

Medicines in Health Systems

Edited by:
Maryam Bigdeli, David H. Peters, Anita K. Wagner

Advancing access,
affordability and
appropriate use

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PREFACE

There is now a much welcomed push by WHO Member States to implement the concept of universal health coverage (UHC) and thus to ensure that all people obtain the health services they need without suffering financial hardship when paying for them.

UHC requires strong, well-run health systems, sustainable and equitable methods to finance health services, sufficient capacities of well-trained and motivated health workers, and – last but not least – access to essential medicines and technologies.

This *Flagship Report* deals with the latter – the challenges to achieve equitable access to essential medicines. With expenditures on medicines reaching extreme levels – with some low- and middle-income countries directing two thirds of their entire health spending on medicines – the need to rethink and redirect action in the field of medicines has never been more pressing. Only with new ways of understanding the scope of the problems can policies, regulations and health interventions be designed to ensure that, when it comes to accessing necessary medicines, no one is left behind, no matter where they live, no matter their age, or sex, or race.

This *Flagship Report* calls for a “systems approach” to position medicines within the complexity of any health system. This approach moves beyond the idea that medicines are little more than a series of interactions between patients and public health services. A health systems approach to medicines may facilitate the understanding of the system’s integral relations and connections, allowing for innovative and contextual responses in developing and implementing new medicines and new medicines policies and regulations.

As evidenced throughout this report, medicines access, affordability and appropriate use must be a core focus for any effort to strengthen health systems and to advance universal health coverage. This *Flagship Report* calls for greater accountability of stakeholders, and stimulates some fresh thinking among decision-makers, researchers, civil society, and development partners. This *Flagship Report* will undoubtedly inspire important conceptual and practical on-the-ground work.



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EXECUTIVE SUMMARY

The World Health Organization (WHO) defines essential medicines as those medicines that respond to the priority health needs of a specific population. They should be available at all times in adequate amounts, be affordable, and have a proven efficacy, quality and safety. When observing these criteria, essential medicines are one of the most cost-effective elements for any health system, with an immediate and long-lasting health impact.

WHO has deemed medicines and health technologies one of six health system building blocks. Yet as a fundamental element, medicines and health technologies do not lie in isolation from the other components of a health system. To appreciate the many interconnections and actors that influence and shape medicines, a systems approach is required.

A systems approach features prominently in this report. This allows us to situate medicines against the full complexity of a health system, understanding how interventions in the pharmaceutical sector influence the rest of the health system and vice versa. In applying a systems approach, we come to understand that improving access to medicines can promote health equity, and contribute to both stronger health systems and the goals of universal health coverage (UHC).

As health systems and the actors who shape them feature many core interactions and connections, it is essential to examine the ways in which the access to, affordability, and use of medicines affect and are affected by decisions in other parts of the health system.

Drawing on the work of the Alliance for Health Policy and Systems Research (AHPSR) (11, 12), this report applies a systems approach to

medicines. Through various country case-studies, the report illustrates major challenges and advances in the access, affordability and appropriate use of medicines in low- and middle-income countries (LMICs).

Only through an appreciation of the dynamic interplay – often unpredictable and always changing – among health system components and actors can we arrive at a full understanding of a health system, and specifically how medicines policies and medicines interventions affect and are affected by the system's constant adaptation and complexity.

Following a description of how the access to medicines field has evolved since the 1970s, we explore specific links between medicines and UHC, then move to the role of innovation in developing and delivering medicines, and then to a focus on the pluralistic health systems around medicines, with particular attention on health market systems. We conclude with some action-oriented guidance and recommendations for decision-makers to inform, monitor, and evaluate the inevitable reforms required to improve medicines access, affordability, and use in LMIC settings.

As demand-side barriers are of critical importance in accessing medicines, it is essential to move past the traditional conceptual confines of medicines as goods transacted in a series of interactions between patients and public health services.

This report argues that only with sound decision-making – informed by the aspirations of universal health coverage, a fuller understanding of the interrelationships between actors in systems, and guided by health system strengthening efforts – will we make viable

and sustainable progress in increasing equitable, affordable access to medicines that are appropriately used by providers and patients in LMICs.

As multiple dynamics, factors and systems influence pharmaceutical and health sector governance, it is essential to map out, analyse, and involve these actors of influence.

Essential Medicines in LMICs

Despite increased global attention to medicines – with rights to medicines enshrined in national constitutions, and as part of Millennium Development Goal 8 – there remain some core problems with essential medicines in LMICs. Cost-effective, quality-assured medicines are not guaranteed to be available, prescribed or used appropriately. Medicines may be counterfeit or substandard, and they may not be accessible due to financing barriers or poor advice from providers and drug sellers. Essential medicines reflect, in short, the principal shortcomings of the health systems in which they are distributed and delivered.

To ensure that medicines are, as per WHO, “available within the context of functioning health systems at all times in adequate amounts, in the appropriate dosage forms, with assured quality and adequate information, and at a price the individual and the community can afford,” any medicines strategy must pay specific attention to a fuller understanding of the bottlenecks in ensuring equitable access to and appropriate use of medicines across various LMIC populations. What policies can improve both the affordability and the appropriate use of medicines? And how can we strengthen accountability and good governance structures in the public and private sectors?

The challenge: providing equitable, affordable access to appropriately used essential medicines

This report focuses on three specific medicines dynamics: the equitable access to essential medicines, their affordability, and their appropriate use.

- **Equitable access.** The actual medicines that patients access will differ from country to country, depending on multiple factors including disease burden, health system infrastructure, and the financial capacity (of households and of health systems). Within and across LMICs, vulnerable populations often lack access to essential medicines, due to geographic, economic, cultural, or other barriers. Equitable access to medicines means that each person receives medicines available in a system according to her or his needs, and that the quality of care and the quality of medicines is the same for everyone.
- **Affordability.** For households, high out-of-pocket payments can have clinical repercussions (e.g. those in need forego or interrupt their treatment), economic repercussions (e.g. high out-of-pocket expenditures reduce household spending on other necessary items), and societal repercussions (e.g. community divisions stemming from inequitable medicines access due to cost). For many health systems, medicines constitutes a large and growing proportion of total spending and certain essential medicines (e.g. novel cancer treatments) may be unaffordable, creating health-equity ramifications across a society. Ensuring that medicines are, in fact, affordable is a key dimension of access.
- **Appropriate use.** When medicines are available, they need to be appropriately used by all involved, including prescribers,

dispensers, households and patients. Multiple factors contribute to their misuse, including a lack of regulatory enforcement, insufficient disease and treatment knowledge, and unintended effects of health and pharmaceutical system policies. Ensuring the appropriate use of medicines is critical to reducing disease burden in LMICs, to preserving the future efficacy of proven treatments, and to spending scarce resources wisely.

Our strategy: addressing medicines challenges using a systems approach

Conceptualizing access to medicines as a foundational element for a health system allows us to move past the more traditional approach to medicines. Integrating medicines within a holistic concept that better reflects how real-world, complex systems actually function allows us to appreciate how medicines affect and are affected by decisions and interventions in other parts of the health system. This report examines many of these health system connections – between medicines and governance, for instance, and between medicines and information, arguing throughout that an increased attention to these connections is paramount.

As different elements of systems – including the development, production, marketing, registration, selection, financing, procurement, distribution, prescribing, dispensing and ultimately the use of medicines – must function in a coordinated fashion to ensure that medicines benefit lives, the routine inclusion of multiple stakeholders is another aspect of vital importance. Recognizing the many dynamics, factors and systems that influence pharmaceutical and health sector governance, we must map, analyse, involve, and try to align actors of influence in medicines decision-making, and actively guide health market systems.

When we recognize that access to medicines depends on much more than a series of interactions between patients and public health services, we understand that innovations for developing medicines and implementing medicines policies are essential to bring both new and existing medicines to people. This raises challenging questions around novel, high-cost medicines and generics which, to be resolved, require routine multi-stakeholder engagement in fair and inclusive decision-making processes.

A Framework for moving forward

Following discussion and analysis of the medicines situation across LMICs, this report concludes with three core arguments for the medicines agenda in LMICs:

1. Include access to medicines and their appropriate use as an explicit focus in health system strengthening and efforts towards universal health coverage.

As LMICs currently spend a disproportionate amount of households' and systems' budgets on medicines, any attempts to strengthening health systems and achieving UHC must include a primary focus on medicines.

2. Recognize the needs for transparency and governance in the medicines sector within and across health systems, and then strengthen governance capacities.

For essential medicines in any LMIC health system and globally, there are multiple authorities and governance structures. Pluralistic health care delivery and financing systems require innovative forms of governance different from those systems that organize public health care delivery alone. Moreover, the governance and regulation of essential medicines transcends national boundaries, requiring both local and international collaboration and innovation.

3. Build more robust connections between information, medicines and decision-making. Recognizing that data on medicines lie in a fragmented manner across a health system – and that information is central to a systems approach to medicines – there is an urgent need to develop innovative means for generating information from data and for connecting not only information and medicines policies, but the actors who gather, shape, control and make decisions based upon that information.

An overview

In **Chapter One**, we lay the groundwork for the rest of the report by introducing and exploring key medicines concepts, including how a systems approach allows us to better understand medicines interventions and health system connections. **Chapter 2** offers a historical perspective on concepts regarding medicines access, affordability, and use, drawing important parallels between the evolution of the field of essential medicines with the global agenda of health systems strengthening and universal health coverage. **Chapter 3** argues for an explicit focus on medicines when moving towards universal health coverage. The chapter discusses how two key aspects of implementing universal health coverage – information and financing – can support policies that facilitate the equitable and affordable access to, and appropriate use of, medicines. **Chapter 4** discusses how innovation can meet three key challenges in access to medicines: the lack of optimal treatment options for some health conditions; under-use of high-quality, lower cost generic medicines in most health systems; and the lack of equitable, affordable access to specialty medicines. **Chapter 5** explores health market systems, examining how medicines are delivered, and how patients and communities access medicines in markets. The chapter offers

alternative ways of delivering and accessing medicines in pluralistic health systems. **Chapter 6** concludes by drawing lessons from the examples and complex situations discussed in the preceding chapters. Finally, the **Web Annex** presents all of the case-studies that informed this report, along with other useful resources. It can be accessed at: www.who.int/alliance-hpsr/resources/flagshipreports/en/

As population needs and the health systems to meet those needs continue to evolve in an increasingly connected world, old challenges will persist and new ones will arise. No one stakeholder or single approach will suffice to ensure that medicines contribute to improving individual and population health and well-being. The emerging synergies between efforts to improve health equity, to strengthen health systems, and to provide universal health coverage, offer unprecedented opportunities to make appropriately-used medicines accessible and affordable across LMICs.

The time is now – for communities, for nations, for our community of nations – to act upon these synergies, and respond to the pressing medicines needs in LMICs.

ACRONYMS

ADDO	Accredited Drug-Dispensing Outlets
AHPSR	Alliance for Health Policy and Systems Research
AMP	Accelerating Medicines Partnership
ANVISA	Agência Nacional de Vigilância Sanitária (Brazilian Health Surveillance Agency)
ART	Antiretroviral Therapy
ASAQ	Artesunate and Amodiaquine
ASU	Antibiotics Smart Use
A4R	Accountability for Reasonableness
CEWG	Consultative Expert Working Group
CHAI	Clinton Health Access Initiative
CSIR	Council on Scientific and Industrial Research
CSMBS	Civil Servant Medical Benefit Scheme
DDW	Diseases for the Developing World
DLDB	Duka la Dawa Baridi (Private medicine outlets)
DNDi	Drugs for Neglected Diseases Initiative
EAG	Ethics Advisory Group
EML	Essential Medicines List
FDA	Food and Drug Agency
GDP	Gross Domestic Product
GFATM	Global Fund to Fight AIDS, TB and Malaria
GPO	Government Pharmaceutical Organization
HAI	Health Action International
HPHC	Harvard Pilgrim Health Care
HTA	Health Technology Assessment
IAVI	International AIDS Vaccine Initiative
ICIUM	International Conference on Improving the Use of Medicines
IFPMA	International Federation of Pharmaceutical Manufacturers & Associations
INRUD	International Network for Rational Use of Drugs
LCSs	Licensed Chemical Sellers
LMICs	Low- and Middle-Income Countries
MDG	Millennium Development Goals
MEDS	Mission for Essential Drugs Supply
MeTA	Medicines Transparency Alliance

MMV	Medicines for Malaria Venture
MOHSW	Ministry of Health and Social Welfare
MSH	Management Sciences for Health
NCD	Noncommunicable Diseases
NCMS	New Rural Cooperative Medical Scheme
NGO	Nongovernmental Organization
NHIS	National Health Insurance Scheme
NHSO	National Health Security Office
NICE	National Institute for Health and Care Excellence
NLEM	National List of Essential Medicines
OSDD	Open Source Drug Discovery
PATH	Programme for Appropriate Technology in Health
PDP	Product Development Partnership
PHC	Primary Health Care
PREPFAR	President's Emergency Plan for AIDS Relief
QUAMED	Quality Medicines for All
R&D	Research and Development
REACT	Response to Accountable Priority-Setting for Trust in Health Systems
ReAct	Action on Antibiotic Resistance
SEAM	Strategies for Enhancing Access to Medicines Program
SP	Seguro Popular (Mexican Social Security)
SSS	Social Security Scheme
STGs	Standard Treatment Guidelines
SUS	Sistema Único de Saúde (Unified Health System)
SWO	Social Welfare Office
TFDA	Tanzania Food & Drugs Authority
TRIPS	Trade Related Intellectual Property Rights
UC	Universal Coverage
UHC	Universal Health Coverage
UMICs	Upper-Middle-Income Countries
WHA	World Health Assembly
WHO	World Health Organization



1

WHY A HEALTH
SYSTEMS APPROACH?

