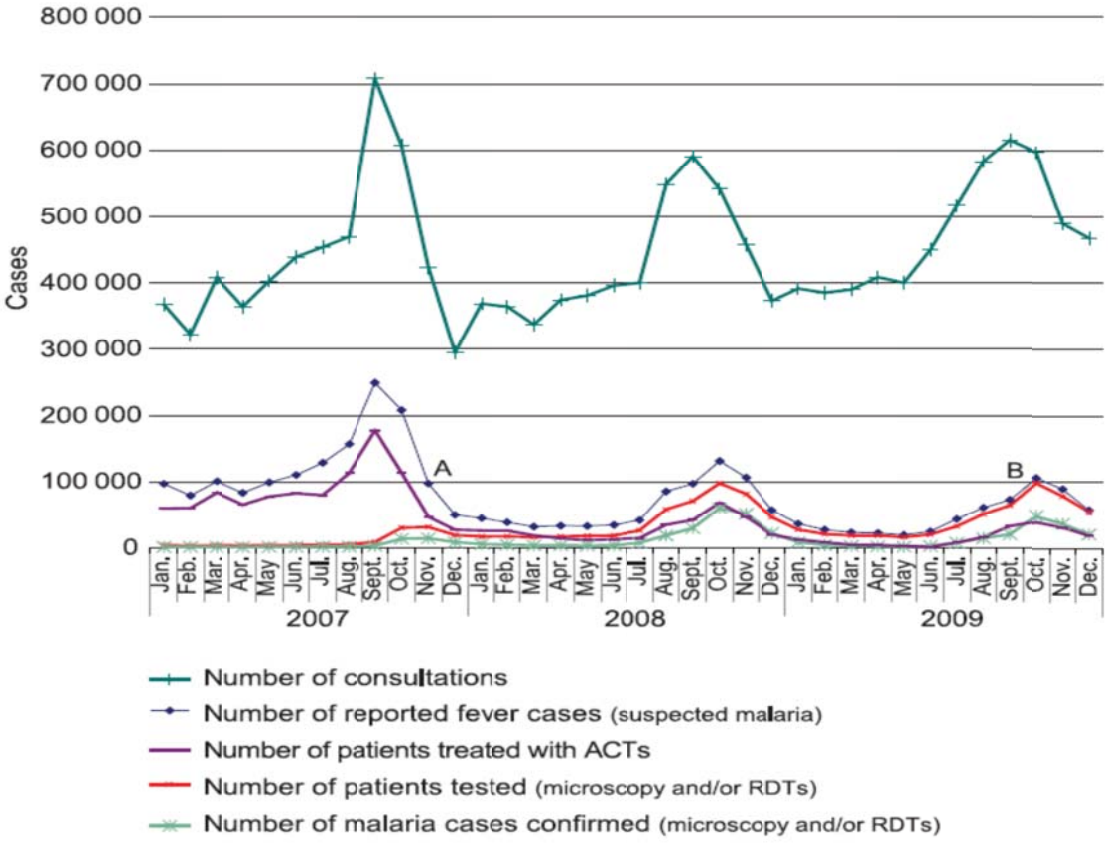
1. From the introduction in 2007 to the end of 2009, the use of RDTs rose from zero to virtually 100% of all presented febrile cases.
2. Increased diagnostic specificity: since the beginning of 2008, the proportion of patients treated with ACT dropped from 60–80% of all presented febrile cases to 15–50% (following the actual malaria season in Senegal), in line with the RDT results.
3. Total ACT exposure in the population decreased, which led to decreased pressure towards resistance.

Figure 7. Percentage of febrile patients tested, diagnosed positive and treated with artemisinin-based combination therapy in Senegal, 2007–2009



Source: Major reduction in anti-malarial drug consumption in Senegal (14)

Figure 8. Number of febrile patients presenting, suspected to have malaria, tested, diagnosed positive, and treated with artemisinin-based combination therapy in Senegal, 2007–2009



Source: Major reduction in anti-malarial drug consumption in Senegal (14)

Financial outcomes

No overall cost-benefit analyses have been published on the RDT intervention in Senegal. The purchase of the tests put an extra burden on financial resources, whereas the reduced number of procured ACTs probably offset these extra costs. Furthermore, RDT-negative patients could be prescribed antibiotics, which in Senegal are more expensive than ACTs.

Longitudinal statistics of antibiotic prescriptions were not available, but some unpublished reports indicate that many of the RDT-negative patients did not receive antibiotics. Cost-benefit models based on situations elsewhere imply that an overall cost avoidance may be expected for the improved management of febrile illness (both malaria and non-malaria) (15,16,17). Patients are receiving earlier and more accurate diagnoses and medicinal treatments and are therefore able to maximize the benefit of antimalarial medicines.

An important economic issue for resource-limited countries such as Senegal is access to ACTs medicines for the less well-subsidized populations. This access may be limited because, while the Government contributed to the cost of ACTs, patients still had to pay some of the cost. Thus, Government savings could be reinvested in the development of a

system in which everyone has access to both appropriate diagnostics and medicine treatments (13). Malaria control can only be achieved when the whole population receives the treatment it needs.

Success factors

The success of the intervention in Senegal can be attributed to the following factors:

1. Commitment by the Ministry of Health to the programme, including adequate funding for the scale-up and clear policy change.
2. Well-developed training of health-care workers at all levels of society.
3. Multi-stakeholder advocacy of a nationwide use of RDTs.
4. Close monitoring of the incidence of malaria rates at district level: a standardized evaluation strategy performed by all districts was submitted to the central monitor point.
5. Provision of medicine- or non-medicine-based therapy for patients with negative RDT results.
6. Engagement of academia (the University in Dakar) and senior physicians.
7. Presence of a quality assurance system based on lot-testing showing that the RDTs were working, to mitigate concerns of false-negative results. The choice of RDT was based on WHO recommendations and results of the validation were published in peer-reviewed academic journals (18,19).

Conclusions

In conclusion, the Senegal case study has shown that nationwide implementation of malaria RDTs is feasible in a relatively short period of time. Scaling up the availability of reliable, quality diagnostics such as RDTs helps to discriminate parasitological confirmed malaria cases against other febrile illnesses, for which appropriate alternative disease management is required.

Prioritization of early and accurate diagnosis is essential to improve health outcomes of medicine treatment and can also be cost-effective when more expensive medical health care can be avoided by treating the right patient with the right medicine at the right time. This case study proves that this can be achieved by scaling up the availability of the right diagnostics.

CASE STUDY 5 – HIV antenatal screening (SWAZILAND)

Practical recommendation 3.2: Mandate early screening in at-risk segments of the population to ensure patients are diagnosed in time to maximize the benefits of treatment.

Executive summary

- Swaziland is the country with the highest human immunodeficiency virus (HIV) infection prevalence among pregnant women in the world.
- Effective medicines for the prevention of mother-to-child-transmission (PMTCT) and treatment of HIV are available. However, due to lack of screening, many pregnant women are not receiving them.
- The Government of Swaziland prioritized HIV screening in maternity units by introducing a nationwide training intervention for maternity nurses, thereby increasing the proportion of HIV-positive mothers receiving antiretroviral treatment (ART) and decreasing HIV infection among young children.

Background

Although remarkable progress has been achieved in the battle against the HIV pandemic, many challenges remain, especially for countries in the developing world. One of the key achievements in the last decade has been the provision of ART to infected mothers, to prevent mother-to-child-transmission of HIV. In June 2001, the United Nations General Assembly adopted the Declaration of Commitment on HIV/AIDS. A focus of this Declaration was improved PMTCT and the reduction of infant HIV infections (20). Since then, WHO has led the process of updating technical PMTCT guidelines to support countries in this major health issue. With other partners, WHO has also supported countries to develop and implement PMTCT health-care services (21,22).

Swaziland has the highest prevalence of HIV in pregnant women in the world, increasing from 3.2% in 1992 to 42% in 2008. WHO data from 2000–2003 show that 47% of neonatal deaths in Swaziland were attributed to HIV/AIDS, in contrast to 7% in the rest of the African Region (23,24).

The Swaziland Government acknowledged the urgency of reducing childhood HIV infections and prioritized the availability of appropriate medicines to do so. As a result, significant improvements have been achieved in access to these medicines, and integration of PMTCT in 80% of antenatal care facilities throughout the country by 2007. The Joint United Nations Programme on HIV/AIDS (UNAIDS) estimated that in 2007, 67% of all HIV-positive pregnant women in Swaziland received ART. However, given the extremely high HIV prevalence in Swaziland, a large number of HIV-positive pregnant women still remained untreated, leading to many newly infected infants every year, as well as illness and death of their mothers.

The Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) performed an analysis of PMTCT programme data in 2007, revealing several potential improvements in the management of the protocol for women presenting at maternity units in Swaziland (24). EGPAF supported the Swaziland Government to identify and address these missed opportunities. This led to improved detection of HIV infection in pregnant women, and administration of appropriate ART drugs before delivery, and thus decreased the infant HIV infection rate and neonatal deaths attributed to HIV/AIDS. This case study describes the intervention, why it was successful, and what recommendations can be extrapolated to other countries.

Intervention

The maternity unit (i.e. in the labour ward) was the main focus of the PMTCT intervention as this is where pregnant women have the last opportunity to receive ART before the delivery process starts. It is essential that the medicines are given to the women in labour, because the highest risk of transmission occurs during and following delivery.

According to national guidelines of Swaziland at the time of the pilot study, the first-line regimen for ART was lamivudine (3TC), zidovudine (AZT) and nevirapine (NVP) and any pregnant woman treated would receive these drugs, which also are effective in preventing transmission to their infants (25). HIV-positive women not eligible for ART received a regimen of AZT from 28 weeks of pregnancy, and during labour they received a single dose of NVP (sdNVP) with a 'tail' of AZT/3TC for one week (25). For maternity sites with minimal capacity, sdNVP was also the minimal required ART in Swaziland. Thus, since every HIV-positive pregnant woman in Swaziland should have had at least NVP in their blood plasma, NVP detection was a good measurement to screen for provision of appropriate ART.

Assessment of the management of PMTCT at maternity units included an evaluation of compliance with the national PMTCT guidelines. Maternity nurses in Swaziland receive national training to learn about PMTCT practice. In addition to provision of ART for HIV-positive women, those with unknown HIV status or who tested negative more than 3 months prior to their presentation at the clinic were to be tested before delivery. The 2007 assessment revealed that this testing guideline was often not followed by the maternity staff.

To improve compliance to the recommended testing policy and performance of the maternity staff, the EGPAF developed an additional, targeted training session in PMTCT, as infant infections were expected to decrease by improving the nurses' skills in this service delivery. The EGPAF team formed a partnership with the Sexual and Reproductive Health Unit of the Swaziland Ministry of Health to integrate the training intervention into the national maternity nurse training programme in 2008–2009. First, the intervention was piloted in a quasi-experimental setting to evaluate its impact.

The EGPAF one-day course included the following key targets:

1. Identify the HIV-status of the presenting mother at the time of arrival (positive, negative or unknown).

2. Test or retest if needed to confirm the HIV status of the mother.
3. Provide the correct ART.
4. Increase the confidence and skills of maternity nurses to counsel mothers in optimal PMTCT.

The Ministry of Health was engaged at the national and regional levels in the design and conduct of the pilot, targeting primarily maternity nurses. EGPAF worked closely with the maternity clinics to enrol women at the clinic sites and collect the umbilical cord blood samples. For the pilot study, the maternity clinics across Swaziland were selected from those that received support from EGPAF, and included over 60% of deliveries in the country during the study period.

Based on the results of the pilot, the policies on retesting women before delivery were strengthened. The 2010 Swaziland guidelines for PMTCT included a new clause specifying that an HIV retest should be done after 32 weeks' gestation or at delivery for all women who tested HIV-negative earlier in pregnancy.

The observation that nearly 5% of HIV-negative pregnant women became infected with HIV during pregnancy resulted in implementation of a 'combination prevention' policy nationwide in all clinics providing antenatal care. Combination prevention includes:

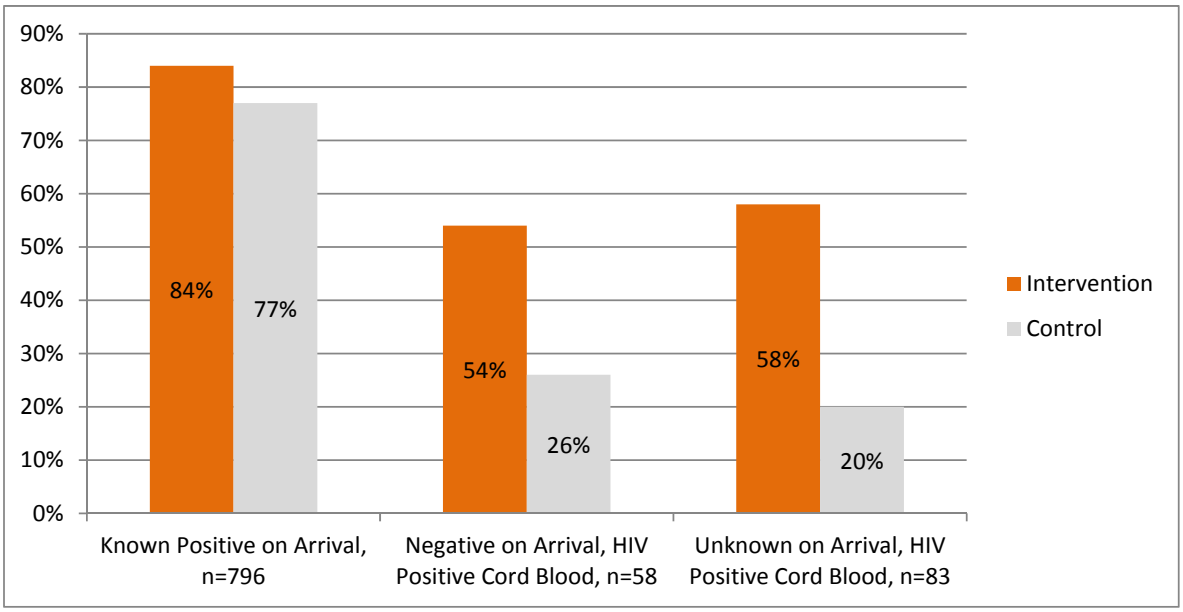
- Retesting 8 weeks after initial testing and every 6 months thereafter.
- Preventive counseling.
- Partner testing/counselling.
- Identification of sero-discordance and referral for treatment.
- Condom demonstration and distribution.
- Infant feeding counselling.

This policy is also a key component of the Swaziland National Strategic Framework for Accelerated Action for Elimination of New HIV Infections among Children by 2015 and *Keeping Their Mothers Alive* initiative, adopted by the Ministry of Health in 2012.

Health outcomes

Data from the first pilot study were analysed and showed promising results that were published in a peer-reviewed journal. Data clearly showed higher rates of NVP presence in the umbilical cord blood of mothers who delivered at the intervention maternity sites compared with control sites (Figure 9).

Figure 9. Rate of NPV detection in cord blood of HIV-positive mothers presenting at the maternity clinic sites, grouped by their situation at arrival, 2008–2009



Source: Swaziland Health Profile, 2006

Financial outcomes

No official published data are available on the cost of this intervention. The pilot study was performed by a private-funded organization and required no financial resources from the Government. When the pilot data were available, no further investment was needed to implement the new screening policy. Using the pilot data from Swaziland, other countries may also intensify their HIV screening policy without placing a significant burden on their budget.

Success factors

The key success factor of this intervention was the comprehensive pilot study carried out before the training became national policy. The pilot study conducted a quantitative statistical analysis of the effect of the training intervention and was performed in 60% of the country's maternity clinics, covering over 70% of births in the country. This was possible given the small size of Swaziland.

Conclusions

This case study shows the clear benefits of a targeted training effort in Swaziland to increase proper screening of pregnant women presenting at maternity care facilities. Although the concept applied in this case to HIV testing and consequent provision of ART, well-developed training of medical staff is important for other diseases and medicine treatments. To obtain the maximal benefit from medicine treatment, providing the right medicines to the right patient must go hand-in-hand with educating health workers in accurate screening.

CASE STUDY 6 – Antibiotics smart use (THAILAND)

Practical recommendation 4.1: Sensitize and promote the engagement of prescribers, dispensers and patients through multi-stakeholder workshops, determining educational requirements for health-care professionals, and public information campaigns.

Executive summary

- In the past five years Thailand has been at the forefront among developing countries in its active engagement to control antimicrobial resistance through the "Antibiotics Smart Use" program. The Antibiotics Smart Use (ASU) is a voluntary program deployed in selected provinces in Thailand between 2007 and 2012 to foster a more responsible use of antibiotics by directly engaging prescribers, dispensers and patients.
- Phase 1 of the project was intended as a pilot for the broader initiative and it was deployed in 2007-08 showing encouraging results. Phase 2 was designed to be a scalability test of the Antibiotic Smart Use initiative, and it was deployed over 13 months (2008-09) in three provinces and two hospital networks, ultimately involving 44 hospitals and 627 primary health centres. Phase 3, currently ongoing, is intended to achieve sustainability for the Antibiotics Smart Use program by stimulating policy advocacy, resource mobilization and public education throughout.
- In Phase 1, the overall amount of antibiotics prescribed in the community hospitals targeted by the initiative declined between 18% and 23%, while the decline in primary health centres declined even further between 39% and 46%. The outcome of phase 2 confirmed the outstanding results of the pilot phase of the program, and phase 3 is currently underway to ensure the benefits of the Antibiotic Smart Use program are maintained. The National Health Security Office (NHSO) has adopted ASU as a key indicator of quality of service in pay-for-performance agreements with community hospitals.

Background

Antimicrobial resistance is increasingly recognized as a key public health concern for both developed and developing countries due to its potentially alarming socioeconomic impact on health. Bacteria naturally develop resistance due to the selective pressure applied by both responsible and irresponsible use of antibiotics, which effectively limits the efficacy of any one antibiotic over time. This realization, coupled with negligible innovation in antibiotics over the last decades, highlights the critical need for responsible use of antibiotics to slow down the development of antimicrobial resistance.

In the past five years Thailand has been at the forefront among developing countries in its active engagement to control antimicrobial resistance. Antibiotic consumption alone represented 16–22% of national medicines expenditure, and both inappropriate prescription and cases of antimicrobial resistant infections were steadily increasing (26). To address these concerns, the 'Antibiotics Smart Use' (ASU) programme was developed in partnership with

key national and international stakeholders to foster a more responsible use of antibiotics in primary care and hospital settings.

ASU is a voluntary programme that has been deployed in selected provinces in Thailand since 2007 with the engagement of prescribers, dispensers and patients. The intervention seeks to change the perception and behaviour of prescribers and patients regarding the use of antibiotics to treat three common conditions in primary health care: upper respiratory tract infections, acute diarrhoea and simple wounds. The three-phase intervention used multiple tools to raise awareness and affect behaviour, ranging from training group discussions to local policies and targeted reminders.

Intervention

Phase 1 of the project was intended as a pilot for the broader initiative and was deployed in 2007–2008 by the Thai Food and Drug Administration (FDA) in partnership with WHO. The scope for the pilot was 10 community hospitals and 87 primary health centres in the Saraburi Province (27), targeted with information materials prepared by the Thai FDA and activities to sensitize patients and prescribers to the importance of a more responsible use of antibiotics. Training was offered to medical personnel, while informative brochures were provided to patients in order to gain their active support. The success of the intervention was to be measured through four key metrics: change in knowledge and awareness; change in quantity of antibiotics prescribed; change in number of patients receiving antibiotics; and level of patient treatment satisfaction (28).

Phase 2, designed as a scalability test, was deployed over 13 months (2008–2009) in three provinces and two hospital networks, ultimately involving 44 hospitals and 627 primary health centres (27). The three provinces were of different sizes in order to test scalability, and both private and public hospitals were involved. Once again, prescribers and patients were engaged through information material and activities, and private pharmacies were included in the target audience. In this second part of the initiative, over 10 000 health professionals and patients were trained, and 22 ASU projects initiated in 15 provinces. This formed the decentralized ASU network of people and centres that were leveraged in Phase 3 (26). The success of the second phase was to be measured through similar metrics as those chosen for the pilot phase: antibiotics use; percentage of patients receiving antibiotics; patient treatment satisfaction; and knowledge and awareness (28).