In recent years a human rights argument has framed access to essential medicines as part of a broader movement to improve the equitable access to health and accelerate the achievement of UHC.

1.1 Introduction to Essential Medicines

The World Health Organization (WHO) defines essential medicines as those medicines that respond to the priority health needs of a specific population. The WHO Model List of Essential Medicines provides guidance for the development of national and institutional essential medicine lists. Not only does this guidance allow countries to select medicines for their own context, it has led to the global acceptance of essential medicines as a powerful means of promoting health equity, pursuing universal health coverage (UHC), and, ultimately, strengthening health systems (1).

Essential medicines should be available at all times in adequate amounts, in appropriate dosage forms, and be cost effective. To respond effectively to a population's health needs, they must have a proven efficacy, quality and safety. When respecting these criteria, essential medicines are one of the most cost-effective elements for any health system, with an immediate and long-lasting health impact. In low- and middle-income countries (LMICs), simple iron-folate preparations can reduce maternal and child mortality from anaemia during pregnancy; inexpensive artemisinin-based combination therapies can prevent malaria fatalities; and affordable medicines can reduce heart attacks and strokes (1).

Despite this health impact – and despite a thriving medicines market – there remain critical problems with essential medicines in LMICs. They are often not easily available or accessed. They can be unaffordable and of poor quality. They are used inappropriately. They reflect, in short, the principal shortcomings of the health systems in which they are distributed and delivered.

To address this issue, in recent years a human rights argument has framed access to essential

medicines as part of a broader movement to improve the equitable access to health and accelerate the achievement of UHC (2-4). To that end, many LMICs have enshrined the right to health – including access to medicines – in their national constitutions (5). This has in turn contributed to the inclusion of access to essential medicines in Millennium Development Goal 8, and the increasing – though incomplete – use of the essential medicines concept across United Nations agencies and other international organizations (6, 7).

Despite some global attention on the issue, however, much work remains to be done. Crucially, governments, the international community, nongovernmental organizations (NGOs) and the pharmaceutical industry must move the medicines agenda beyond intellectual property rights and increasingly respect their legal and ethical responsibilities in working towards the equitable access to medicines in LMICs. This includes specific attention to:

- ▶ a fuller understanding of the bottlenecks in ensuring equitable access to medicines across LMIC populations;
- ▶ improving both the affordability and the appropriate use of medicines;
- ▶ increasingly using fair and transparent priority setting processes to determine which medicines to select and include on a national essential medicines list (8, 9);
- ▶ determining innovative pricing and financing strategies for medicines, along with more efficient models of supply; and
- ▶ developing incentives for the appropriate use of medicines.

LMIC governments and the international community must recognize and follow through on their responsibilities to achieve these access goals. Furthermore, this focus on access

to medicines can help advance steps towards universal health coverage – a principle where people can obtain the health services they need without incurring financial hardship. Giving people access to the high quality, affordable medicines they require can only occur within a context of stronger health systems that have removed barriers to the full and equitable participation of populations across LMICs.

This global attention on UHC and strengthening health systems opens some important windows for access to medicines (10). To take full advantage of these opportunities, we must adopt a *health systems approach* and situate medicines against the full complexity of a health system to visualize how interventions in the pharmaceutical sector influence the rest of the health system and vice versa. In applying a health systems approach, this report deepens our understandings of the many ways to improve access to medicines within a broader system that is increasingly able to satisfy the health needs of the people it serves. Such an analysis generates some strong recommendations for decision-makers to act upon, and presents priority topic areas for researchers.

1.2 Introduction to the Flagship Report

The goal of this Flagship Report is to provide an analysis of essential medicines using a health systems approach. This approach advances an innovative and holistic perspective that will ultimately enhance informed decision-making to improve medicines access, affordability and appropriate use in LMICs. Drawing on the work of the Alliance for Health Policy and Systems Research (AHPSR) (11, 12), this report uses concrete examples through country case-studies to contrast the stated

goals of medicines policies with their actual outcomes and implementation challenges. The report also offers guidance and recommendations for decision-makers to inform, monitor, and evaluate the inevitable reforms required to improve medicines access, affordability, and use in LMIC settings.¹

This report's central contribution lies in its application of a health systems approach to essential medicines. Recognizing that the introduction of a new or modified intervention generates both predictable and unpredictable responses from the health system, a health systems approach allows us to anticipate how pharmaceutical interventions affect other health system functions and are, in turn, affected by them. What, for instance, are the governance or financing or service-delivery implications – across a system – when expanding access to an essential medicine? A medicine may be an essential life-saving measure, but without adequate attention to how it will be financed in the medium and long term, or to how it will be stocked and delivered – consistently and reliably – and how it will be used appropriately, the intervention will become yet another vertical effort that fails to integrate with the health system, seeing its impact fading over time.

A health systems approach allows for a comprehensive mapping of relevant actors and their influence and power on medicines access. Some of these actors may be an active part of the health system (e.g. nurses providing health care and local officials implementing medicines policies), and some may lie well beyond the actual delivery of health care (e.g. bilateral donors funding specific interventions or pharmaceutical companies' marketing practices). Arriving at a deeper understanding of health system actors – including an appreciation of their power, interests and ability to effectively collaborate – is a crucial missing

Global attention on UHC and strengthening health systems opens some important windows for access to medicines.

This report uses concrete examples through country case-studies to contrast the stated goals of medicines policies with their actual outcomes and implementation challenges.

1. Whereas the report recognizes that there are vulnerable populations in all countries – with growing inequities threatening people in need of essential medicines for acute and chronic conditions no matter their geography – the report focuses on LMICs.

Only with sound decision-making – informed by the aspirations of UHC and guided by health system strengthening efforts – will decision-makers make viable and sustainable progress in increasing access to medicines in LMICs.

piece in access to medicines. Through this increased understanding of relevant actors, a systems approach allows us to then visualize the many decision-making points and processes within a health system – in priority setting, for instance, in policy formulation, and in policy implementation (10).

The challenge of course lies in finding new ways of influencing those decision-making processes with voices and experiences from across the health system. We argue throughout this report that only with sound decision-making – informed by the aspirations of UHC and guided by health system strengthening efforts – will decision-makers make viable and sustainable progress in increasing access to medicines in LMICs.

1.3 Definitions and concepts

In any context, access to medicines is much more than simply an intellectual property issue. Access to medicines depends on which medicines are selected for inclusion on a national essential medicines list, and whether they are available, affordable and appropriately used. As these dimensions of access are of fundamental importance to the report, we define them below.

1.3.1 Selection and availability of medicines

WHO updates its Model List of Essential Medicines every two years (13), selecting medicines “with due regard to public health relevance, evidence on efficacy and safety, and comparative cost-effectiveness” (14). WHO states that “essential medicines should be available within the context of functioning health systems at all times in adequate amounts, in the appropriate dosage forms, with assured quality and adequate information, and at a price the individual and the community can afford” (14).

The WHO Model List of Essential Medicines

serves as a guide for developing national and institutional essential medicine lists. Effective implementation of essential medicines lists will depend on several factors: standard treatment guidelines for health conditions, including communicable and noncommunicable diseases that are relevant to the population (15-17); changing population-health conditions and treatment options; the capacity of skilled health care providers and levels of care; infrastructure conditions such as the state of storage facilities and transport issues; the availability of quality-assured products; affordability; and financing, with a particular focus on out-of-pocket costs.

1.3.2 Affordability

There are different ways to define affordability, with assessments typically focused on two levels: affordability for patients/households, and affordability for the health system itself. At the patient/household level, an inability to afford medicines can have clinical repercussions (e.g. those in need forego or interrupt their treatment), economic repercussions (e.g. high out-of-pocket expenditures reduce household spending on other necessary items), and societal repercussions (e.g. community divisions stemming from inequitable medicines access due to cost). The WHO/Health Action International (HAI) Project on Medicine Prices Availability and Affordability measures patient affordability by estimating the number of daily wages – using the salary of the lowest-paid unskilled government worker – required to purchase a course of treatment (18).² Such measurements provide a precise snapshot of a medicine’s affordability in any given context, helping to quantify the impoverishing effect of purchasing medicines (19).

2. Cameron et al. (2009) studied affordability for both acute and chronic conditions – specifically a course of antibiotics for a bacterial infection, and one month of treatment for diabetes.

Several authors (20, 21) have furthered this work by constructing three indicators of the financial burden of medicines spending at the household level:

- (1) high (and potentially catastrophic) health care spending, defined as 40% or more of total expenditures after accounting for food costs, over a period of 4 weeks;
- (2) undesirable financial coping strategies, such as using savings, borrowing money, or selling assets to pay for health care; and
- (3) an unbalanced proportion of household health care spending on medicines.

At the health system level, there are no set benchmarks for what is an affordable medicine. Can LMIC health systems afford the medicines they put on their essential medicines list? Can they, for instance, afford a high-cost cancer treatment on their list? Health system affordability depends on medicines prices and also on the budgets health systems can command to spend on medicines. Commonly-used indicators of health system spending on medicines include the proportion of total health expenditure on medicines, total pharmaceutical expenditure as a percentage of GDP, and per capita pharmaceutical expenditures (22). Ultimately, however, we need to ensure that spending on medicines aligns with the needs of all population groups, defined by socioeconomic status (e.g., expenditure quintiles), geographic location (e.g. urban or rural), racial or ethnic category, health status, and other characteristics that allow for the identification of potentially vulnerable populations. Spending medicines budgets without strong regard for who benefits from that spending could lead to disproportionate gains for specific population groups (e.g. the urban elite, given their typical proximity and access to decision-making

processes).

1.3.3 Appropriate use

WHO defines the appropriate use of medicines as when “patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost to them and their community” (23). Historically, this concept was referred to as the “rational use” of medicines – but in this report, we prefer the term “appropriate use” as stakeholders have various reasons for using particular medicines and the “rational” use of medicines may in fact still be inappropriate (as inappropriate use includes overuse, underuse, or inefficient use of medicines, including, for example, using antibiotics for viral infections or non-adherence to chronic treatment regimens).

Several major initiatives such as the 1985 Conference of Experts on the Rational Use of Drugs in Nairobi, Kenya (24), the International Network for Rational Use of Drugs (25), and the three International Conferences for Improving Use of Medicines (26), have increased global awareness of the problem of inappropriate use of medicines, and have encouraged programmes and policies to target the appropriate use of medicines in LMICs.

1.4 Essential Medicines and Health Systems

Essential medicines and medical technologies are core elements of a health system (27, 28). Thinking of access to medicines as a foundational element for a health system allows us to integrate medicines within a holistic concept that better reflects how real-world, complex systems actually function. Figure 1.1 conveys the many interactions and connections among a health system’s building blocks, which were first described by WHO in 2007 (27).

Thinking of access to medicines as a foundational element for a health system allows us to integrate medicines within a holistic concept that better reflects how real-world, complex systems actually function.

Figure 1.1: Interconnectedness of health system components (12)



A systems approach that recognizes the interconnected nature of health system components – and the policies and interventions that play out across them – represents a true paradigm shift in access to medicines (29).

While these building blocks divide a health system into convenient, conceptual pieces that provide, above all, for analytical simplicity, the systems approach as advocated throughout this report goes much further. We argue that only through an appreciation of the dynamic interplay – often unpredictable and always changing – among health system components and actors can we arrive at a full understanding of a health system, and specifically how medicines policies and medicines interventions affect and are affected by the system's constant adaptation and complexity.

A systems approach that recognizes the interconnected nature of health system components – and the policies and interventions that play out across them – represents a true paradigm shift in access to medicines (29). According to Bigdeli and colleagues (2013), this shift reveals three key factors that characterize access to essential medicines (29):

1. As health systems – and the actors who shape them – feature many core interactions and connections, it is essential to examine the ways in which the access to, affordability, and use of medicines affect and are affected by decisions in other parts of the health system.

Essential medicines connect to the other core health system components in the following ways:

- ▶ **Service delivery** processes affect how medicines reach patients and whether they are appropriately prescribed, dispensed, and taken.
- ▶ Well-trained **health care providers** are required for appropriate prescribing and dispensing practices as well as for supporting patient adherence to prescribed use.
- ▶ **Information systems** play a critical role in supporting the appropriate use of medicines (e.g. through monitoring prescription practices and adherence), supply management (including avoidance of stock-outs), pricing, and payment.
- ▶ **Financing systems** are crucial to ensure equitable access and affordability of medicines. Without national policies stipulating access to essential medicines for vulnerable populations, many households are unlikely to access medicines when necessary – or will access them at the risk of further impoverishment.
- ▶ **Good governance and effective stewardship** are essential to all aspects of medicines in health systems, including registration, selection, quality assurance, procurement, financing, prescribing and dispensing of medicines.