Phase 3, ongoing, aims to achieve sustainability for the ASU programme by stimulating policy advocacy, resource mobilization and public education (27). One of the key expected outcomes of the second phase was the creation of a decentralized ASU network of health-care professionals and institutions, so that the initiative could naturally spread beyond the target hospitals if successful.

The sensitization of all key stakeholders – prescribers, dispensers and patients – to the benefits of a responsible use of antibiotics, and their active involvement in promoting such practices, are the cornerstones of this initiative. The initiative itself was structured in three progressively larger phases which achieved widespread and grass-roots involvement of patients and prescribers and facilitated measurement of the efficacy of the approach.

Health outcomes

To date, all four key metrics demonstrated the efficacy of the intervention (25,27). As a proxy measurement of increased sensitization, the response rate of health-care professionals invited to take part in the training sessions exceeded 60%, with the highest percentage of participants being nurses. This is very encouraging as it shows that the education campaign to raise awareness and change perceptions on the responsible use of antibiotics reached both prescribers and dispensers.

The overall amount of antibiotics prescribed in the targeted community hospitals declined by 18–23%, while the decline in primary health centres was even greater at 39–46%. Prescription reduction alone is a success, and is supported by a similar reduction in the percentage of patients receiving antibiotics for upper respiratory tract infection, diarrhoea or simple wounds, from 54.5% to 25.4%. The reduction in antibiotics use was not achieved at the expense of reduced positive clinical outcomes: 97.1–99.3% of patients fully recovered after their health visit, with small variations depending on the treatment setting. Finally, up to 90% of patients were satisfied with the treatment outcome and intended to return to the same health-care setting for the next medical visit.

An explicit evaluation of the outcomes of the initiative will be published by the relevant authorities in Thailand as soon as Phase 3 is completed.

Financial outcomes

The outcome of Phase 2 confirmed the outstanding results of the pilot phase (27). In the first four months of the second phase, the use of antibiotics declined sharply, delivering estimated savings of Thai Bhat 6.6 million (approximately US$ 220 000 per year). For example, the percentage of patients treated with antibiotics for upper respiratory tract infections declined from 50.4% to 37.5% within months of the beginning of the initiative. Furthermore, 96–99% of patients treated without antibiotics in the participating centres recovered from their illness.

A key positive outcome of Phase 2 has been the public support of the National Health Security Office for the initiative, which has adopted ASU as a key indicator of quality of service in pay-for-performance agreements with community hospitals (26). This acknowledgement opened the door to nationwide policy support, and highlights how national guidelines and policies on the responsible use of medicines do not necessarily have to be promoted through a top-down approach by the Ministry of Health; rather, this initiative was tested using a bottom-up approach that was eventually supported through national policy.

Success factors

The key success factors of the Antibiotics Smart Use program are its multidisciplinary approach, a clear focus on stakeholder engagement, and demonstrated results at each step of the way. The ASU approach has been successful in creating a decentralized network of participating centres and professionals who can claim ownership for the quality and

outcome of their contribution. Furthermore, the measurement of the health and economic outcomes of each phase have been key factors in promoting expansion of the initiative. Finally, the policy support granted by the National Health Security Office guaranteed the legitimacy needed to spread the project nationwide in Phase 3 and ensure that all citizens can enjoy the benefits of a more responsible use of antibiotics.

Conclusions

The Antibiotics Smart Use programme is a clear example of how the responsible use of medicines can be tested and up-scaled, if successful, via a bottom-up approach through the support of key stakeholders, and lead to effective national guidelines and policies.

CASE STUDY 7 – Medical use of opioids (INDIA)

Tactical recommendation 4.2: Reassess regulatory requirements on the dispensing of selected medicines to ensure their wider availability and accessibility. Sensitise and promote engagement of prescribers, dispensers and patients through multi-stakeholder workshops, educational requirements for health-care professionals and information campaigns.

Tactical recommendation 4.3: Reduce redundant paperwork and the administrative burden of prescribing/dispensing particular essential medicines to ensure appropriate patient access.

Executive summary

- Use of medicines produced from substances controlled under the international drug control conventions, such as strong opioid analgesics and long-acting opioids for treatment of opioid dependence, is suboptimal in most developing countries.
- Improving medical access to opioid analgesics (pain relievers) will improve treatment of moderate and severe pain and the quality of life for patients in India and in the rest of the world.
- The Indian State of Kerala organized a symposium to simplify the regulations of opioid procurement and use. This resulted in a large increase in the prescribing and use of opioids in the State.
- Along with simplification of the regulations, Kerala developed a system to monitor the use of opioids which generated a comprehensive picture of opioid use. This showed there was minimal misuse.
- An essential part of the initiative to improve access was palliative care education of physicians, pharmacists and nurses.
- The experience in Kerala (which had political commitment and multi-stakeholder involvement) demonstrates that it is possible to improve the use of medicines and has important lessons for other states in India as well other countries.

Background

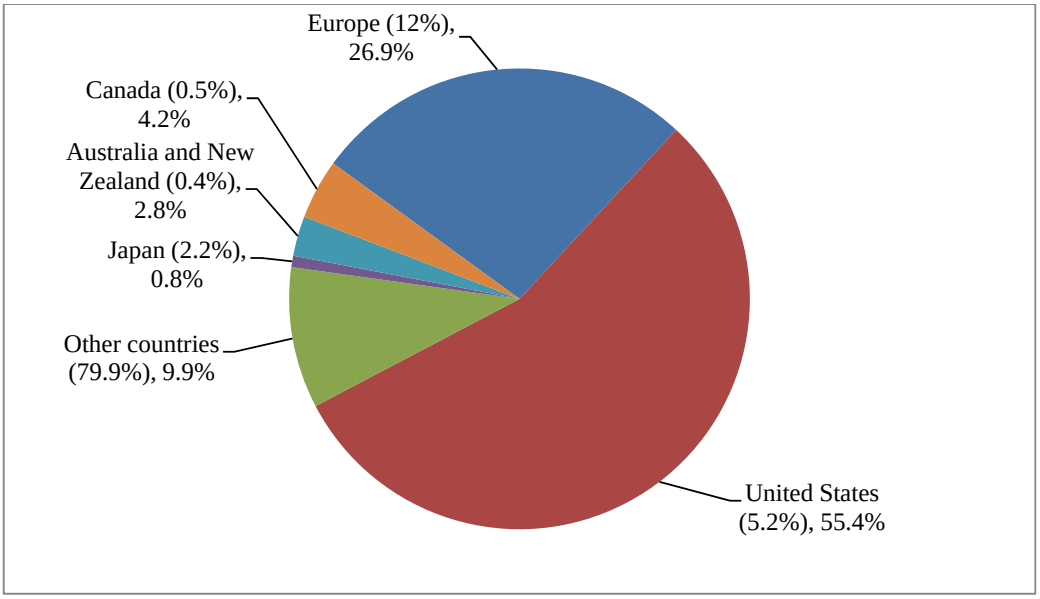
Various medicines produced from substances controlled under international drug control conventions are not readily available for medical use in most countries, even when they are considered to be essential medicines. One such group is strong opioid analgesics (pain relievers). They are essential in the treatment of moderate and severe pain, including in palliative care. However, in many developing countries, lack of access to effective pain medicines is due to excessive regulatory and policy restrictions, the lack of knowledge on treatment among health-care professionals, attitudes among health-care professionals, patients and their families, and economic issues.

The International Narcotics Control Board (INCB) Annual Report demonstrates significant disparities in morphine use in the world (Figure 10) (29). WHO data from 2006 estimates that 5.5 billion people (83% of the world's population) live in countries with low to non-existent access to controlled medicines and have inadequate access to treatment for moderate to severe pain. These data also show a strong positive correlation between ranking on the Human Development Index and the consumption of strong opioid analgesics (30). In these countries, tens of millions of pain patients suffer each year from inadequate treatment (31) for conditions such as :

- end-stage HIV/AIDS (1 million patients)
- terminal cancer (5.5 million patients)
- injuries caused by accidents and violence (0.8 million patients)
- chronic illnesses
- recovery from surgery
- labour pain (110 million births each year)
- paediatric illness.

Other conditions where controlled medicines are essential for treatment include epilepsy, post-partum bleeding (cause of maternal mortality), opioid dependence (including the prevention of HIV and hepatitis C transmission) and psychiatric conditions (30). The particular medicines needed in these conditions are derived from controlled substances.

Figure 10. Global distribution of morphine consumption, 2010



The percentages within parentheses are the proportion of the world's population in the country; the percentages without parentheses are the proportion of the total available morphine consumed by the country.

Source: Report of the International Narcotics Control Board (29)

All countries have a dual obligation with regard to these medicines based on legal, political, public health and moral grounds. The dual obligation is to ensure adequate availability of controlled substances for medical and scientific purposes, while simultaneously maintaining a system to monitor potential dependence (e.g. methadone and buprenorphine), abuse, diversion and trafficking. In order to develop a policy that incorporates both access to rational medical use and the prevention of dependence, governments should carefully review existing regulations and laws. Although opioid abuse and dependence is harmful for the individual, its use for medical and scientific purposes is evident and essential: morphine, for example, is one of the only effective medicines for patients suffering from moderate and severe pain and should therefore be available to those in need (32).

In this case study, India shows how successful policies eventually resulted in restoring the balance in the regulation of opioid use, particularly for the treatment of pain in palliative care. In 1998, to reduce over- and underuse in palliative care, the Government of India (GOI) proposed an amendment to State law aimed at simplifying opioid regulations. This amendment would have authorized the State's Medicine Controller to license palliative care programmes within Recognized Medical Institutions (RMIs), requiring no further licences to purchase, import and/or possess opioids (33,34).

In Kerala, a symposium was organized in 1998 to improve opioid practice in palliative care pain management services, chaired by the State Minister of Health. His commitment to engage both local stakeholders and representatives of other departments was essential. The symposium made important decisions on opioid policy and palliative care development.

However, in other states of India opioids remained underused. The unsuccessful efforts of the GOI were a result of a number of factors described below (35).

The three objectives of this case study are to analyse the policy change in Kerala, to describe reasons why the intended policy change could not be replicated in other parts of the country, and to identify more universal and generalizable recommendations on how other governments, working within the health-care system, could improve the responsible use of controlled medicines such as opioids.

While this case history describes the specific situation of opioid access in palliative care, it must be clear that palliative care is only one of many medical applications of opioid medicines. To address the issue of opioid accessibility on a larger, nationwide scale, the GOI adopted in 2012 a new controlled substances policy that covers improved access to adequate palliative care, extrapolating this access to other conditions where opioid pain management is essential, and access to treatment of opioid dependence (36).

Intervention

The first decision of the symposium was to simplify opioid licensing rules as recommended by the GOI. The second step was the creation of a voluntary advisory panel of palliative care physicians. These were selected because of their experience in the field and commitment to treat pain in terminal diseases such as cancer. To ascertain whether the minimum mandatory requirements were met by a potential institute to be licensed, a member of the panel performed an on-site visit. Minimum mandatory requirements included the presence of a physician with at least one month of palliative care training in an approved institution, safe storage facilities and an opioid documentation system that monitors dispensing and use (35, 37).

A basic principle of the Kerala symposium was to engage all key stakeholders for a broad consensus on the use of opioids. Therefore a local champion, appointed by the Government, was given the responsibility to invite all involved stakeholders to maximize attendance. Invited stakeholders included palliative care physicians, a state Medicine Controller representative, a Health Department officer, an Excise Department representative, and representatives of the collaborators. The collaborator group comprised the Pain Policy Studies Group at University of Wisconsin, Madison, WI, United States of America (a WHO Collaborating Centre for Pain Policy and Palliative Care), the Indian Association for Palliative Care and the Pain and Palliative Care Society of Calicut. All these organizations were committed to the simplification and improvement of opioid rules in Kerala.

Health outcomes

Following low opioid consumption from 1985 due to the introduction of the Narcotic Drugs and Psychotropic Substances Act, manufacture (as an indicator of consumption) rose again in 2007 (Figure 11). The rise in 2000 and 2001 were due to efforts of the GOI aiming at a nationwide scale-up of opioid accessibility, following introduction of the amendment. However, for reasons described below, these policies did not result in an actual improvement of opioid accessibility.

As a result of the symposium in Kerala, over 140 palliative care services became licensed to prescribe and dispense oral morphine in the State. This contrasts with the rest of Indian states where no or few clinics provide palliative care. Thus, by expanding palliative care facilities where opioids were allowed, availability of opioids medicine was improved. Governmental data show that institutes in Kerala procured 75 kg of morphine sulphate in 2010, 33% of the total amount of morphine sulphate procured nationwide. The population of Kerala is only 2.5% of India, clearly indicating that opioid availability in Kerala is superior to the national average.

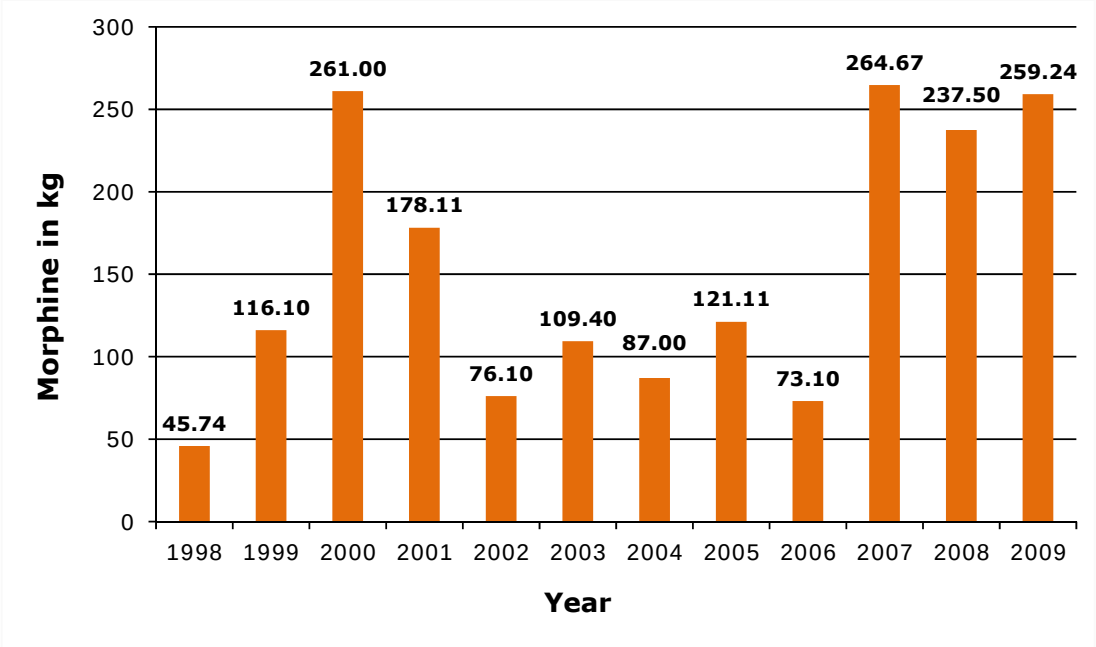
Other states that have adopted the Kerala model have not shown clear improvements in the short term. However, some small but significant regulation changes may eventually lead to an improvement in morphine use. In addition, official data show a steady increase nationwide in morphine manufacture since 2007, implying sustained improvement in opium access since the intervention was implemented (Figure 11).

Regarding misuse, no increased dependence prevalence has been reported since 2001, and a survey detected no diversion of opioid analgesics (33).

Financial outcomes

Opioids are in general affordable medicines, relatively easy to produce, transport and store. The success of the Kerala intervention is therefore not expressed in terms of financial gains. On the other hand, there are no financial barriers for increasing access to opioids, underlining the high relevance of this case history for all low- and middle-income countries as well as for the rest of the world.

Figure 11. Quantity of morphine manufactured in India, 1998–2009



Source:
Government of India. National Policy on Narcotic Drugs and Psychotropic Substances, New Delhi, 2012 (36)

Success factors

In contrast to other states, Kerala has achieved some remarkable results that could serve as a template for other states or countries. Using the WHO guidelines and its checklist (32), a policy for medical use of controlled substances should be developed through a multi-stakeholder approach. The policy should then be implemented through negotiations and advocacy by committed professionals at national and local levels. Based on the Kerala recommendations, a workshop should include at least the following six key elements (35):

1. A local champion committed to the case.
2. Senior governmental officials sensitized to the need for palliative care and oral morphine.
3. Development and implementation of palliative care education programmes for doctors and nurses.
4. Interaction of the local champion, governmental officials and collaborators to ensure adoption of optimal opioid use, develop Standard Operating Procedures (SOPs) and establish a follow-up monitoring schedule.
5. Collaboration with organizations such as WHO to benefit from their experience.
6. Strong commitment of palliative care pioneers and NGOs to develop a network of facilities and education programmes, and create consensus on appropriate opioid prescribing practice.

Key failure factors

The GOI experienced a number of hurdles in their efforts to improve the responsible use of morphine nationwide. Eight of these are described below. (35)

1. In 2000–2001, the GOI distributed large quantities of morphine free of charge to its states. However, the morphine could not be used because essential support at regulatory level and the engagement of medical professionals were not in place. The whole consignment was therefore wasted and morphine consumption dropped.
2. The follow-up schedule to the symposium was inadequate. Governmental organizations need to initiate incentives and activities early to maintain the process. The absence of a solid timeframe created critical bottlenecks in some states.
3. Socio-geographical factors created barriers to increased morphine consumption, for example in the border states in northern India, which suffer higher substance abuse than other states.
4. The transfer of committed key officials to other departments was detrimental to expansion of the initiative.
5. In states such as Sikkim, Tripura and Jammu-Kashmir, although the amendment was adopted, morphine use remained suboptimal because of a lack of trained palliative care physicians.
6. An effective system was not in place to update the regulations.

7. The scope of the amendment was limited to easing restrictions in palliative care; pain clinics and post-operative pain treatment were not served by the policy change.
8. The policy to allow cancer patients access to pain management with opioid analgesics was clear but other patients, such as those with end stage AIDS, were denied access.

Conclusions

Prioritizing the removal of regulatory barriers to access can be achieved while maintaining a necessary level of regulation; the Kerala example has demonstrated this. However, the suboptimal use of opioid analgesics in India shows that simplifying regulations and purchasing large quantities are not sufficient. Other activities such as education/information on palliative care for all stakeholders are needed. In Kerala, opioid consumption improved by strongly embracing a national initiative, coupled with commitment from the local government, academia, educational efforts and strong advocacy.

CASE STUDY 8 – Upscaling zinc in diarrhoea treatment (BANGLADESH)

Tactical recommendation 4.1: Sensitize and promote the engagement of prescribers, dispensers and patients through multi-stakeholder workshops, determining educational requirements for health-care professionals, and public information campaigns.

Tactical recommendation 4.2: Reassess regulatory requirements on the dispensing of selected medicines to ensure their wider availability and accessibility. Regulations should permit over-the-counter availability of medicines of appropriate risk/benefit.

Executive summary

- Diarrhoea is a major cause of death in many developing countries.
- Zinc treatment in addition to oral rehydration solution (ORS) reduces mortality and morbidity from diarrhoea.
- In Bangladesh, the Government scaled up the procurement and use of oral zinc tablets from 2006 to 2009.
- As a result, awareness on the need for zinc supplementation increased among health-care providers and caregivers, and the use of zinc increased.
- Consistent with the long-term trend, the under-five mortality rate dropped in Bangladesh below the regional level.
- The Government was not responsible for the full project, but its enabling function was essential for its success.
- The Scaling Up Zinc for Young children (SUZY) project is an excellent example of effective guideline implementation and removing barriers to increase the responsible use of medicines.