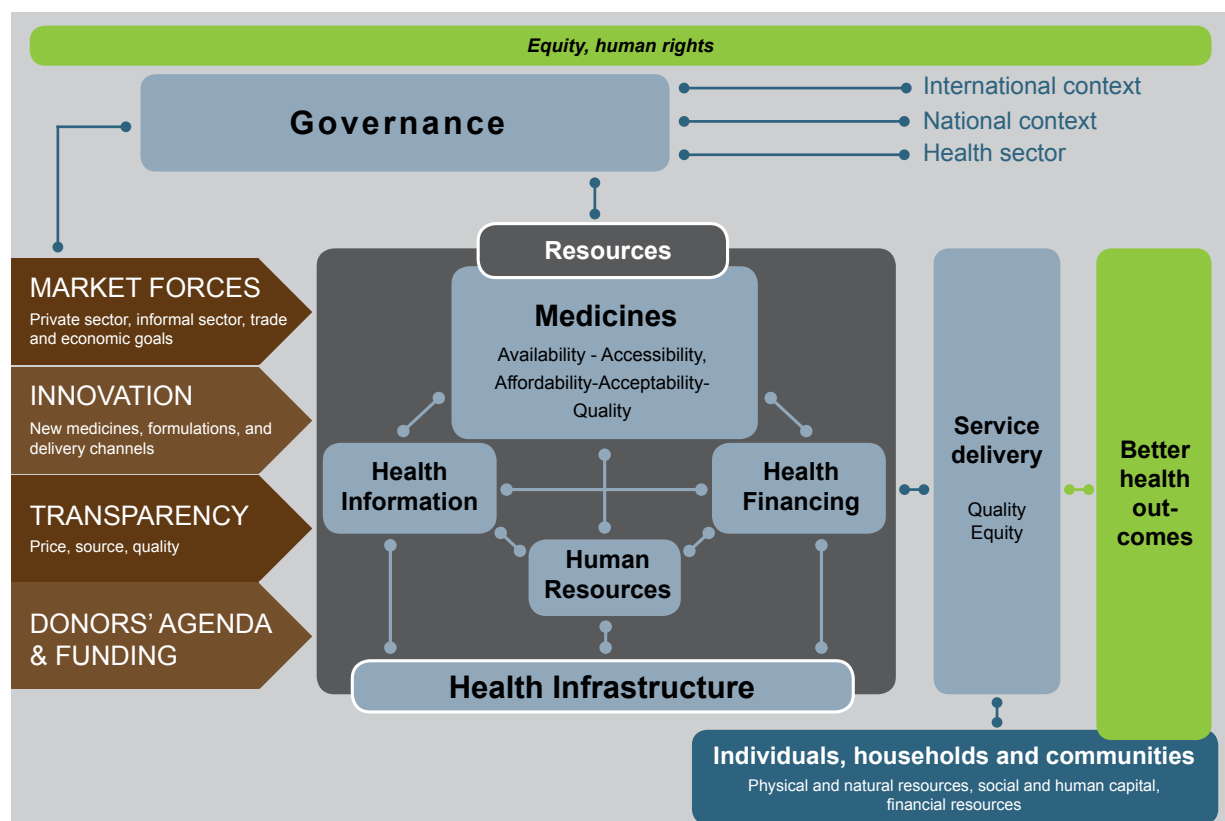
2. As demand-side barriers are of critical importance in accessing medicines, it is essential to move past the traditional conceptual confines of medicines as goods transacted in a series of interactions between patients and public health services. Access to medicines, and their affordability and use, are influenced by multiple factors at the patient, household, community and systemic levels. Understanding the cost and perceived quality of medicines and health services, patient demand and health-seeking behaviour, and sociocultural barriers (among others) are critical elements that expand our area of inquiry and generate more systems-based knowledge.

3. As multiple dynamics, factors and systems influence pharmaceutical and health sector governance, it is essential to map out, analyse and involve

these actors of influence. This would include mapping and analysing international development efforts, global and bilateral trade agreements, local politics, public and private market forces, informal and unregulated providers, research and development priorities, industry priorities, and intellectual properties rights. An analysis of these dynamics, factors and systems – focused on the converging and diverging interests that influence the health system – will greatly assist in an understanding of the forces for and against change, the perspectives any medicines policy will need to navigate or address, and ultimately move us towards a broadened vision of health system stewardship.

Figure 1.2 illustrates the conceptual framework that guides this report (reproduced from 29). It shows how the medicines sub-system is nested within the broader health system and

Figure 1.2: Access to medicines from a health system perspective adapted from Bigdeli et al. (29)



in constant interaction with other sub-systems. These dynamic relationships are characteristic of a complex system, and must be considered in order to understand how innovations and interventions in one part of the system will affect other parts of the system (30-32). As Kannampallil and colleagues rightly observe, “complex systems cannot be understood by attending to their individual components in isolation” (33).

1.5 Applying systems thinking to access to medicines

Health systems have both predictable and unpredictable behaviours and reactions to individual interventions. Research tends to assess the predictable outcomes of these interventions, ignoring the unpredictable or unintended consequences of the system’s response. This contributes to an inaccurate and incomplete picture of the full effects of an intervention.

Relationships between system components

are governed by a set of inherent rules that are highly context-specific. Sheikh et al. (34) designate values and norms, relationships and power, and ideas and interests, as the “software elements” of health systems. The system’s reaction to an intervention creates new relationships and often reconfigures these existing “software elements” (34).

Understanding access to medicines through a health systems approach must take into account several additional factors. First, studying effects over time is important since adaptation – in which the effect changes with time – is common in complex systems. For example, interventions may have a so-called “flash effect” – they seem successful immediately but less so in the medium and longer term. Another characteristic of complex systems is the inclusion of multiple actors, with their perspectives, connections and the ways in which they interact influencing each other’s behaviour, which in turn affects the system. When

Box 1.1: Systems thinking for health systems strengthening (12)

The Alliance published its 2009 Flagship Report on *Systems Thinking for Health Systems Strengthening*. This 2009 *Flagship Report* discussed the linkages between the concepts of systems thinking and health system strengthening, arguing that systems thinking provides “a way forward for operating more successfully and effectively in complex, real-world settings. It can open powerful pathways to identifying and resolving health system challenges, and as such is a crucial ingredient for any health system strengthening effort”. This current *Flagship Report* expands on the work and thinking of the previous report, applying systems thinking to the area of access to medicines.

As described in the 2009 report, systems thinking is a process that “works to reveal the underlying characteristics and relationships of systems... Health systems are constantly changing, with components that are tightly connected and highly sensitive to change elsewhere in the system. They are non-linear, unpredictable and resistant to change, with seemingly obvious solutions sometimes worsening a problem.” Anticipating how an intervention might “flow through, react with, and impinge on” sub-systems is crucial, creating “the opportunity to apply systems thinking in a constructive way...” (12).

assessing an intervention in a complex system, we must attempt to predict actors' behaviours and reactions, as these may lead to potential unintended consequences in the system. Identifying these potential unintended effects of interventions before the intervention is implemented is critical in ensuring that intended outcomes overshadow the unintended.

Systems thinking has particular relevance for medicines as their access, affordability, and use are determined by multiple processes both within and outside the health system – and at multiple political and socioeconomic levels. Predicting patterns of behaviours from various perspectives and based on different sources should help us better plan, implement, and assess interventions that improve access to medicines (and in turn, better health outcomes). While such predictions are essential, they are often challenging to make in practice.

This report responds to that challenge by offering concrete examples of specific medicines issues through a systems approach. The report uses case-studies to describe challenges and the approaches to meet those challenges in real-life contexts.

1.6 Overview of the chapters

Following this introduction, **Chapter 2** offers a historical perspective on concepts regarding medicines access, affordability, and use. It examines how these concepts have evolved over time since the 1970s and 1978's Alma Ata Declaration, and then briefly discusses issues around the quality of medicines. The chapter draws an important parallel between the evolution of the field of essential medicines with the global agenda of health systems strengthening and universal health coverage.

Chapter 3 argues for an explicit focus on medicines when moving towards universal health coverage. The chapter discusses how

two key aspects for implementing universal health coverage – information and financing – can support policies that facilitate the equitable and affordable access to, and appropriate use of, medicines. The chapter describes medicines management strategies used in financial risk protection schemes in several countries at different stages of implementation of universal health coverage. It then discusses the importance of ethical considerations in designing medicines policies for universal health coverage.

Chapter 4 discusses how innovation – broadly defined as “a process to create or improve products, processes, technologies and/or ideas to generate positive changes in efficiency, value and quality” (162) – can meet three key challenges in access to medicines. These include: the lack of optimal treatment options for some health conditions; underuse of high quality, lower cost generic medicines in most health systems; and the lack of equitable, affordable access to specialty medicines.

Chapter 5 explores health market systems, examining how medicines are delivered, and how patients and communities access medicines in markets. The chapter offers examples of alternative ways of delivering and accessing medicines in pluralistic health systems – through accreditation of drug outlets, expert patients groups, provider and regulatory networks, and social business initiatives. These new approaches are promising yet have broader system implications that require careful consideration.

Chapter 6 concludes by drawing lessons from the examples and complex situations discussed in the preceding chapters. Acknowledging the many challenges of ensuring the equitable, affordable access to and appropriate use of medicines, the chapter offers tools and recommendations for understanding

Systems thinking has particular relevance for medicines as their access, affordability, and use are determined by multiple processes both within and outside the health system – and at multiple political and socioeconomic levels.

medicines situations in complex health systems that will ultimately inform sound decision-making.

The **Web Annex** presents all of the case-studies that informed this report, along with other useful resources. It can be accessed at: www.who.int/alliance-hpsr/resources/flagshipreports/en/



2

EVOLVING CONCEPTS IN ESSENTIAL MEDICINES AND HEALTH SYSTEMS

KEY MESSAGES

- ▶ Since the 1970s, the concept of essential medicines has evolved beyond the selection of essential medicines to include product quality, sustainable supply chains, equity in access, efficiency and appropriateness of medicines use, and affordability for both households and health systems.
- ▶ In many LMICs, the availability of essential medicines remains poor, particularly in the public sector, and available medicines are often unaffordable, of questionable quality, and used inappropriately.
- ▶ In parallel, a focus on health systems has also evolved over time and now targets universal access to, and equitable financing of, health care, including essential medicines.
- ▶ It is crucial that stakeholders consider essential medicines and health systems in relation to each other, so that improving access to medicines is an explicit target for health systems strengthening and an understanding of health systems informs policies and programmes for medicines.

2.1 A historical perspective

This chapter provides a historical perspective on the development of essential medicines and health systems, describing the current environment in which each is situated, and then identifying priority issues related to the access, affordability, and use of medicines in health systems in LMICs.

To provide a sequential understanding of many of the aspects central to this chapter, an extensive table (Figure 2.1) shows some notable milestones in the evolving concepts of essential medicines, health systems, and the interplay between the two.

2.1.1 Essential medicines since the 1970's

The idea of selecting a list of essential medicines originated in military medicine, particularly during the Second World War, and was adopted in some LMICs (e.g., Bangladesh and Sri Lanka) in the 1970s (35, 36). WHO formalized the concept of medicines selection with the publication of the first essential medicines list (EML) in 1977 (37). In 1981, WHO created the *Action Programme on Essential Drugs* – now called the Department of Essential Medicines and Health Products – while Management Sciences for Health published the first edition of *Managing Drug Supply*, a leading reference on how to manage essential medicines in developing countries (38).

While this initial focus lay on creating a list of medicines, in the 1980s and 1990s multiple stakeholders, including governments, NGOs, and pharmaceutical companies, began to consider factors such as supply, appropriate use, product quality, and affordable pricing. The International Network for Rational Use of Drugs (INRUD) was established in 1981 “to design, test, and disseminate effective strategies to improve the way drugs are prescribed, dispensed, and used, with a particular emphasis

on resource-poor countries” (25). In 1985, key stakeholders, including patients and consumers, discussed the appropriate use of essential medicines at a landmark conference in Nairobi (24). This meeting resulted in the WHO Revised Drug Strategy, which put the “emphasis beyond selection [onto] procurement, distribution, rational use, and quality assurance for the public sector” (37).

The first International Conference on Improving the Use of Medicines (ICIUM) convened in 1997, followed by ICIUM conferences in 2004 and 2011, which brought together researchers, policy-makers and, most recently, industry stakeholders. Above all, these conferences sought a global consensus on interventions designed to improve the use of medicines and on a research agenda to address particular knowledge gaps (26). There was also attention paid – particularly by northern European development agencies – to support research and capacity strengthening on the use of medicines in LMICs (25, 26). With a growing focus on improving the quality of essential medicines, the WHO began a Prequalification Programme in 2001 to assess the quality, safety and efficacy of medicines for HIV/AIDS, tuberculosis and malaria (39). This service has since been expanded to cover medicines and products for other priority diseases and for reproductive health.

More recently, there has been a focus on household access and affordability with the development of measurement tools to increase transparency and the creation of evidence-informed policy. The WHO/HAI pricing survey methodology, first published in 2003, provided a new approach to measuring prices of medicines at different points in the supply chain (40). This had a particular focus on end-user prices and in promoting greater transparency of global medicines prices. Over this period, WHO led the development of a toolkit for

country assessments that includes health facility and household surveys to measure the supply of medicines, how they were prescribed, along with their price, accessibility, and use (41). Currently, as described in this report, there is a growing focus on the availability, access, affordability, and use of medicines in the context of complex, real-world health systems.

2.1.2 Health systems: from Alma Ata to UHC

Alongside this evolution of the access to medicines field were important developments in the concept and understanding of the health system. The 1978 Alma Ata Declaration was the first international commitment to primary health care and “a first attempt to unify thinking about health within a single policy framework” (27). It emphasized the importance of essential medicines in health systems when it identified the “provision of essential drugs as one of eight key components of primary health care” (37). In 1987, the Harare Declaration and Bamako Initiative spearheaded efforts to improve primary health care systems in Africa through decentralization (i.e. a district health system approach) and user fees for medicines (i.e. revolving drug funds) (42). In the 1980s and 1990s, user fees were widely promoted as a means to finance struggling health systems, though this approach would contribute to “widespread ‘financial catastrophe (for households) associated with direct payments for health services’” (43). Three decades after the widespread adoption of user fees, there is now a worldwide movement toward more equitable financing of health care and risk protection through universal health coverage.

The 2000 WHO World Health Report (44) emphasized the goals of quality and equity, particularly fairness of financial contributions, of national health systems. In 2005, WHO Member States made a commitment to work

towards universal health coverage (45). The 2010 WHO World Health Report (46) provided guidance for countries to raise sufficient resources, improve efficiency of health systems, and achieve universal health coverage.

During this time, there has also been a growing recognition, largely as a result of the World Bank’s 1993 World Development Report (47, 48) and the 2001 WHO Report of the Commission on Macroeconomics and Health (49, 50), that greater investment in health by both LMICs governments and donors will accelerate economic development in LMICs.