Background

Childhood diarrhoeal disease is a major problem in developing countries, contributing significantly to childhood morbidity and mortality (38). Zinc treatment during a diarrhoea episode has been proven to reduce this disease burden in low-income countries. It is estimated that the lives of nearly 400 000 children under five years of age could be saved each year through adequate zinc treatment. In turn, this would support the MDG 4 to reduce mortality in children of this age group by two thirds by 2015. According to a joint WHO/UNICEF statement in 2004, increasing the use of zinc in childhood diarrhoea treatment is one of the best ways to achieve a rapid impact (39).

Indeed, findings of a community randomized trial in Bangladesh clearly indicate reductions in diarrhoea incidence (15%), diarrhoea-caused hospitalizations (24%) and non-injury death rates (51%) in the intervention group (40). In addition, acute lower respiratory infections and causal hospitalizations decreased among zinc users. The efficacy of zinc addition in diarrhoea treatment is supported by other studies conducted in low-income countries in Asia and Africa, including India, Mali, Pakistan and the United Republic of Tanzania (41).

At the start of the project in 2006, only 5–15% of children <5 years old suffering from diarrhoea were receiving zinc treatment in Bangladesh, depending on where they lived (42). Hence, the Bangladesh Government decided to initiate a project to improve overall zinc use against childhood diarrhoea. The goal of the project was to implement zinc treatment in addition to oral rehydration therapy (ORT) as the standard therapy for all young children suffering from diarrhoea in Bangladesh.

Intervention

The policy interventions carried out by the Bangladesh Government in 2006 to scale up the use of zinc comprised five fundamental actions (42):

1. Development of two committees by the Ministry of Health and Family Welfare in collaboration with the SUZY team:
    a. National Advisory Committee, headed by the Health Secretary
    b. Planning and Implementation Committee, headed by the Joint Secretary, Public Health, and supported by the WHO Country Office.
2. Revision of the National Diarrhoea Treatment Guideline and approval of a 20 mg dispersible zinc tablet formulation for children <5 years suffering from diarrhoea.
3. Approval to brand the product as 'Baby Zinc'. This approval, leveraging the intellectual property and marketing of this zinc formulation, became attractive for the pharmaceutical manufacturer.
4. Obtaining an over-the-counter sales waiver: 20 mg oral zinc formulation became available in pharmacy retail stores without prescription, so caregivers did not have to see a prescriber first to obtain zinc tablets. The standard ORS was already available over-the-counter.
5. Permission to proceed with a public promotional campaign to promote Baby Zinc.

The governmental policy changes engaged the private sector in areas including manufacture, promotion and education. A Project Performance Framework was created to describe all preparatory activities including a timeline to monitor and evaluate the project, policy interventions, laboratory research and development of the formulation, and the promotional campaign to engage stakeholders. This process was to be completed within 18 months (42).

The three primary endpoints of the SUZY project were (1) changes over time in carer awareness of zinc as a treatment for childhood diarrhoea, (2) the actual use of zinc to treat child diarrhoea, and (3) the use of ORS. This information was obtained by repeated impact surveys carried out in households comprising approximately 3200 children with an active or recent case of diarrhoea. Between 2006 and 2008, seven of these surveys were conducted and stratified by socioeconomic/geographic area (43).

An essential part of the SUZY project was to ensure that all key stakeholders were engaged in and supported the scaling up of zinc use for diarrhoea. To achieve full support of the stakeholders, nearly one third of the project's overall budget was reserved for the promotional campaign (42). Governmental and professional organizations, including the Ministry of Health and Family Welfare and the Bangladesh Paediatric Association, fully supported the messages delivered through the campaign.

Health-care providers (physicians and pharmacists)

The goals of the zinc campaign were to create awareness of zinc as a treatment of childhood diarrhoea and its protective effects against recurrence; to include the use of zinc in clinical practices; and to reach all health-care providers in all regions. Therefore, approximately 2000 representatives working in all geographic areas were trained to educate health-care providers. In addition, information pamphlets were developed and sent out to all parts of the country by the Government.

Caregivers (parents)

Newspaper and television commercials, billboards, posters, a catch-phrase, as well as educational efforts such as a drama series, talk shows and health education programmes, were developed to reach the caregivers. Marketing specialists and social scientists worked together to develop the content of the commercials.

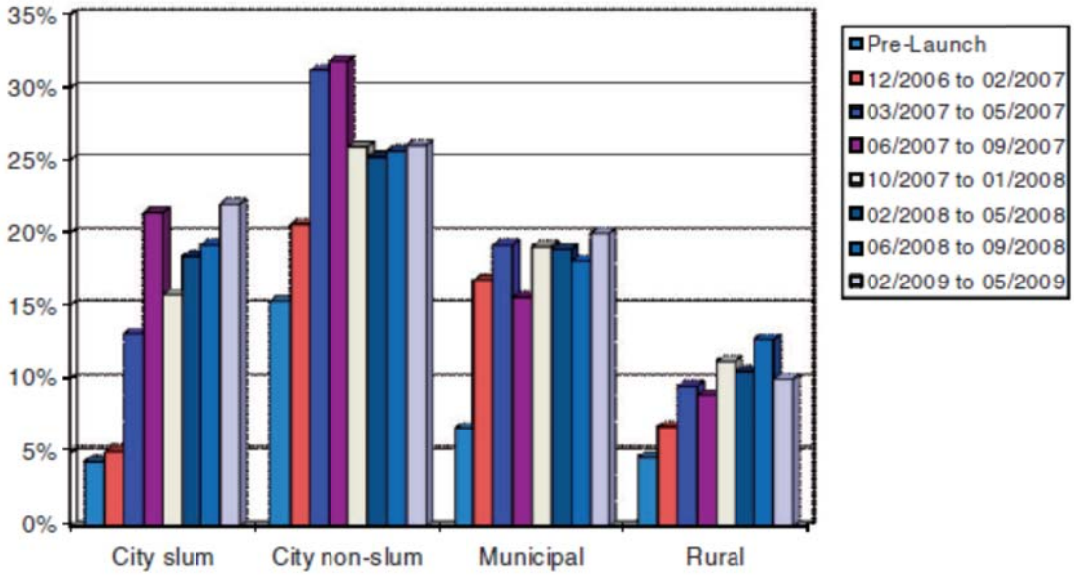
Health outcomes

The results indicate a rapid increase in caregiver awareness of zinc as a treatment of diarrhoea and an increase in the actual use of zinc for childhood diarrhoea (Figure 12). At the end of the scale-up project, the use of zinc had clearly increased for all regional strata in Bangladesh.

Adding zinc to childhood diarrhoea treatment reduced mortality, morbidity and morbidity-associated hospitalization. WHO health statistics indicate that the under-five mortality rate in Bangladesh dropped below the regional average in 2008 for the first time (WHO country profile Bangladesh). Specifically, a 2004 WHO report showed that diarrhoea mortality represented 21.1% of mortality from communicable, maternal, perinatal and nutritional

conditions among Bangladeshi children aged 0–14 years. In 2008, when the SUZY project had been running for two years, this percentage was reduced to 12.4%. This risk reduction cannot be completely attributed to the scale-up of zinc use, since other major improvements in the health sector and general living conditions had also been made during this period (41,42). Nevertheless, the risk reduction in combination with the scientific evidence show that the scale-up of zinc treatment for diarrhoea is likely to have had a positive contribution to reducing child mortality.

Figure 12. Trends in zinc use in Bangladesh categorized by household location, 2006–2009



Source: Larson et al., 2011 (42)

Zinc supplementation also improved overall quality of life in a borderline zinc-deficient population including Bangladesh (44). Appetite, physical activity and the happiness of children also improved, as did that of their caregivers. Anecdotal witness reports have described mothers saying 'my son is shining again' after starting zinc treatment for their child.

Financial outcomes

Randomized studies in countries such as India and the United Republic of Tanzania have shown that hospitalizations are reduced as a result of an increased use of zinc, thereby making diarrhoea treatment cheaper when ORS is complemented with zinc. Caregivers in Bangladesh purchase the zinc therapy over the counter. At US$ 0.25 for the recommended 10-day treatment, this purchase significantly reduces the likelihood of an expensive hospitalization. A cost-effectiveness study conducted in the United Republic of Tanzania (40) showed that the cost to avert one child death due to diarrhoea was approximately US$ 3200, compared with US$ 2100 to provide zinc to all children suffering from acute diarrhoea. Thus, the cost of averting one child death from diarrhoea is reduced by US$ 1100 when zinc is added to the treatment (40). Although these results were obtained in a different

region, it is believed that zinc treatment for childhood diarrhoea can be considered highly cost-effective.

Success factors

Several factors that made this project successful were identified. Firstly, the approval of a 20 mg oral zinc tablet formulation and its introduction into the National Diarrhoea Guideline were essential in making the medicine available on the market. Secondly, the preparation and use of a Project Performance Framework provided a good structure to monitor and evaluate the project. Thirdly, a promotional campaign was designed with the support of all key stakeholders including the Ministry of Health and the Bangladesh Paediatric Association. Nearly one third of the overall project budget was allocated to the campaign to maximize stakeholder engagement. Finally, the Bangladesh Government created the circumstances necessary for the scale-up of zinc treatment and thus the ultimate success of the project.

Conclusions

Important lessons on successful guideline implementation can be extracted from the Bangladesh zinc project. A number of processes needed to be completed in order to produce, promote and scale up the use of zinc in clinical practice. The Project Performance Framework enabled these processes to be completed in only 18 months and, thanks to a multi-stakeholder approach, improvements were made within a relatively short period of time in a low-income country. Adequate resources should be spent on promotion to engage all stakeholders and maintain their engagement. In addition, regulatory burdens should be removed where possible, for example by allowing over-the-counter access.

Chapter V – Focusing on adherence

Strategic recommendation 5: Promote initiatives that put patients at the centre of treatment in order to maximize adherence to therapy.

Adherence to treatment focuses on individual patient behaviour in the context of the proper use of medicines. The term adherence is used in this report as the overarching term for compliance and persistence. Compliance refers to the medicine being taken at the time, frequency, dose and circumstances advised by the prescriber. Persistence refers to the patient's continued use of the prescribed medicine as long as needed without interruption. Reasons for poor adherence include lack of perceived susceptibility to, and severity of the disease, adverse reactions associated with the medicine, lack of financial resources to continue the treatment, inconvenience of taking the medicines as directed and simply forgetting to take them.