2.1.3 The impact of HIV/AIDS on health systems and essential medicines

The HIV/AIDS epidemic has had massive implications for both essential medicines and health systems. As the HIV epidemic spread, with more and more patients requiring antiretroviral therapy (ART), pharmaceutical companies defended their intellectual property rights, which maintained high prices for ART, putting these life-saving medications out of reach for most LMIC populations (51). South Africa in particular struggled with a devastating HIV/AIDS epidemic, with the government eventually enacting the Medicines and Related Substances Control Amendment Act in 1997, which allowed for the provision of more affordable HIV medicines through parallel imports and compulsory licensing (52).

In 1998, however, 41 companies sued the government of South Africa, claiming that the act was in violation of the Trade Related Intellectual Property Rights (TRIPS) agreement protecting drug patents (51). Following public outcry highlighting the urgent life-saving importance of these medicines, the case was dropped in 2001. However, the publicity surrounding the court case spurred global access campaigns and the creation of donor-driven access-to-medicines programmes, especially

around HIV/AIDS, TB and Malaria (e.g., Clinton Health Access Initiative, Global Fund, PEP-FAR, and UNITAID) (53-56). Ensuring access to medicines that prevent or treat these three diseases has since become the focus of major global health efforts.

While these vertical disease-focused programmes have improved access to medicines through increased donor support, novel and enhanced funding and purchasing mechanisms, and improved supply chains, they have created a raft of unintended consequences. These consequences have seen the global focus shift away from other essential medicines, and from other issues such as the appropriate use of medicines, and the role of medicines in overall health system strengthening efforts.

Recent attention to these unintended consequences has, however, helped to shift the global focus back to health system strengthening and improving access to medicines for noncommunicable diseases (57). Governments use flexibilities in the TRIPS agreement that encourage efforts to make medicines more affordable in LMICs – allowing, for instance, for the production or importation of generic products of patented medicines when there is a public health emergency (58, 59). Donors are now analysing the HIV/AIDS access campaigns for lessons on how to strengthen health systems and improve access to essential medicines for noncommunicable diseases within the context of a complex, real-world health system (60).

2.2 Current situations of medicines in LMICs

In this section, we examine some of the current key issues relating to access to medicines in LMICs. This includes sub-sections on the general LMIC situation around the availability of medicines; affordability issues for

patients and for health systems; prescribing practices, dispensing and use; health-seeking behaviour and reliance on the informal health sector; traditional medicines; quality control and regulation; and investing in research and development.

2.2.1 Availability of medicines

The availability of essential medicines, particularly in the public sector, is still poor in many LMICs. Beginning in 2003, WHO/HAI surveys have found that the availability of widely-used generic medicines was 57% in the public sector and 65% in the private sector (61). In both sectors, medicines for chronic conditions were less widely available than those for acute conditions (62).

Where people live in relation to the nearest health facility affects their geographical access to medicines. As a result, those in rural areas typically have much poorer access to medicines – a fact further compounded by lower treatment adherence in rural areas (63). Rural households are also more likely to incur catastrophic health expenditures (64). Distance and poor road conditions can also interrupt the medicines supply chain, leading to an erratic supply of medicines, including stock-outs (65).

2.2.2 Affordability for patients

The price of medicines varies widely across countries, as well as by region and between the public and private sector (18). Medicines are often wholly unaffordable for poorer patients (18). Without a financial risk protection scheme (e.g. health insurance with a comprehensive medicines benefit) and a functioning public health care delivery system in most LMICs, patients pay high out-of-pocket costs for medicines. Out-of-pocket spending can be financially devastating as medicines account for the largest category of out-of-pocket

Three of the top ten sources of health care inefficiency involved medicines.

health expenses in LMICs – in 2002-03, approximately half (41%-56%) of households spent 100% of their health care expenses on medicines (20).

Medicine expenditures often lead to catastrophic levels of household spending and impoverishment, with the poor being particularly vulnerable (66). Health insurance, which can reduce or eliminate out-of-pocket spending on medicines, provides a form of financial risk protection and has been shown to improve access to medicines in LMICs (67). However, many insurance programmes do not provide a comprehensive essential medicines benefit.

2.2.3 Affordability for health systems

On average, total pharmaceutical expenditures in both public and private sectors account for over a quarter of total health expenditure in LMICs (30% in low-income countries and 28% in lower-middle income countries), with some LMICs spending up to two-thirds (67%) of their total health expenditure on pharmaceuticals (22). A high proportion of health spending on medicines may constitute good value for money. However, high expenditures on medicines may in fact threaten the sustainability of a health system, as in Ghana where, in 2008 – three years following the implementation of the National Health Insurance Scheme – spending on medicines consumed nearly half of the scheme's expenditures (see Chapter 3).

Given resource constraints, LMIC health systems cannot afford to spend money inefficiently. In 2010, WHO determined that three of the top ten sources of health care inefficiency involved medicines – specifically the high prices of medicines; the use of substandard and counterfeit medicines; and the inappropriate and ineffective use of medicines (46). Health system reforms aimed at increasing access to medicines may also serve to increase

expenditures, a dynamic that requires more emphasis on the appropriate and efficient use of medicines (68). Risk protection schemes and health care delivery systems in LMICs can use purchasing, selection, utilization management, and contracting strategies to provide incentives for health system stakeholders (e.g. pharmaceutical industry, providers, and patients) to sell, dispense and use medicines more appropriately and more efficiently (see Chapter 3).

2.2.4 Prescribing practices, dispensing and use

Over half of the medicines used in LMICs are used inappropriately; according to the World Medicines Situation 2011, only 30-40% of LMIC patients are treated according to clinical guidelines and only about 50% of patients anywhere adhere to treatment regimens (69). Recent studies have identified health system shortcomings – including unreliable medicines procurement and supply systems; insufficient numbers of adequately trained prescribers and dispensers; inadequate knowledge of prescribers, dispensers and patients about medicines; and perverse incentives for prescribers and dispensers – as the major causes of suboptimal use of medicines (70, 71). These shortcomings require targeted system strengthening policies to improve the use of medicines (69).

In a 2012 report (70), WHO promoted various actions for improving medicines situations at the national level. These included the development and mandated use of a national essential medicines list; investments in improving national medicines procurement and supply systems; promoting early screening and accurate diagnoses; facilitating the implementation of evidence-based treatment guidelines; promoting patient-centred treatment initiatives; monitoring medicines use to guide evidence-informed policy-making; and ensuring

Over half of the medicines used in LMICs are used inappropriately

government commitment to and stakeholder engagement in the appropriate use of medicines (70).

2.2.5 Health-seeking behaviour and reliance on the informal health sector

Over-the-counter treatments, when used properly, can reduce pressure on the health system and give patients – especially those with poor access to formal health care providers – greater control over their medical conditions (72). However, in many countries, prescription-only medicines are widely sold without a prescription, resulting in patients self-medicating without proper instruction (72). This type of self-medication may not be effective and potentially compromises patients' safety when treatments require diagnosis by trained practitioners, proper instructions on drug regimens, or follow-up with a provider (83). People may also self-medicate when they have poor access to health care providers or perceive public health facilities to be inefficient or of low quality. Health insurance coverage for medicines can potentially reduce reliance on self-medication and thereby improve the appropriate use of medicines.

There are a host of social factors that influence health-seeking behaviour specific to medicines. Medicines are sometimes not acceptable due to cultural reasons, stigma (e.g. enrolment in an HIV medicines programme signals HIV/AIDS status (73)), or perceptions about low product quality (e.g. belief that generic medicines from local manufacturers are inferior (74)). Evidence of gender inequities in access is thus far not conclusive (75,76) – the issue remains to be investigated further.

2.2.6 Traditional medicines

Patients in many LMICs rely on traditional medicines or complementary and alternative medicines (77), either because of cultural

beliefs or because of poor access to the formal health system. While these traditional medicines or complementary and alternative medicines may have clinical benefit, there is concern regarding their lack of regulation and insufficient data on safety, efficacy and quality (77). WHO encourages countries to develop a national policy on these medicines and when safety, efficacy and quality can be established, these medicines may be eligible for inclusion in a national essential medicines list and a health insurance system's medicines reimbursement list.

2.2.7 Quality control and regulation

Challenges in ensuring the quality of medicines in LMICs include a lack of reliable data on the extent of the problem, and a lack of agreement between stakeholders about how to deal with those quality issues (78). These challenges have to be addressed within wider system constraints that include a lack of regulatory capacity, a general inability to test and monitor data, and a substantial market for counterfeit medicines in LMICs (79, 80). WHO has defined standards of acceptable product quality, safety and efficacy, and it uses these criteria to evaluate medicines for priority diseases and to "prequalify" medicines for UN agency and other LMIC purchasers (39). Cost-effective, rapid technologies are needed to monitor the quality of medicines in supply systems, and improved information exchange about quality between key stakeholders (81).

An example of an initiative for supporting the exchange of information on medicines quality is QUAMED (Quality Medicines for All), an alliance of non-profit organisations (82). QUAMED was launched in 2011 by the Institute of Tropical Medicine (Antwerp, Belgium) with a mission to improve the quality of the medicines available in LMICs. The organization collects independent information on quality of

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In many countries, pre-prescription-only medicines are widely sold without a prescription, resulting in patients self-medicating without proper instruction.

Challenges in ensuring the quality of medicines in LMICs include a lack of reliable data on the extent of the problem, and a lack of agreement between stakeholders about how to deal with those quality issues.

Research and development (R&D) on innovative products, formulations, and drug delivery technologies are important components of improving access to essential medicines in LMICs, especially for HIV/AIDS, tuberculosis, malaria and neglected tropical diseases.

medicines from multiple sources (e.g. public sources such as WHO, audits of international wholesalers and local distributors and manufacturers, and registration files submitted to regulatory authorities) and partners with NGOs and non-profit procurement centres to share information on the quality of medicines and to build the capacity of LMIC partners to procure quality medicines.

2.2.8 Investing in research and development

Research and development (R&D) on innovative products, formulations, and drug delivery technologies are important components of improving access to essential medicines in LMICs, especially for HIV/AIDS, tuberculosis, malaria, neglected tropical diseases (83) – and also for the medicines children require (84). Driven by strong advocacy, global access campaigns for HIV/AIDS have resulted in patent flexibilities for public health emergencies and national disease priorities (51, 85); enshrined the right to health and medicines in many LMIC constitutions (2); and led to the creation of organizations dedicated to expanding access to medicines for HIV/AIDS, tuberculosis and malaria, such as the Global Fund, PEPFAR, Clinton Health Access Initiative, and the Global Drug Facility (53-56, 86). Similar campaigns are needed for neglected tropical diseases, since many of these can be prevented or treated with available medicines, and more research is needed to develop strategies to make these medicines accessible, particularly for remote populations (87).

The problem of low investment in R&D for medicines for neglected diseases due to low market demand in poor countries is now well recognized. Of the 850 new therapeutic products registered in 2000–11, only 37 (4%) were for neglected diseases (88). WHO has tried to address this problem by establishing

a Consultative Expert Working Group on Research and Development: Financing and Coordination, which has made far-reaching recommendations to change incentives for R&D (see Chapter 4).

The pharmaceutical industry, from small local manufacturers to large multinational R&D firms, has an important role to play in improving access to medicines in LMICs. Increasingly, companies recognize that improving access to medicines in LMICs is a corporate social responsibility goal – and a viable business strategy (89). There are numerous tools that industry can use to expand access to innovative products, such as: differential or tiered-pricing according to the economic capacity of the buying country or population group; voluntary licensing to generic manufacturers for production of generic versions of patented medicines; investing in R&D for neglected diseases; *pro bono* research; creating wholly-owned local subsidiaries in LMICs; public-private partnerships for R&D; and participating in patent pools, in which several patents are donated by medicine producers to drive R&D in a particular area (89, 90).