Poor adherence can impair the efficacy and safety of medicines so that not only the intended treatment outcome may not be fully achieved, but unnecessary adverse events and hospitalization may occur. The negative effects of non-adherence on health outcome and the cost and efficiency of treatment are of great concern, especially in therapy areas with worryingly low long-term adherence rates such as chronic, noncommunicable diseases.

Non-adherence is an acknowledged and documented problem in the use of medicines, and the competence to tackle the issue is increasingly integrated in the education of medical professionals in both developed and developing countries. However, there is only limited evidence available on interventions effective in improving adherence in the real-world setting. Changing the behaviour of individuals is a complex social process and many factors may play a role. This chapter showcases a community-based intervention in Ethiopia targeting tuberculosis patients to minimize non-adherence by providing closer patient support during therapy.

Governments should take the lead in promoting, through national health policy, comprehensive initiatives to improve adherence to medicine treatment. In order to achieve this complex goal, partnerships with the private sector should be explored so that health-care professionals and the treatment are brought as close as possible to patients and their lifestyles. Furthermore, to close the current knowledge gap on how to minimize non-adherence, governments should support and promote academic research to identify risk factors and determinants of non-adherence, the results of which can be used to stratify the risks and develop innovative interventions.

CASE STUDY 9 – Community interventions (ETHIOPIA)

Tactical recommendation 5.1: Promote the creation of, and provide technical support to community-based initiatives aimed at improving patient engagement and adherence to treatment.

Tactical recommendation 5.2: Facilitate health-care professionals in providing closer therapy support to patients to motivate their health-seeking behaviour.

Executive summary

- Tuberculosis (TB) is a major problem for public health and society in many low-income countries.
- For many reasons, including frequent HIV comorbidity and related multiple medicine treatments, adherence to TB treatment medicines is suboptimal.
- In Estie District, Ethiopia, a grass-roots patient-centred initiative was implemented by and for TB patients, supported by the local government.
- The Government enabled the success of the intervention by providing education, organizing TB club events and monitoring the impact.
- The case of Estie District demonstrates how governments can facilitate patient empowerment to improve treatment adherence in a very resource-limited setting.

Background

As reported by WHO in 2010, TB is a major communicable disease with a global incidence of 8.8 million 1.1 million deaths from TB among HIV-negative patients and an additional 0.35 million associated with HIV (45). Effective medicine treatments are available; however, suboptimal adherence to the treatment is a major problem. Reasons for this may include HIV comorbidity and therefore the high pill burden for the patient, and medicine interactions (46). WHO recommends the empowerment of patients in TB treatment to increase their engagement and treatment adherence. The concept of patient empowerment to improve treatment adherence has been discussed for other diseases such HIV/AIDS (47,48). Several studies have identified patient empowerment and community engagement as effective means to improve adherence to TB treatment (49). Nevertheless, although such empowerment is a well-known concept, it remains under-developed in many countries (48).

TB has high prevalence, incidence and mortality rates in Ethiopia, placing a serious burden on the public sector. This case history describes a patient-centred initiative in 1996, introduced in the Ethiopian Estie District (population 290 000) where patient empowerment was concretized by the formation of TB clubs. The district is in a remote area with no access to electricity and poor communication and transportation infrastructure. Health care was provided in very basic conditions, with one health centre and ten clinics (health stations) in the whole district and no individual doctor–TB patient counselling before 1996. As a result, adherence to TB treatment was suboptimal; patients were frequently and inappropriately extending or stopping their antibiotic courses. The smallest administrative subdivision in the

district where people live together is called a *kebele*. The formation of TB clubs within these *kebeles* was promoted by the governmental District Medical Officer, providing a strong endorsement of this approach, supported by research in other countries and WHO guidelines (47,48,50).

Intervention

The intervention started with a grass-roots initiative from the community living together in a *kebele.* In 1996, the Estie District public health administration decided to improve the TB patient follow-up procedure at the sole health centre in the district. At that time, no individual patient–doctor interaction took place during these follow-up visits: 500 patients had an appointment on the same day and were seen by the doctor in large groups. In the new approach, more days were reserved for TB patients and appointments could be distributed over several weeks. All appointments for all TB patients living within one *kebele* were scheduled on the same day. As a result, 'intra-*kebele*' relationships were established among TB patients since they had to travel and be at the health centre together. These patients then formed TB clubs, usually of 3–10 persons. The purpose of the TB club was for members to stimulate each other to adhere to treatment, help identify new TB cases and share experiences of the course of the disease, the progress of the treatment and adverse drug reactions (50).

The TB clubs received support from the local District Medical Officer, which included educational materials prepared by the Ministry of Health and the Regional Health Bureau, written in the regional language Amharic. Further public sector support was provided by local health workers and community health agents who supervised meetings and educated the TB clubs in identifying new cases. The TB clubs elected a leader who was literate and functioned as the contact person for the health workers and the district government, coordinated the club meetings and was responsible for distributing the education materials to the club members. The task of the leader was also to report any treatment failures or adverse drug reactions to the local health facility.

This initiative was a clear example of a patient-centred approach in improving adherence to medicine treatment; there was no primary involvement of any prescribers or dispensers. However, their role in supporting the TB clubs was essential through follow-up with the TB club leaders and provision of materials. In addition, health workers monitored TB club attendance and initiated follow-up with cured patients.

In rural areas such as Estie District in Ethiopia, community leaders (e.g. Coptic priests and mullahs) are important stakeholders in the health-seeking behaviour of the population. TB club leaders sought therefore to collaborate with them to encourage TB patients to attend the club meetings.

Health outcomes

Adherence was measured by calculating the proportion of actual vs expected attendance at a follow-up TB appointment at the district health centre. TB patients from a particular *kebele* absent at a follow-up appointment were defined as non-adherent. The District Medical Officer tracked the attendance per *kebele* and could therefore monitor the impact of the TB clubs on attendance, before and after TB clubs were introduced. Table 2 shows that adherence increased after the introduction of the TB clubs in 1996. As a result, health outcomes from TB medicine treatment improved. Although no published results on mortality are available, data from the WHO Global Tuberculosis Programme show that TB mortality in Ethiopia decreased by more than one third between 1996 and 2008, implying a contribution from the TB clubs to this positive trend (50).

Table 2. Adherence to treatment, before and after the introduction of the TB club approach in Estie District, Ethiopia

	Actual/Expected attendances	
	1996	1997
January	195/286 (68.2%)	224/240 (93.3%)
February	215/291 (73.9%)	239/247 (96.8%)
March	230/306 (75.2%)	251/259 (96.9%)
April	230/296 (77.7%)	278/281 (98.9%)
May	225/290 (77.6%)	297/299 (99.3%)
June	219/287 (76.3%)	302/308 (98.1%)

Source: Getahun H & Maher, D., 2000 (50)

Financial outcomes

The TB clubs were cost-effective because they were a grass-roots and voluntary initiative requiring no expensive interventions. The existing District Medical Officer was responsible for the follow-up meetings with the TB club leaders and monitoring was performed by the district health centre. The economic outcome of the initiative was therefore characterized by the use of existing resources rather than an investment in new approaches.

Success factors

This case history shows that patient empowerment is an effective concept in improving treatment adherence. By making the community self-responsible for health, capacities to contribute to individual and community TB treatment were developed in a remote and low-income area in Ethiopia. The following key factors contributed to the impact of TB clubs:

- The rational reorganization of TB follow-up visits at the district health centre that included the *kebele*-grouped appointment schedules.
- The introduction of individual patient–doctor interaction, creating an incentive for patients to attend the TB appointments.
- The identification of a committed leader of the TB club, who is literate and has organizational capacities.

- The TB club activities were tailored to the local community: meetings were scheduled during weekends or holidays, taking cultural and religious events into account, and materials were provided in the local language.
- The engagement of local influential community leaders, including priests and mullahs.
- The voluntary nature of the intervention: commitment came primarily from the patients, with the Government functioning as the facilitator.

Conclusion

The introduction of TB clubs in Estie District in Ethiopia is an excellent example of how adherence to medicine treatment can be improved in a basic, resource- and income-limited area. This model has been proven effective in other countries and regions of the world (49). Although the Government was not the lead, it provided essential support and functioned as the primary enabler of the intervention. While the initiative in Estie District was a spontaneous event, governments in other TB-burdened countries may follow the example and create TB clubs within their communities. Addressing adherence to medicine treatment is a complicated process, especially for settings with few resources, financing capabilities and infrastructure. Nevertheless, governments can prioritize treatment adherence by supporting patient empowerment and stimulating self-responsibility of the population.

Chapter VI – Health system capabilities

Strategic recommendation 6: Monitor medicine use, from purchase to health outcome, to evaluate the real-world efficacy of treatment and guide evidence-based policy-making.

Health-care systems rely on a broad range of capabilities in order to fulfil their purpose of providing effective, accessible and affordable care. According to WHO, six 'building blocks' are needed for a fully functional health-care system: service delivery, health workforce, health information, medical technologies, health financing, and leadership and governance. Although this report focuses on the responsible use of medical technologies, and on medicines in particular, it is worth highlighting the importance of the service delivery aspect of a responsible use of medicines.

Policy-making aimed at improving the efficacy and efficiency of the procurement system can be crippled by the inability to monitor medicines use. Electronic records of specific medicines expenditure and waste due to expiry before use, provide a clear picture of the level of implementation of the essential medicines list and of the quality of the procurement system. Furthermore, medicines expenditure data can be compared with prescription records to identify prescribing trends, e.g. the average number of medicines per prescription, and the amount of medicines dispensed without prescription. Ultimately, expenditure and prescription records should be matched with patient use and measured health outcomes to be able to monitor longitudinally the cost and real-world effectiveness of medicines. Although this is not yet practised at the national level, it has been demonstrated at the hospital level to improve resource allocation, and will become the gold standard in the near future due to its unmatched ability to inform targeted, evidence-based policy-making.