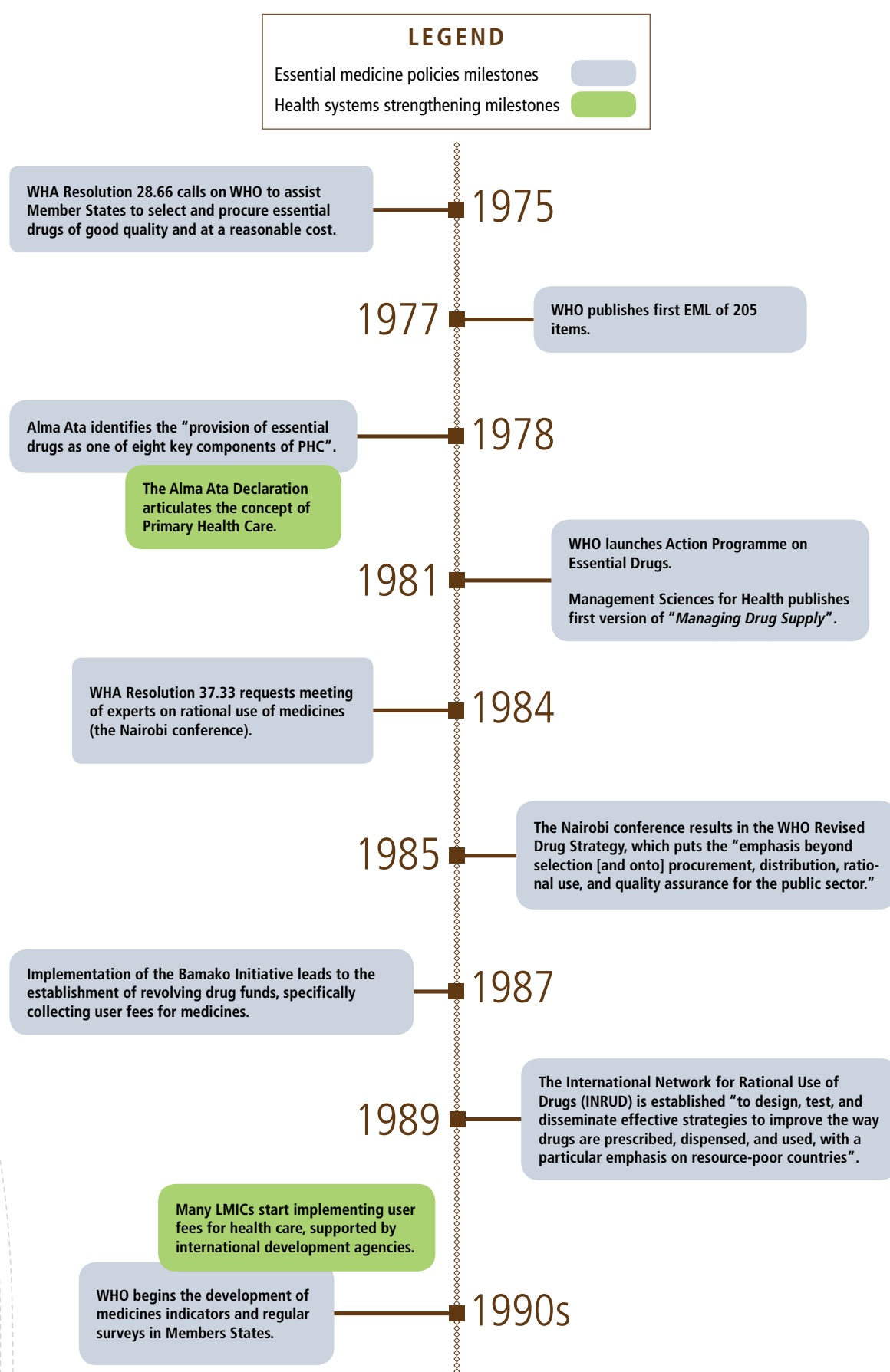
More recently, some pharmaceutical companies have started so-called social business or shared-value initiatives that target both the generation of social value for populations in LMICs, and profit (91, see Chapter 5). The Access to Medicines Index collects data on industry efforts to improve access to medicine in LMICs and publically recognizes companies for their investments and initiatives (92, 93). The Index's objective is to create another form of competition between companies, based on recognition of their investments in access to medicines rather than on market share or sales volumes.

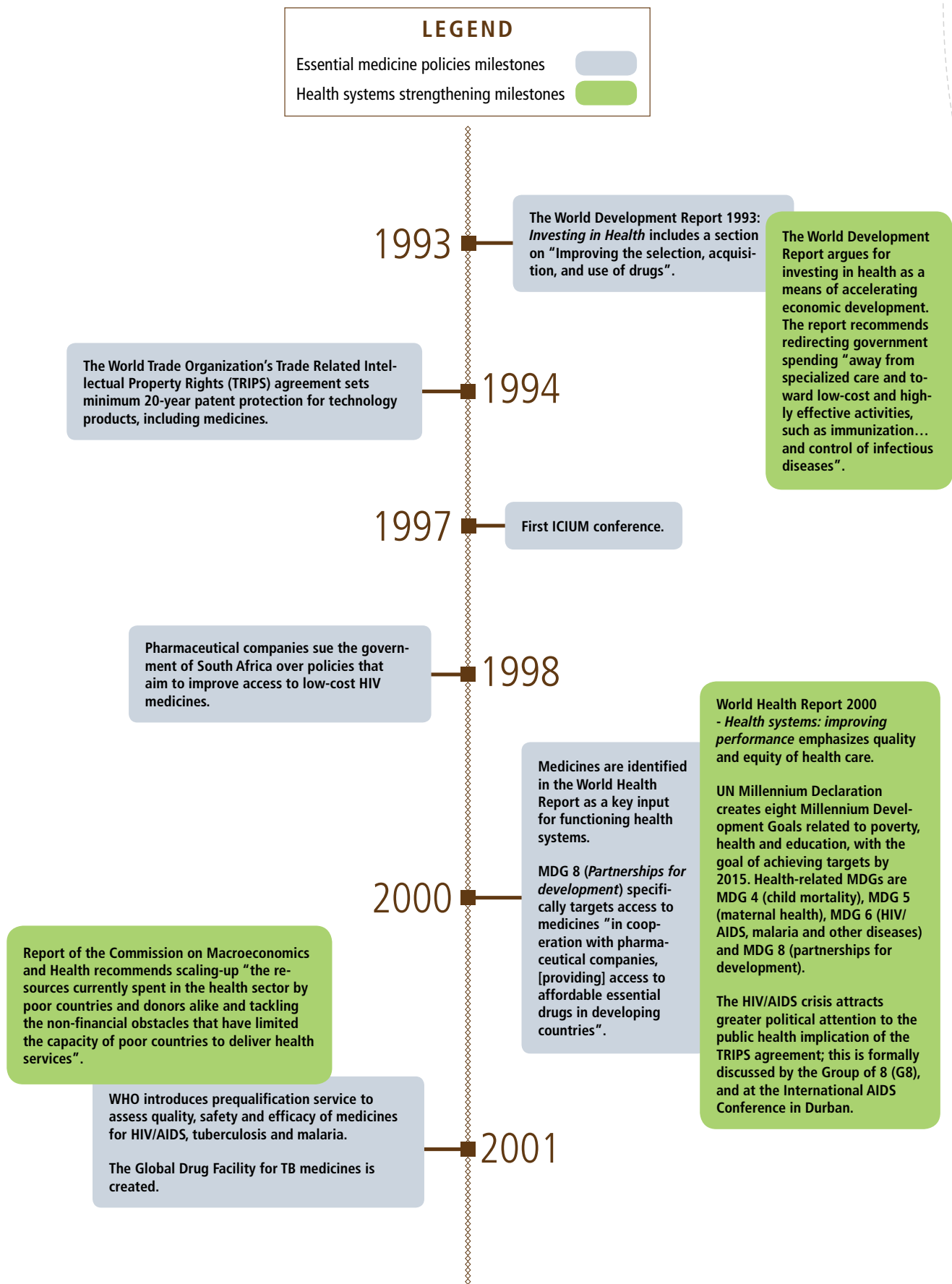
2.3 The future of medicines in LMIC health systems

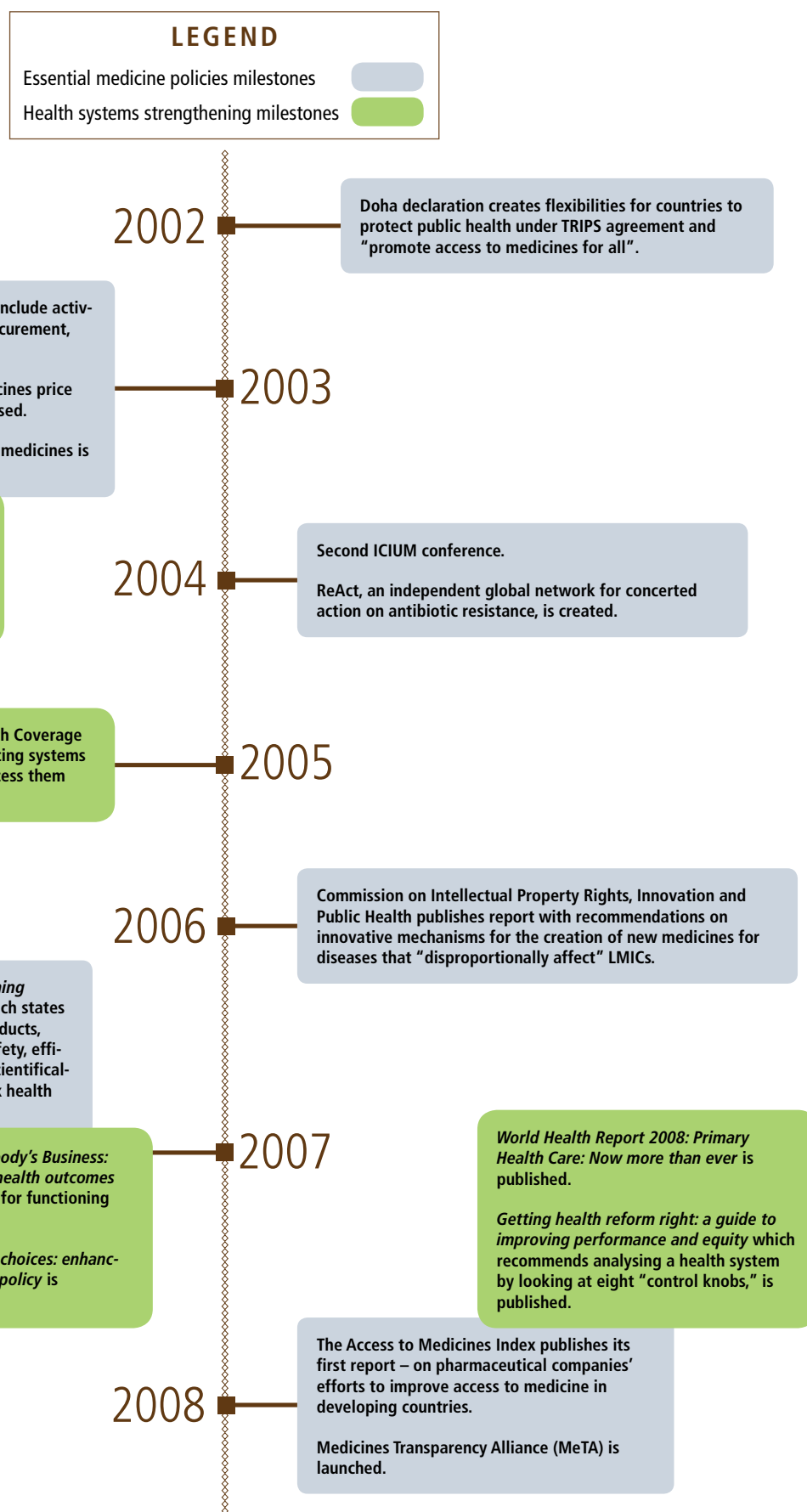
Recent decades have seen great progress in improving the access, affordability, and appropriate use of essential medicines. During this time, understanding has grown about how to create sustainable and equitable health systems in LMICs. From a health systems perspective, many countries have now identified achieving universal health coverage as their top health system priority (10). At this junction, it is essential to bridge the considerable work done towards improving access to medicines, and their affordability and appropriate use in LMICs with the promising agenda of health systems strengthening and universal health coverage.

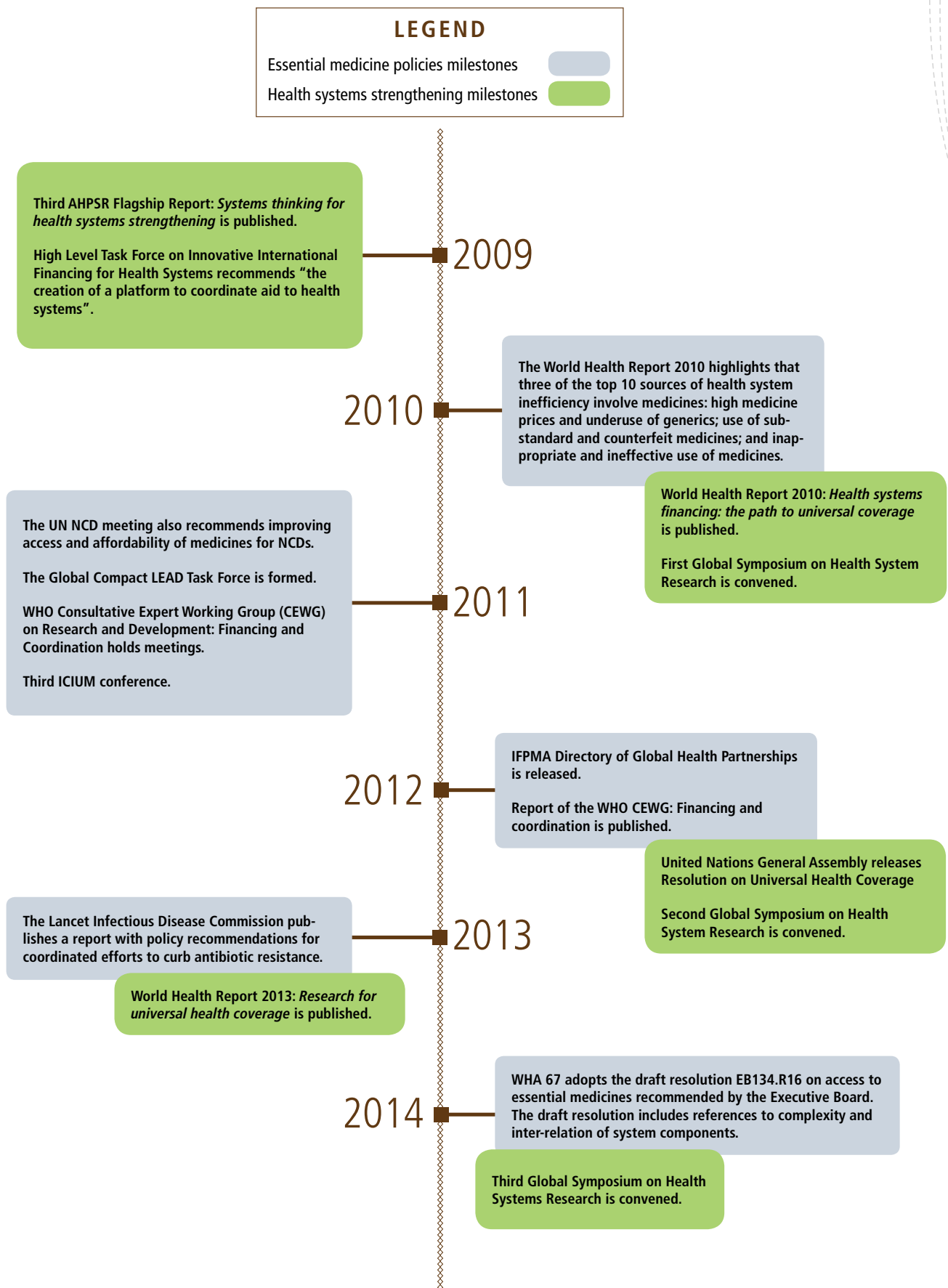
Figure 2.1: Timeline of milestones in development of essential medicines and health systems concepts

A more comprehensive timeline with full references is available in the Web Annex: www.who.int/alliance-hpsr/resources/flagshipreports/en/









3

THE ROLE OF
MEDICINES IN
ACHIEVING UNIVERSAL
HEALTH COVERAGE

KEY MESSAGES

- ▶ An explicit focus on medicines is necessary for health systems to achieve the goals of universal health coverage.
- ▶ Using a system approach to medicines, combined with information and financing levers, can contribute to achieving UHC goals and to supporting strategies to maximize equitable access, appropriate use, and efficiency, and to ensure household and system affordability.
- ▶ Competing objectives of medicines policies create ethical challenges that require informed, inclusive, and fair decision-making processes.
- ▶ Health systems working towards UHC must routinely monitor the impacts of medicines policies and adapt strategies accordingly.

3.1 Introduction

While defined in different ways (94), universal health coverage (UHC) is the focus of high-level global health discussions (95-99) and a declared goal of governments in more than 50 countries (95). WHO's approach to UHC is in Box 3.1 below.

In this chapter, we describe how a systems approach to medicines, combined with using information and financing levers, can contribute to achieving UHC goals. We summarize medicines policies and management strategies in four countries working towards UHC, and discuss the importance of a systems approach. We go on to emphasize the need for policies to engender equity in health care, and suggest that equity could be advanced through fair decision-making processes. Finally, we outline categories of the information necessary to

effectively monitor and adapt policies that address the equitable access to medicines, their appropriate use, and their affordability for households and systems.

3.2 Why is an explicit focus on medicines needed to achieve UHC?

The key facets of UHC are the "provision of, and access to, high-quality health services" for all people and "financial protection for people who need to use these services" (46). Achieving these goals sustainably requires "constant attention to waste and inefficiency" in health systems (99).

Medicines are indispensable for delivering key aspects of UHC – including coverage, service provision, and risk protection (46) – because they are a requirement for high-quality care, contribute significantly to household health expenditures, and are one of the major causes

Medicines are indispensable for delivering key aspects of UHC – including coverage, service provision, and risk protection (46)

Box 3.1: Universal Health Coverage (3)

The goal of UHC is to ensure that all people obtain the health services they need without suffering financial hardship when paying for them. For a community or country to achieve UHC, several factors must be in place, including:

1. A strong, efficient, well-run health system that meets priority health needs through people-centred integrated care (including services for HIV, tuberculosis, malaria, noncommunicable diseases, maternal and child health) that:
 - ▶ informs and encourages people to stay healthy and prevent illness;
 - ▶ detects health conditions early;
 - ▶ has the capacity to treat disease; and
 - ▶ helps patients with rehabilitation.
2. Affordability – a system for financing health services so people do not suffer financial hardship when using them.
3. Access to essential medicines and technologies to diagnose and treat medical problems.
4. A sufficient capacity of well-trained, motivated health workers to provide the services to meet patients' needs based on the best available evidence.

of health system inefficiency. Moreover, the policy mechanisms to manage, pay for, and facilitate the appropriate use of medicines are interwound with those guiding the improvement of health systems as a whole. Hence, policy-makers committed to achieving UHC must explicitly focus on medicines through targeted, well-implemented, and continuously adapted policies. Even systems with a long history of working towards UHC must develop new mechanisms for managing the financing of medicines (see Thailand's policy for coverage of high cost medicines in Chapter 4) and incentivizing their appropriate use in changing environments.

3.2.1 The inappropriate use of medicines can threaten equity, quality, affordability, and efficiency

When used appropriately, medicines contribute to the health and well-being of individuals and populations. When used inappropriately, medicines can exacerbate health system inequities, endanger health, waste resources, and threaten the sustainability of health systems. Given that about half of the medicines in primary care settings are inappropriately prescribed and dispensed (100, 101), ensuring quality and appropriate use is of primary concern for health systems and financing schemes.

More than US\$1,000 billion is spent globally on medicines every year (102), accounting for up to 67% of total health expenditures in LMICs (22) – mostly paid out-of-pocket by consumers. Spending on medicines in LMICs will need to increase even further as donors decrease their financial support for expanded access programmes for HIV/AIDS, malaria, and tuberculosis treatment.

As discussed in Chapter 2, medicines account for three of the top 10 sources wasting scarce

health system resources. These include higher than necessary medicines prices, substandard and counterfeit medicines and the inappropriate use of medicines (46). Medicines-related waste occurs through cost-inflating taxes and tariffs (101); the underuse of generic products (46); the unreliable availability of medicines in public sector facilities (62, 103); the overuse of antibiotics (often for children with respiratory infection or diarrhoea) (104), resulting in drug resistance (105); and the underuse of proven therapies, particularly among the poor and for chronic conditions (e.g., hypertension, diabetes) (106, 107). Meanwhile, many households face poverty from having to pay for medicines (108, 109) and many patients die prematurely because they lack access to life-saving medicines (110).

3.2.2 Decision-makers must balance competing policy objectives

Governments and other stakeholders in health systems must balance the competing objectives of policy decisions relating to medicines, all of which are closely connected to the goals of achieving UHC. In an ideal world:

- ▶ all patients – particularly those in vulnerable populations – would be able to access the medicines they need, according to evidence-based treatment guidelines;
- ▶ products would be of proven quality;
- ▶ appropriately prescribed and dispensed medicines would be available where and when patients need them;
- ▶ patients would take these medicines as necessary to achieve their clinical effects;
- ▶ households and health systems would have the resources to pay for medicines;
- ▶ patients and providers would be satisfied with the way the health system functions;

- ▶ local manufacturers would be profitable while providing high-quality priority products at affordable prices;
- ▶ research companies would develop innovative products for unmet health needs; and
- ▶ all stakeholders would adhere to good governance and ethical business practices and actively contribute to equitable systems.

The four main policy objectives with respect to medicines in health systems – widely available high-quality generic and innovative products; equitable access; appropriate and safe use; and affordability for households and systems – inevitably compete in many ways (Figure 3.1). For example, price pressures to contain costs may contribute to low quality – or the outright lack – of products in the market, and providing subsidized medicines may strain a system’s resources. Limiting the coverage of

medicines to preserve financial sustainability – for example, by only subsidizing medicines used in inpatient settings – may increase out-of-pocket household spending on medicines in ambulatory care, impoverish households, decrease access, impede appropriate use, and negatively impact health (111). In addition to competing objectives, other system characteristics add further complexity. Weak regulatory capacity, information imbalance, lack of coordination among – and opportunities for economic gain by – different stakeholders provide perverse incentives for suppliers, distributors, prescribers, dispensers and patients to increase the consumption, cost, and inefficiencies of medicines in systems.

3.2.3 Decision-makers can use information and financial levers to balance competing objectives

Although the various objectives of medicines policy may compete with each other, a systems

The four main policy objectives with respect to medicines in health systems – widely available high-quality generic and innovative products; equitable access; appropriate and safe use; and affordability for households and systems – inevitably compete in many ways.

Figure 3.1: Approaches to balance competing medicines policy objectives



approach offers opportunities for innovative solutions. Countries implementing and expanding financing schemes to meet UHC goals will also have levers – information and financial incentives – to help balance competing medicines policy objectives (Figure 3.1 lists some approaches that rely on these levers).

For instance, financing schemes can access information on the demographic characteristics, health care needs, and utilization patterns of members because they enrol members and pay for their care. Financing schemes can also access information about the demographics and behaviour of health care providers, including their prescribing patterns and associated costs, because they employ or contract with them.

As financial intermediaries, financing schemes have leverage to determine what types of care, and medicines, they pay for; they can also provide incentives to health care providers for purchasing, prescribing, and dispensing, and to patients for using the most clinically appropriate, safe, and cost-effective medicines. Since they pay for large quantities of medicines, financing schemes can also be in a position to negotiate product prices with suppliers (See Chapter 4), dictate standards of product quality, react to unethical promotion practices, and demand supply chain efficiency. By virtue of their access to information, schemes can help to shape patient demand for care, through educational outreach and provider and patient targeted incentives to encourage screening, prevention, and cost-effective care.

Information and financing levers may help policy-makers balance the competing aims of equitable and affordable access, availability of high-quality, needed medicines, and appropriate use. International (111, 112) and local data on burden of disease, combined with information on patterns of utilization within schemes,

are needed to prioritize health conditions in a population, and to signal potential inappropriate medicines use patterns. Evidence-based clinical guidelines (113) can inform medicines reimbursement lists. Economic assessments (including health technology assessments and budget impact analysis) (114), can inform decisions about the coverage of treatments, and frameworks for transparency (115) can guide decision-making processes (116). Participation in international collaborations on product quality assurance (117) can strengthen capacity for the efficient and reliable supply of medicines (118).

Several medicines management approaches, such as implementing standard treatment guidelines and selecting medicines for essential medicines lists, have been used for many years in LMICs (120). In section 3.2, we describe examples of approaches used in selected countries.

Policies and programmes that target costs of care (e.g. reference pricing or generic substitution) or quality of care (e.g. disease management programmes) have been used extensively in high-income countries. More recently, countries and systems have implemented policies that seek to incentivize use of high-value care through pay-for-performance programmes. These financially reward prescribers for achieving quality, efficiency and “value” by reducing out-of-pocket expenses for medicines known to improve health outcomes. However, evidence on the effects of value-focused policies is mixed in high-income countries (121-124) and virtually non-existent in LMICs (125).

3.3 Medicines management in China, Ghana, Indonesia and Mexico

To illustrate how health care financing schemes have balanced competing objectives with respect to medicines, we conducted case-studies in four countries striving towards UHC:

Table 3.1: Overview of health care financing schemes in China, Ghana, Indonesia and Mexico

Country	Reported % population enrolled in any scheme in the country	Scheme covering the poor	
		Year of inception: funding arrangement	Provider mix
China	94%-99% (126)	NCMS (2003): Premiums and federal and local government subsidies	Largely private contractors
Indonesia	40%-63% (127, 128)	JK (2005) ¹ : General tax revenue	Largely public sector providers
Ghana	33% (129)	NHIS (2004): Value added tax and mandatory social security contributions by formal employees	Mixed public/private providers
Mexico	75-100% (130, 131)	SP (2003): Premiums and general tax revenue	Nearly exclusively public providers

Legend: NCMS: New Rural Cooperative Scheme, JK: Jamkesmas, NHIS: National Health Insurance Scheme, SP: Seguro Popular: ¹Since 2014 Jamkesmas has become the National Social Security Body (*Badan Penyelenggara Jaminan Sosial* or BPJS) Detailed information about the case-studies is in the web annex.

The case-study investigations uncovered a wealth of information on health system structures within which the schemes operated, on the populations, sources of overall scheme financing, and on the medicines that were selected for service provision and paid for by the scheme.

the New Rural Cooperative Medical Scheme (NCMS) in China; the National Health Insurance Scheme (NHIS) in Ghana; Jamkesmas (JK) in Indonesia; and Seguro Popular (SP) in Mexico (Table 3.1). The countries were selected to balance a mix of population coverage (showing different stages of moving towards UHC), funding arrangements (tax-based vs. premium-based), geographical differences, and provider networks (public vs. private).

In performing these case-studies, we explored five crucial policy and management areas (67):

- ▶ the selection of medicines that schemes provide or subsidize;
- ▶ strategies for procurement and reimbursement;

- ▶ contracting with or paying providers who prescribe and dispense medicines;
- ▶ medicines utilization management tools; and
- ▶ systems for monitoring prices, prescribing behaviour, and user satisfaction.

We reviewed documents and interviewed key informants to understand whether the schemes used specific strategies for selecting medicines (lists of covered medicines [formularies]; patient cost sharing; and regulations for dispensing a generic for a prescribed brand-name product). We also investigated what policies were in place for purchasing (price negotiations, bulk purchasing, and reference pricing); contracting (fee-for-service, capitation, or case-based provider payments,

reimbursement rates, and preferred provider networks); and management of utilization (pay-for-performance, separation of prescribing and dispensing, disease management programmes). We also asked schemes whether they monitored member satisfaction, and purchasing and prescribing patterns.

The case-study investigations uncovered a wealth of information on health system structures within which the schemes operated, on the populations, sources of overall scheme financing, and on the medicines that were selected for service provision and paid for by the scheme. Much less information was available on medicines procurement, and even less on how schemes contract suppliers, manage the use of medicines, and monitor prescribing or member satisfaction. Some evidence on the impact of medicines financing on medicines access was found in China, Ghana and Mexico, but not in Indonesia.

Table 3.2 summarizes the management and policy approaches of the four schemes in 2013 (further details are in the web annex). All schemes had formularies that defined the medicines they covered, and these were based on national essential medicines lists, although selection criteria may not always have been based on evidence of clinical effectiveness. Some schemes (Indonesia and Mexico) required the use of generics when available. All schemes paid 100% of the costs of covered medicines without patient co-payments. However, in China, schemes only start covering medicines after patients have paid a deductible, and they discontinue coverage after a maximum insurance payment has been reached (coverage cap) in a given time frame. Informants did not mention restrictions on coverage for specific medicines or populations, such as requirements of documenting failed treatment with a first-line therapy before a second-line therapy would be covered (prior

authorization).