The following case study in Namibia illustrates how a centralized monitoring system can be successfully implemented even in sparsely populated countries with limited resources. The benefits of closer control of the supply of medicines and the measurement of their use from point-of-purchase to health outcomes are great, and allow health-care professionals to target better their interventions to improve, for example, adherence rates.

CASE STUDY 10 – Antiretroviral supply and adherence monitoring (NAMIBIA)

Tactical recommendation 6.1: Institute a system of centralized monitoring of medicines purchasing to inform budgeting and ensure optimal funding allocation to essential medicines.

Tactical recommendation 6.2: Collect medicines utilisation data at the national level to identify and evaluate prescribing trends and expenditure.

Tactical recommendation 6.3: Design a system to measure patient use of medicines, preferably at the point of dispensing, to assess patient adherence to therapy.

Tactical recommendation 6.4: Design a system to collect and aggregate information on patient health outcomes to measure real-world efficacy and safety of medicines use.

Executive summary

- HIV/AIDS is a major problem in Namibia (51). Efforts to scale up antiretroviral (ARV) coverage highlighted the need for better control of medicines supply and dispensing to avoid stockouts and measure the effectiveness of the programme through population coverage and patient compliance.
- In 2005, the Namibian Ministry of Health and Social Services, supported by the Rational Pharmaceutical Management Plus programme, introduced an electronic dispensing tool (EDT) to facilitate the monitoring of medicine use nationwide.
- The EDT software, computers and user training were provided to all facilities offering antiretroviral therapy (ART) services. As at March 2012, 49 ARV-dispensing pharmacies throughout Namibia were using the EDT.
- The centralized national database was used to generate national and regional reports on ART patient numbers and status as well as ARV stock consumption and stock levels. This information is used by the Ministry for planning and budgeting purposes.
- The EDT allows pharmacists to monitor the adherence rate of each patient and an average for the facility through pill count and pill coverage. More support can therefore be provided to patients at higher risk of developing complications and ultimately failing treatment due to non-adherence. The EDT is also used to generate HIV Drug Resistance Early Warning Indicators that can identify facilities whose patients are at highest risk of developing drug resistance (52).

Background

Income inequality and the very low population density in Namibia are challenges for the health-care system to reach the 2.3 million people living in ~800 000 km². Since gaining independence in 1990, the Namibian Government has focused on the crippling HIV/AIDS epidemic affecting the country through the National AIDS Control Programme and several short- and medium-term interventions (53). In 2003, Namibia secured funds from the US President's Emergency Plan for AIDS Relief to scale up the coverage of ART in the country (54), with the goal of providing ARV treatment to over 80% of the affected population (55): the effort has continued through 2010 and is yielding encouraging results (53).

The initiative to scale up ARV coverage highlighted the need for better control of medicines supply and dispensing in order to avoid stockouts, and to measure the effectiveness of the programme not only through population coverage but also patient compliance. The largely paper-based tracking system used in the country was deemed insufficient to collect and centralize data on the use of medicines, especially due to the challenges of implementing such system in a sparsely populated country.

In 2005, The Namibian Ministry of Health and Social Services, with support from the US Agency for International Development (USAID), introduced an electronic dispensing tool (EDT) that had been developed by Management Sciences for Health, to facilitate the monitoring of medicine use throughout the country.

Intervention

USAID funded the Strengthening Pharmaceutical Systems programme (55) to customize and enhance the EDT. The tool was thus able to improve the traceability of ARV supply, better assess consumption rates at each facility, and track patients. For example, the system was able to identify which patients were not achieving optimal adherence levels, to identify provinces/regions where consumption was higher, and consequently to budget medicines supply accordingly to reduce stockouts.

Throughout Namibia, 35 ARV-dispensing pharmacies (49 as of April 2012) were provided with computers, training and specialized tools to record and match ARV dispensing to specific patients. A clear picture was available of when patients has their prescriptions dispensed, and which facilities were dispensing to which patients. Furthermore, all facility- and patient-level data were aggregated in a national database so that trends and key metrics could be easily evaluated at the district, regional and national levels (56). Finally, hand-held scanners were provided to dispensers as part of the programme to extend the coverage of the EDT to more remote areas of the country; the data collected were sent to the national database via 3G cell phone technology with support from Namibia Mobile Telecommunications Limited (56).

The EDT intervention targeted mainly the medicine dispensers as they were the "gateway" between patients and their therapy. The engagement of key pharmacies was fundamental, as the system was intended to monitor the use of medicines while reducing the administrative burden of dispensing ARVs. The EDT was welcomed by pharmacists as it allowed them to

focus more on patient care to improve health-care delivery rather than filling in paperwork manually.

Health outcomes

The new system was successfully implemented in all ARV-dispensing pharmacies, and the project and facilities were handed over to the Ministry of Health in 2010 (55). The centralized national database can be used to monitor prescription data collected at the pharmacy level to predict more easily pharmacies that needs to be resupplied to avoid stockouts, and this information is fed back into the budgeting process to ensure better accuracy. Furthermore, usage data can be aggregated at the district, regional and national levels to monitor areas of the country that dispense the highest amount of ARVs, and that can be targeted appropriately to ensure that medicines are used responsibly.

The EDT allows health workers to monitor the adherence rate of each patient through pill count and time of prescription refill: this information is used to provide more support and attention to patients at higher risk of developing complications and ultimately failing treatment due to non-adherence. Patient-level data can then be used to monitor WHO Early Warning Indicators (55) to identify areas at heightened risk of developing ARV resistance and inform policy to address the issue.

Finally, it is easy to see how the output of the EDT can be used to better inform pharmacovigilance. Heterogeneous information sources have been successfully used in Namibia to connect adverse events with their potential medicinal cause. A good example of this practice is assessment of the connection between anaemia and Zidovudine-based ART (56,57) to inform treatment choices. Such monitoring would have been virtually impossible with the previous paper-based system. The longitudinal monitoring of medicines dispensing, use and health outcome at the patient level is invaluable in providing real-world evidence on the efficacy and safety of medicines. Data from the EDT have also been used in the quarterly ART reports and the nationwide ART adherence baseline survey currently underway.

Financial outcomes

Although no official published data are available on the cost-effectiveness of the implementation of the EDT, or on the short-term financial investment required, such investment will be effective in the long term. By monitoring dispensing, procurement of medicines is more accurate and wastage of expired medicines is reduced. In addition, it enables pharmacists to monitor and evaluate adherence and target education to non-adhering patients, reducing medication errors and avoidable hospitalizations.

Success factors

The EDT implementation has been widely successful in Namibia due to several factors, including the design of the tool. Pharmacists readily accepted the system as it reduces the administrative burden of dispensing ARVs, increasing therefore their ability to support patients in their therapy by providing more advice and better information on the importance of adhering to treatment. Furthermore, pharmacists may be able to spend the time saved by

identifying and following up patients with the lowest adherence rates. This form of risk stratification has the potential to greatly improve treatment outcomes, as it makes the most efficient use of human resources in targeting non-adherence. The intervention truly brought the pharmacists to the core of the medicines use evaluation effort, and this is one of the two main drivers of the success of the initiative in such a short period of time.

The ability to operate the system through hand-held devices allowed the reach of the initiative to be extended to remote communities where the use of medicines was prohibitive to track in a consistent and reliable fashion. This greater reach allowed for better budgeting of supplies in remote communities where stockouts might have jeopardized patients' adherence. At the same time supported a more accurate monitoring of adherence even when pharmacists or doctors were not in close proximity to the patient. In a country as sparsely populated as Namibia, the ability to reach such remote communities effectively is essential to the success of any intervention. The fact that the project and facilities were handed over to the Ministry of Health in 2010 and that the number of clinics participating has increased demonstrate that it is sustainable and 'locally' owned.

Conclusions

The introduction of EDT has proved effective in Namibia in monitoring medicine use to improve policy-making, and the ability to operate it through hand-held devices ensured its efficacy even in remote communities that are traditionally hard to reach with policy-making. Namibia provides a clear example of how longitudinal medicine use monitoring can be implemented and scaled up not only in high-income countries, and how the information collected through such a system can provide invaluable direction in policy-making.

EDT is also a good example of how developing countries can leverage technology to overcome physical barriers to the provision of health care, such as in sparsely populated lands. The efficacy of these systems is of course not limited to ARVs but can be used to monitor medicine use more generally at the point of prescription and dispensing. In Namibia, the Ministry of Health is currently piloting a broader e-health system in two referral hospitals in Windhoek, which is intended ultimately to monitor, among many other functionalities, all medicine use in every public facility in the country. The ability to monitor medicines use and adherence will be an invaluable tool in informing policy-making to promote the responsible use of medicines.

Chapter VII – The importance of leadership commitment

Strategic recommendation 7: Ensure sustained, top-down commitment of national authorities and promote active, bottom-up engagement of prescribers, patients and dispensers to the principles and policies fostering the responsible use of medicines.

Government commitment through policy-making and sustained financial support is essential in the pursuit of a more responsible use of medicines. Commitment does not stop at the will to improve health care: goodwill is rather the very beginning of commitment. Government commitment comprises three key elements: provide resources to upscale effective interventions to achieve their full potential; provide sustained support to successful interventions for as long as needed to ensure the permanence of the results; and directly engage national and regional stakeholders to promote top-down commitment coupled with bottom-up engagement of prescribers, dispensers and patients.

As illustrated by case studies throughout this report, and particularly by the case in this Chapter, the scale of the intervention can often be a key determinant of success. In large countries, governments should make sure that even the more remote regions are reached. In countries with several ethnic or religious groups, the government should address their respective concerns and needs. Finally, the government should make sure that people obtaining health care outside the reach of the public sector also benefit from the intervention.

In addition, the effort undertaken should be supported as long as needed to sustain the positive impact of a project. A frequent mistake is that when the goals of a project are accomplished, the efforts and investments are gradually terminated and thereby the benefits reduced. The case history of polio elimination in India is a clear example of the need for sustained commitment to immunization: if immunization coverage had decreased, polio would have had the chance to spread again and the benefits achieved would have been lost.