The four schemes used pooled procurement to lower medicines procurement prices. In addition, three schemes (China, Indonesia, Mexico) engaged in direct price negotiations either for all medicines procured by the scheme or only for single source products, and they have introduced electronic procurement systems to enhance transparency in the process. Ghana and Mexico set maximum prices at which suppliers are reimbursed by the scheme. Indonesia set maximum retail prices for all retailers, not only those affiliated with the scheme.

Most schemes limited coverage to accredited health care service providers. Prescriber and dispenser payment strategies varied: Ghana, Indonesia and Mexico used fixed prescriber payments whereas in China, payment was linked to service volume and type. Whereas Indonesia and Mexico had fixed dispenser payments in the public sector, dispensing charges in China and Ghana were included in the product reimbursements.

All schemes implemented a variety of strategies to manage utilization, including separating the incomes of public prescribers from medicines sales. Most reported well-established programmes for developing and implementing standard treatment guidelines and for disease management. However, payment for performance in relation to standard treatment guidelines had not been used to incentivize individual prescribers or dispensers.

In general, publicly-available documentation in these four countries provided little information on monitoring and evaluation activities of the schemes. No scheme reported mechanisms to routinely monitor utilization. All schemes had introduced the monitoring of procurement processes. Only Mexico routinely monitored and published information on patient satisfaction with the dispensing of medicines

at the country level.

The case-studies found some information on how financing medicines affects the availability, access, and use of medicines, and household and system affordability in China, Ghana and Mexico. Early cross-sectional appraisals of China's health system reforms found lower medicines prices in primary care facilities, but no clear positive impacts on generally low availability (132), cost per prescription (133) or less-than-appropriate use. In Ghana, medicines expenditures had drastically increased (134), although for some, access to medicines seems to have improved (135). However, whether increased spending has improved equity in access and appropriate use is questionable, given evidence of supplier-induced demand (136) and medicines utilization changes that did not match enrolment patterns (137). In Mexico, there was no drop in household medicines spending after 10 months (138) or in comparison to households not insured by Seguro Popular (139).

3.3.1 Systems striving towards UHC face common policy implementation challenges

These case-studies highlight common challenges faced by different health systems. For instance, decentralization in China, Indonesia, and Mexico has led to differences in the implementation of medicines policy across provinces, and may contribute to geographic and socioeconomic inequities in access and use. For numerous reasons, including increasing numbers of individuals enrolled, a rise in prevalence of chronic conditions requiring long-term therapy, greater availability of new, higher cost medicines, and higher demand for these medicines, the use of medicines and their expenditures increase over time in any system. If rising costs are not managed effectively, they may threaten the long-term sustainability of schemes (140).

Evidence from Thailand shows that financing schemes tend to address medicines in an explicit way only when spending on medicines threatens the viability of the scheme (141), and that they then focus primarily on prices rather than on appropriate use of medicines and the mechanisms that influence use. This approach is reflected in the four schemes studied, where responses to containing expenditure growth have included budget caps on pharmaceutical expenditures (Mexico) and medicines price limits (all four countries). Providers are mostly paid through fixed salaries, irrespective of the quality of their prescribing efficiency or the health outcomes actually achieved.

3.3.2 Using financial and information levers to increase quality and efficiency

Given that about half of the medicines in primary care settings are inappropriately prescribed and dispensed (100, 101), ensuring quality and appropriate use must be of primary concern for health systems and financing schemes.

Expenditure-focused policy instruments can be blunt and have unintended effects: while policies such as state-level caps in the China and Mexico case-studies could contain spending on pharmaceuticals, they do not necessarily direct spending to more clinically appropriate medicines or eliminate wasteful spending on clinically unnecessary or substandard products. Medicine sales are difficult to regulate in the private sector, even when, as in Ghana, private sector providers are part of the NHIS network. Incentives to sell higher-priced products may drive higher medicines expenditures in such systems. Different mechanisms of provider payment may incentivize more cost-effective use of medicines. So far, performance-based payment strategies have been underused in the schemes studied.

Given that about half of the medicines in primary care settings are inappropriately prescribed and dispensed (100, 101), ensuring quality and appropriate use must be of primary concern for health systems and financing schemes.

For numerous reasons, including increasing numbers of individuals enrolled, a rise in prevalence of chronic conditions requiring long-term therapy, greater availability of new, higher cost medicines, and higher demand for these medicines, the use of medicines and their expenditures increase over time

Table 3.2: Policy and management approaches in country case-studies

Medicines Management Strategies	New Cooperative Medical Scheme (China)	National Health Insurance Scheme (Ghana)	Jamkesmas (Indonesia)	Seguro Popular (Mexico)
SELECTION				
Formulary	✓	✓	✓	✓
Cost sharing for medicines included in the formulary	✓	✗	✗	✗
Generic substitution	✗	✓	✗ ¹	✗ ¹
PROCUREMENT				
Medicines prices negotiation or rebates	✓	✗	✓	(✓)
Bulk procurement	✓	✓ ¹	✓	✓
Generic reference pricing	✗	✓	✗ ¹	✓
CONTRACTING				
Fixed salary for prescribers	✗	✓	✓ ¹	✓
Fixed reimbursement rates for medicines	✓	✓	✗ ¹	✗ ¹
Preferred provider network (accreditation)	✗	✓	✓	✓
UTILIZATION				
Standard treatment guidelines	(✓)	✓	✓	✓
Payment for performance	(✓)	✗	✗	✗
Separation of prescribing and dispensing	✓	✓	✓	✓
Disease management programmes	✓	✗ ⁴	✓	✓
MONITORING AND EVALUATION				
Routine patient consumer satisfaction monitoring	(✓)	✗	✗ ⁴	✓
Medicines purchasing monitoring	✓ ⁴	✗	✗ ⁴	✓
Prescription monitoring	✗	✗	✗ ⁴	✗

Legend: 1=public sector; 2= mix of capitation and salary; 3= confidential agreements between insurance companies and pharmaceutical manufacturers or wholesalers; 4=information not publically available; ()= Limited use.

The four case-studies highlight the fact that schemes may not have sufficient information about which medicines they pay for. As observed in Ghana and Indonesia, schemes often have inefficient claims-processing systems, which may be paper-based rather than electronic, and often require resource-consuming reviews. Inefficient claims-review systems can lead to delays in payments to facilities, shortages of facility funds to purchase medicines, and medicines stock-outs. Inefficient data processing systems also make it difficult to access timely information about medicine utilization, which is crucial for both routine expenditure monitoring and for designing strategies to encourage more cost-effective use. Access to patient-level clinical and demographic data will be increasingly important in systems covering

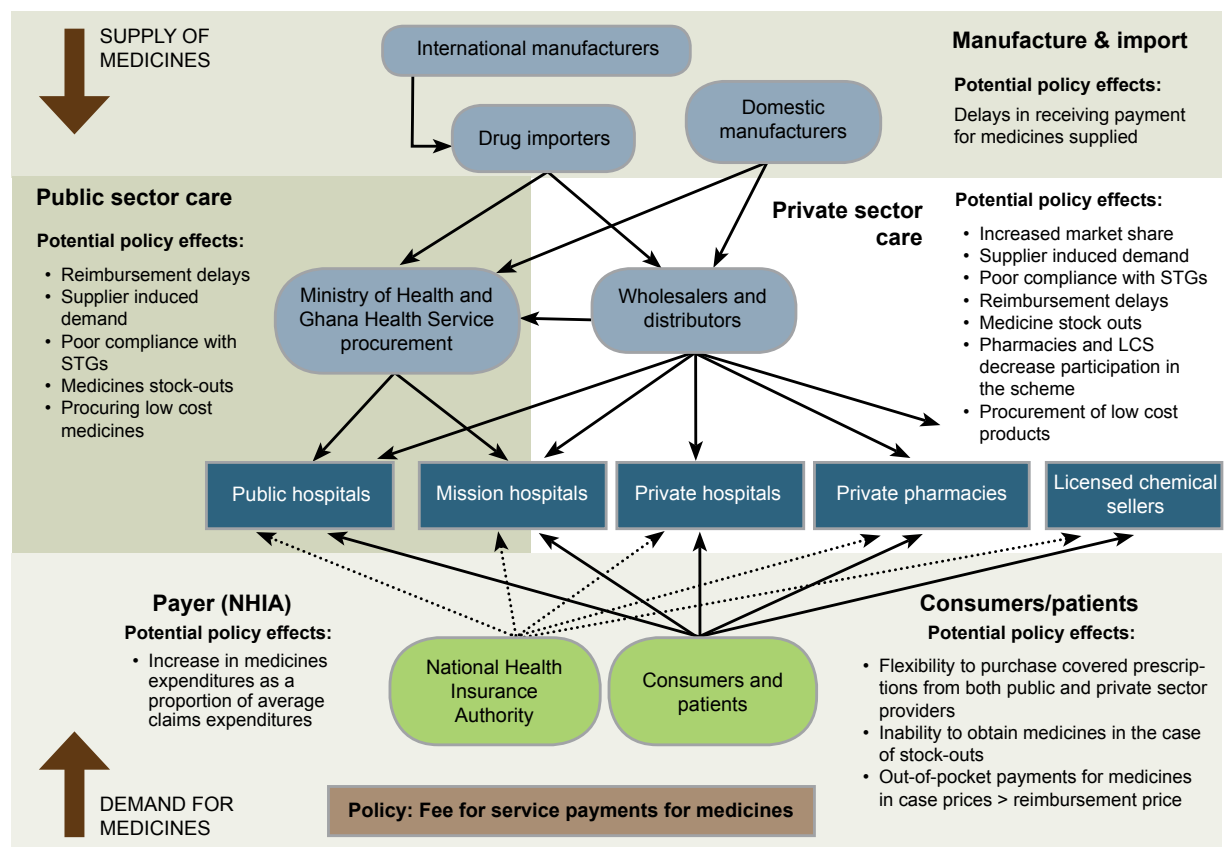
innovative, high-cost biological medicines such as novel cancer treatments that may benefit only a few carefully selected patients. Different tools and approaches than those designed to provide a minimum benefit from medicines are needed to help make decisions about the coverage of specialized high-cost medicines (142). (See Chapter 4).

3.3.3 A systems approach is important when implementing medicines policies

The case-studies highlight how one policy in a complex system can impact the behaviours of multiple actors, which may in turn affect expenditures, quality of care, and patient outcomes in numerous ways. Figure 3.2 illustrates the relationships between key actors in Ghana's pharmaceutical system. Since the

One policy in a complex system can impact the behaviours of multiple actors, which may in turn affect expenditures, quality of care, and patient outcomes in numerous ways.

Figure 3.2: Stakeholders in Ghana's pharmaceutical sector and potential impacts of excluding medicines from case-based provider payments



Legend: STGs=standard treatment guidelines; LCSs=licensed chemical sellers

Notes: full arrows represent the direction of supply or demand of medicines; Broken arrows show reimbursements for medicines from the National Health Insurance Authority.

The case-studies illustrate that medicines policies and strategies – which are crucial to achieve wider UHC goals – vary across different settings, and that information and financing levers with the potential to help balance competing medicines policy objectives are currently underused.

NHIS scheme finances a large proportion of the health care in Ghana, it is closely linked to providers in the public and private sectors, and its policies will affect the behaviours of these providers in both intended and unintended ways.

When case-based provider payment was first introduced in Ghana in 2008, medicines were excluded from the provider payment, and medicines reimbursement to facilities continued on a fee-for-service basis (143). For the various types of providers (e.g. licensed chemical sellers, private pharmacies, private hospitals, public hospitals, and mission hospitals), payments for medicines may have served as a source of income to offset perceived or actual decreases in income from medical services (143). Providers' responses to the payment policy likely contributed to an unintended rise in numbers of prescriptions, cost per prescription, and doubling of NHIS expenditures on medicines (143), which pressured the NHIS both logistically (through the required review of claims) and financially. Reimbursement delays may have led to medicine stock-outs and to providers leaving the NHIS. This cascade of policy effects (described in more detail in the web annex) would have had negative effects on consumers and patients, as they had more difficulty in obtaining access to prescribed medicines.

The case-studies illustrate that medicines policies and strategies – which are crucial to achieve wider UHC goals – vary across different settings, and that information and financing levers with the potential to help balance competing medicines policy objectives are currently underused. A systems approach helps to identify where policies have the greatest potential to advance UHC and medicines objectives – or where those policies might lead to unintended consequences that undermine their objectives. Such a perspective can also

highlight some of the substantial ethical challenges that schemes face when making decisions about medicines coverage.

3.4 Towards UHC: ethical considerations must guide policy decisions

UHC is by definition an ethical endeavour as it urges health systems around the world to implement pre-payment and risk-sharing strategies, ensure the equitable distribution of health resources, and move towards equity in access to health services (45). Equity here refers to “equal access to available care for equal need, equal utilization for equal need, and equal quality of care for all” (144). In the context of this chapter, equity relates to avoiding or minimizing disadvantages that arise from lack of access to medicines (for example, due to an inability to pay for them), especially for the poorest.

In every health system, limited resources are spread across medical services that range from preventive to curative (including pharmacotherapy) and palliative care. Medicines constitute a critical component of expenditures. Even well-intended policies may create inequitable outcomes. For instance, limiting coverage to inpatient care (inclusive of medicines) to protect households from catastrophic payments for sudden high-cost hospitalizations may contain expenditures on medicines by the financing scheme, but may be detrimental for poor households that cannot afford regular payments for common outpatient medicines. In contrast, wealthier households are better able to shoulder recurring expenditures, and they are also more likely than poorer households to be able to access hospital-based care. In working towards UHC, decision-makers must ensure that policies facilitate access to medicines and decrease economic burden equitably, an aspect we address in the subsection below.