Government commitment should entail provision of the needed financial support for the intervention. Governments from low- and middle-income countries with limited resources should collaborate with development organizations to acquire sufficient funding to support their projects. Interventions improving the responsible use of medicines may need more intensive short-term investment, which in the long term can be expected to be cost-effective.

Finally, the government should be ready to translate its commitment into strong advocacy for an intervention at all levels of the public and private sectors. The goal of such advocacy is to create and consolidate broad consensus among stakeholders to sustain commitment. The top-down approach of integrating policies from the national government must always be supported by a bottom-up response from grass-roots institutions, professionals and patients.

CASE STUDY 11 – Polio eradication (INDIA)

Tactical recommendation 7.1: National authorities should provide sustained, top-down policy and financial commitment to initiatives fostering a responsible use of medicines.

Tactical recommendation 7.2: Build consensus on medicine use among national and local stakeholders by stimulating the active engagement of prescribers, dispensers and patients.

Executive summary

- Despite the availability of effective vaccines, polio remained endemic in India until January 2011.
- The Government of India (GOI) made a sustained effort over 17 years to achieve polio eradication through immunization campaigns.
- The success of the immunization campaign was attributed to the sustained commitment of the GOI and the local government institutions.
- The governments at national, state, regional and district levels were all engaged in the polio eradication programme regardless of political background.

Background

In 1988, the World Health Assembly (WHA) adopted a resolution calling for the worldwide eradication of the poliovirus by the year 2000 (resolution WHA41.28). At that point, polio was endemic on a global scale. Figures 13 and 14 show the effect of the immunization on global polio epidemiology. Although this was a major success, the goal of the resolution was not achieved. Figure 14 shows that in 2012, polio remains endemic in three countries: Afghanistan, Nigeria and Pakistan, whereas Angola, Chad and the Democratic Republic of the Congo have imported the virus after initial eradication. Other countries also experienced outbreaks during 2011 from imported poliovirus. This indicates the critical need for sustained efforts in the fight against this devastating, life-impairing and immobilizing disease (58).

One of the most recent polio-free declared countries is India. In January 2012, one year had passed since the last case of wild poliovirus had been reported. India was one of the Member States that ratified the 1988 WHA resolution, but did not start the eradication programme until 1995. In 1997 the National Polio Surveillance Project (NPSP) was established as a collaboration between WHO and the Ministry of Health and Family Welfare to centralize, monitor and coordinate the campaign. The strong incentive of the GOI for a comprehensive multi-stakeholder intervention to eradicate polio definitively in India was fuelled by three motivations: the burden of disease, the international obligation to eradicate polio as India was the main global source of the virus, and belief in the feasibility of eradication. Although the polio virus was eradicated in most parts of the country, two states remained endemic: Uttar Pradesh and Bihar. This last pool of polio virus was finally targeted in 2010 and 2011, resulting in the official eradication in January 2012. This case

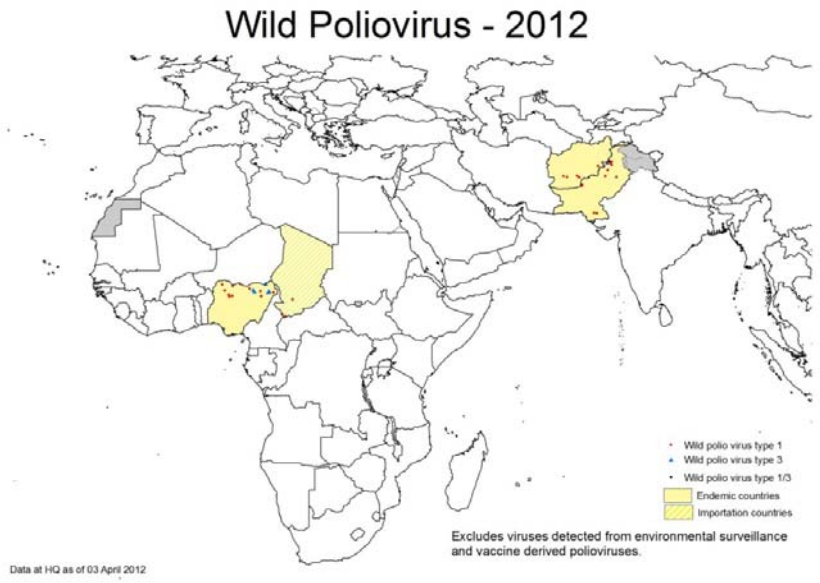
study describes the commitment of the GOI to eradicate polio and how the targeted policies were integrated on a large scale to accomplish this goal (58,59).

Because there is little research on the political commitment for eradication, the facts mentioned in this case history are based on information from WHO experts and GOI publications.

Figure 13. Global polio epidemiology, 1988

Source: Global Polio Eradication Initiative (58)

Figure 14 Wild poliovirus epidemiology, 2012



Source: Global Polio Eradication Initiative (58)

Intervention

All Indian political parties decided to commit to polio eradication at the national, state and district level. This was essential, because the states of India can independently decide whether to implement health policies. By achieving unanimous political commitment, between-state barriers were removed, as all state governments were committed to implement the necessary policies. Because polio immunization is an ongoing process, continuous action was essential and administrations of different political backgrounds worked on the programme.

Normally, the states of India are responsible for the implementation of policies in their health-care systems, and thus allocating GOI funding for health in their state. For the polio eradication programme, however, the GOI established an exclusive budget. To sustain the commitment of the state governments, the GOI funded over 80% of the total project costs.

The Government collaborated with several partners that could contribute to the local implementation of polio immunization. These partners included WHO, UNICEF, the US Centres for Disease Control and Prevention, and Rotary International.

Starting in 1995, two nationwide pulse polio immunization days (NIDs) were organized by the GOI on an annual basis. The targeted age group of these extensive vaccination rounds was 0–5 years. All infants in that group were given two doses of oral polio vaccine (OPV). In addition, the GOI performed several subnational immunization days (SNIDs) and eradication rounds in locally infected areas.

Since the foundation of the NPSP in 1997, regular immunization rounds have been carried out, mobilizing increasing proportions of the population. In 2010, the GOI Central Drugs Standard Control Organisation approved the use of bivalent OPV, targeting type 1 and 3 of the poliovirus (type 2 was eradicated by 1999). In 2011, the GOI collaborated with the private sector, NGOs, health agencies and other professional bodies to scale up the SNIDs, leading to seven small SNIDs focused on the specific cores of polio outbreaks in Uttar Pradesh and Bihar. During these immunization days, approximately 2 million community health-care workers were raising awareness, providing information and mobilizing the population to be immunized. The SNIDs were centrally planned and funded by the GOI. Health-care workers were sent out to all regions of Uttar Pradesh and Bihar with the vaccine to reach every remote location.

The interventions were monitored by UNICEF and the NPSP, which tracked all immunized infants and documented all new polio cases. The GOI was able to evaluate the status of immunization and eradication by reliable data provided by these organizations.

The GOI established a partnership with all key stakeholders in the health-care system that could contribute to maximize the scope of the SNIDs. In addition, key figures in the community were engaged to urge parents to obtain the vaccines for their children, reducing the number of parents who were refusing vaccination on grounds of principle. During the whole intervention, the stakeholders engaged included public health-care workers,

physicians, clerics, imams and teachers. These were engaged in order to mobilize parents who are responsible for obtaining the vaccination for their child.

Health outcomes

As a result of the intervention, India has been free of any new polio case since January 2011. This means that the country has accomplished polio eradication as the minimum period for official eradication is one year. To maintain eradication, continuous efforts are dedicated in India to the universal coverage of immunization against polio. Immunization activities are still performed, and the NPSP continues to monitor and detect polio outbreaks.

Financial outcomes

There was no financial incentive for the polio eradication interventions performed by the GOI. Polio vaccines are inexpensive and can be procured on a large, national scale. The GOI showed its commitment by sustaining investment in the procurement of vaccines and ensuring that sufficient health workers distributed the vaccines to all areas of the country over 17 years. Governments can prioritize universal immunization against viral diseases such as polio by providing the vaccine for free, because the health benefits clearly outweigh the financial burden.

Success factors

Seven innovative approaches contributed to the success of the immunization campaign (58). These approaches evolved over the 17-year experience of the polio eradication programme in India.

1. Commitment to polio immunization of all state governments regardless of political background: all political parties supported the eradication programme to ensure that the effort continued if one government was succeeded by a different political party.
2. High quality standards and responsibility for health-care workers at district level in the polio programme: local project leaders were personally responsible for the required optimal delivery of vaccines, with serious consequences for any laxity.
3. Access: health-care workers were sent out to bus stations, construction sites and used motorbikes and trains to reach the mobile population in India. They also travelled by foot to vaccinate children in the most remote regions.
4. Stakeholders in Muslim communities: key facilitators such as clerics, imams, madrasa teachers and physicians were engaged to persuade reluctant parents to obtain the immunization.
5. Monitoring: sewage samples were collected in high-risk areas to track the spread of the polio virus.
6. Specific targets: 107 high-risk blocks in the States of Uttar Pradesh and Bihar were targeted by focusing on hygiene, sanitation and the availability of clean water besides the routine immunization practice.

7. Combination interventions: the combined use of operational (mobilization of populations living in the remaining polio pools) and technical (introduction of bivalent OPV as most effective for India) innovations.

All seven success factors testify to the strong and sustained commitment of the GOI to accomplish polio eradication.

Conclusions

This case study provides a clear example of successful polio eradication for the remaining polio-endemic countries. It shows that through the strong and sustained commitment of the government, eradication can be achieved even in a large country such as India. However, the battle against polio is certainly not finished. All stakeholders at the governmental, state and district levels must maintain immunization coverage, polio surveillance and preparedness to contain outbreaks.

Overall, this case study shows how a committed Government improved the responsible use of medicines and as a result obtained the maximum benefits of the medicine for its people. Sustained leadership commitment was important for achieving polio eradication. This message is not limited to India; it applies to governments and policy-makers in India and the rest of the world, whether it concerns polio eradication or other issues affecting health. If leaders can stand together behind a specific intervention for as long as it takes to improve the responsible use of medicines, setting aside their opposing political backgrounds and ideologies, it will be their citizens' health (including the politicians) and the country that will be the winners.

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