3.4.1 Striving towards equity-enhancing pharmaceutical policies

To achieve UHC, policy-makers must move towards equity-enhancing pharmaceutical policies. Equity is intimately linked with fairness and social justice, and underscores the legitimacy of policies (see Box 3.2). Equitable policies can help reduce poverty in the long run, especially where investment strengthens human capabilities (145, 146). They also heighten awareness of the discrimination suffered by certain groups of people, boost trust and social cohesion, and reduce political conflict (147). Finally, equity contributes to the sustainability of health systems by determining what will be provided within a resource-constrained setting based on a set of criteria that is fair (148).

Determining whether a pharmaceutical policy is equitable can be difficult as this judgment is intertwined with other social values. Often, a specific situation is further complicated by clinical uncertainties, competing objectives, and different stakeholder interests. Not surprisingly, there is disagreement over which values should drive pharmaceutical policy decisions and there is no fixed formula guaranteed to resolve differences arising from conflicting values or to generate categorically equitable outcomes. Many health systems rely on input about cost-effectiveness from health technology assessment (HTA) for decisions on medicines selection or reimbursement, although different systems vary in how they apply these assessments. While HTA and other forms of economic evaluations are important in informing policy, they tend to be primarily concerned with efficiency, which is just one of

many values.

There are several frameworks for assessing the equity and fairness implications of a policy. Rather than providing the strengths and weaknesses of these frameworks here, we have instead selected a commonly-used and accepted ethical framework – “accountability for reasonableness” (A4R) – to guide our analysis (149, 150). To date, a number of organizations and regulatory bodies have applied this A4R

Box 3.2: Equity

Equity refers to “equal access to available care for equal need, equal utilization for equal need, and equal quality of care for all.” (144) In the context of this chapter, equity relates to avoiding or minimizing disadvantages that arise from lack of access to medicines (for example, due to inability to pay for them), especially for the poorest. Equity is intimately linked with fairness and social justice, and underscores the legitimacy of policies.

framework, to varying degrees, in assessing the equity and fairness implications of policies. These include Harvard Pilgrim Health Care in the USA (see Box 3.3), the National Institute for Health and Clinical Excellence (NICE) in the UK (151), Seguro Popular in Mexico (152), the Response to Accountable Priority Setting for Trust in Health Systems (REACT) project in the United Republic of Tanzania (153), and the National Health Insurance Program of South Korea (154).

A4R seeks to ensure that policies enhance equity by satisfying four decision-making conditions (149):

- Publicity: policies regarding both direct and indirect limits on the provision and

A systems approach helps to identify where policies have the greatest potential to advance UHC and medicines objectives – or where those policies might lead to unintended consequences that undermine their objectives.

Systems need to generate routine, up-to-date information about the medicines that patients need, which medicines they are using and how use differs across member groups, who prescribes them, whether these medicines are clinically appropriate, address the disease burden faced by the population, and how much both the scheme and its members spend on medicines.

reimbursement of medicines and their rationales should be publicly accessible.

- ▶ **Relevance:** the rationale behind decisions should provide a reasonable explanation of how the varied health needs of a defined population are met under reasonable resource constraints. An explanation is “reasonable” if it is grounded in principles and evidence that are accepted as relevant by fair-minded people who are disposed to finding mutually justifiable terms of cooperation.
- ▶ **Revision and appeals:** all decisions and policies must be subject to mechanisms for challenge and dispute resolution, and more broadly, provide opportunities for revision and improvement in light of new evidence and arguments.
- ▶ **Regulation or enforcement:** there must be voluntary or public regulation to ensure that the conditions set out above are met.

To further emphasize the importance of full participation in democratic deliberation, some have proposed *empowerment* as a fifth condition to the A4R framework (155). In the context of this report, empowerment would require effort by policy-makers to minimize power differences in decision-making processes and to optimize opportunities for participation in priority setting.

Arguably, pharmaceutical policies in systems working towards UHC are more likely to be equity-oriented or equity-enhancing if they are generated in a deliberative environment that is fair and inclusive – both in terms of the values encompassed and through participation by members of the health system concerned, especially those that are most directly affected.

In reality, however, it can be difficult to fully account for these fairness and inclusion

requirements of the A4R framework. While the framework attempts to ensure that decisions in pharmaceutical policies are legitimate and fair, the outcomes are not necessarily equitable. Hence, constant monitoring and evaluation of policy outcomes is of utmost importance in ensuring that equity is enhanced or maximized as systems strive towards UHC.

3.5 Information about medicines is key to achieving UHC goals

Information is critical in determining policies for effective, safe, equitable, and efficient use of medicines; affordable access by households; and economic sustainability of schemes. Medicines policies also need to account for contexts such as population demographics, disease epidemiology, treatment approaches, and political and economic environments that are constantly changing. This means that systems need to generate routine, up-to-date information about the medicines that patients need, which medicines they are using and how use differs across member groups, who prescribes them, whether these medicines are clinically appropriate, address the disease burden faced by the population, and how much both the scheme and its members spend on medicines. Without this information, systems will find it difficult to ensure that they are moving in the direction of UHC – i.e. equitable access to quality care and financial risk protection – and that they are spending their resources efficiently.

Information systems need to have mechanisms to capture individual medicine utilization and expenditures, to judge the quality, equity, and efficiency of care and to know whether bundled payment rates, when implemented, are justified. However, when schemes reimburse providers through bundled payment arrangements (e.g. case-based or episode-based payment), information systems may not

Box 3.3: The Harvard Pilgrim Health Care ethics advisory group

Harvard Pilgrim Health Care (HPHC) is a not-for-profit, private health insurance company serving about 1.2 million members in the USA. In 1996, facing the challenge of balancing rising costs with growing patient needs, the organization created an ethics programme, based on “the conviction that virtually every area of our activity has implications for the ethical quality of the care and service our members receive” (156). An ethics advisory group (EAG) composed of health insurance leaders, insurance purchasers, consumers, and physician leaders from contracted practices, and representatives of the larger public (157) meets quarterly to deliberate on cases brought to it by the insurance scheme’s managers who need to consult on the values associated with operational and policy decisions. The EAG’s approach is based on a widely-used framework for conceptualizing the ethics of organizations called “stakeholder theory” which holds that the interests of all the parties involved in any transaction ought to be considered in determining how to act ethically (158). The main goal of the EAG is to “promote increased organizational skill at identifying and addressing ethical aspects of key policy, operational, and budgetary decisions”. (159)

Through active participation, members of the ethics group systematically examine conflicts of values that arise from the legitimate and often competing interests of the various stakeholders whose needs the insurance scheme seeks to meet. Over the years, the EAG has deliberated on a number of challenging medicines-coverage decisions. For example, the 1998 US approval of *sildenafil* for erectile dysfunction raised the question whether an insurance scheme should allocate resources to pay for a medicine considered by some to be “a lifestyle drug” (159). More recently, the EAG discussed the challenge of covering increasingly

available high-cost specialty medicines that provide benefits to only a few patients. Such medicines include *ivacaftor*, a new drug to treat patients with a rare form of cystic fibrosis, currently priced at about US\$ 300,000 per patient per year. Importantly, this EAG meeting included representatives from several pharmaceutical companies (160). In both instances, EAG deliberations provided non-binding guidance to insurance decision-makers.

The experience of how this group has worked within the organization offers several practical lessons. The stakeholders of the EAG can help insurance leaders tease out the value dimensions underlying policy options; voices of members, providers, employers who purchase insurance, insurance programme staff, and the larger community contribute to a growing case portfolio of transparency in difficult discussions about cost and quality of care. Explicit ethical analysis of challenging coverage questions can provide practical decision-making support to insurance leaders and help communicate decisions to different stakeholders (159).

EAG leaders believe that over time, health care ethics will advance through careful observation of decision-making processes by governments, payers, providers, and consumers (159); that values underlying decisions will become more transparent and decision processes more fair, contributing to increased trust between patients, providers, and payers; and that resulting management of costs of care through limit-setting policies may be more just and acceptable by different stakeholders. (160)

Policy-makers seeking to improve medicines situations on the way to UHC need to take a systems approach, considering the converging interests, roles, responsibilities, and resources of all stakeholders.

Pharmaceutical policies in systems working towards UHC need continuous adaptation to a shifting context (e.g. evolving population demographics, disease epidemiology, treatment approaches, political and economic environments) and changing realities. Such adaptations must be informed by the best available evidence.

be designed to capture data on specific medicines prescribed for individual patients, since payment does not depend on the information.

Routine information in at least four categories is needed to inform medicines policy adaptation:

- ▶ spending on medicines (e.g. per member per month);
- ▶ medicine utilization (e.g. number of prescriptions per member per month);
- ▶ quality of pharmaceutical care (e.g. percentages of primary care patients receiving antibiotics, those receiving injections, or newly-diagnosed diabetic patients receiving first-line therapy according to standard treatment guidelines); and
- ▶ fraud and abuse (e.g. number of prescriptions per provider, number of prescriptions dispensed per member).

Key indicators need to be assessed overall, but also disaggregated by therapeutic drug class, provider, and member characteristics (socioeconomic status, location of residence, etc.). Based on key medicines information, policy-makers can develop interventions to strengthen the management of medicines in the scheme as a whole; target policies that increase access within specific disadvantaged groups; develop strategies for volume-based price negotiations with manufacturers; target education programmes for members and providers and incentive policies aimed at improving prescribing; and carry out audits of institutions or providers suspected of fraud.

In the early stages of developing information systems, schemes can plan to combine information from different parts of the health care system. Regular samples of paper-based facility procurement, prescribing, and dispensing records can provide sufficiently detailed

information on utilization to inform policy decisions. Widely-used facility-based indicators of medicine use that can be calculated from relatively small, regular samples of paper-based records include the percentages of medicines procured or dispensed in primary care facilities that are injectables, antibiotics, corticosteroids, or vitamins; the percentages of medicines prescribed that are on essential medicines or reimbursement lists; and the percentage of prescriptions that follow standard treatment guidelines. Chapter 6 and the related web annex elaborate more on medicines indicators and data sources.

Importantly, equity in access to medicines cannot be assessed using only data from the delivery system, because these data do not capture underuse of services by people who cannot access care because of geographic, economic, or sociocultural reasons. Household surveys are needed to understand community need for and barriers to access among vulnerable, disadvantaged populations (161).

3.6 Conclusions and recommendations

The case-studies presented in this chapter illustrate that, despite the overall size of the pharmaceutical market, to date medicines are not a central component of UHC debates. Making UHC a reality will require a much more explicit focus on medicines. Health systems pursuing UHC have information, financial and other policy levers to work towards balancing the competing objectives of availability, access, affordability and appropriate use, equitably and efficiently. Policy-makers seeking to improve medicines situations on the way to UHC need to take a systems approach, considering the converging or competing interests, roles, responsibilities, and resources of all stakeholders – regulators, payers, facility managers, procurement officers, local and multinational drug industries, prescribers, dispensers, and

consumers. These diverse stakeholders have different perspectives on how systems should devote resources to medicines, highlighting the ethical complexities of policy-making that require deliberative, inclusive, and transparent processes. The use of evidence-informed, systems-oriented policy approaches will increase the likelihood of equitable, effective, affordable pharmaceutical policy outcomes, and boost progress towards UHC.

Pharmaceutical policies in systems working towards UHC need continuous adaptation to a shifting context (e.g. evolving population demographics, disease epidemiology, treatment approaches, political and economic environments) and changing realities. Such adaptations must be informed by the best available evidence of what works, for whom, how, and why, in a given situation. Routine monitoring and periodic evaluations of impacts of pharmaceutical policies in health systems are therefore indispensable.



4

INNOVATION TO
ENSURE BETTER
ACCESS TO MEDICINES

KEY MESSAGES

- ▶ Innovation – broadly defined as “a process to create or improve products, processes, technologies and/or ideas to generate positive changes in efficiency, value and quality” (162) – is urgently needed to bring new and existing medicines to people in novel ways.
- ▶ Innovations for developing novel medicines for unmet needs require multiple public- and private-sector partnerships, building on communication technology advances, and delinking research and development (R&D) funding from sales revenue.
- ▶ Innovations to increase the use of quality-assured generic products include multi-pronged strategies involving government regulations of generic product manufacturing and licensing, payers that incentivize the prescribing and dispensing of generic products, and media that communicate the value of quality generics in health systems.
- ▶ Expanding access to increasingly available novel products – often high-cost, biotechnology-based products – raises challenging clinical, ethical, economic, societal, legal and political questions that require multi-stakeholder engagement in fair decision-making processes.
- ▶ The overall effects of innovations on health systems need to be assessed. This includes evaluating the reasons the innovations were introduced, monitoring their intended and unintended effects over time, and determining how the innovations adapted (or were adapted to) local contexts.

4.1 An inclusive definition of innovation

Overcoming challenges in medicines availability requires innovation to identify new diagnostics and therapies for many diseases and populations around the world (163). Innovations are also necessary to ensure that existing products are supplied, prescribed and dispensed correctly, and used appropriately by those who need them, at costs that both households and health systems can afford.

Innovation does not solely mean invention, or the development of a new product or technology. Throughout this report, we consider innovation broadly as “a process to create or improve products, processes, technologies and/or ideas to generate positive changes in efficiency, value and quality” (162). For instance, ensuring that medicines are more widely available and that health market systems work (see Chapter 5) requires stakeholders engaged in different parts of the health system to operate in new ways in developing, regulating, financing, procuring, distributing, prescribing, dispensing, and using medicines. These health system activities are connected to each other; as in the systems approach advanced throughout this report, innovations targeting one part of the health system will require interaction with health system components, institutions or stakeholders to ensure that medicines do in fact improve health.

There are many examples of innovations designed to make medicines better available (164, 165), several of which illustrate how health system activities are integrally connected to other sectors. For instance, the 2013 joint report of the World Health Organization, World Intellectual Property Organization, and World Trade Organization offers a crucial, in-depth discussion of issues at the intersection of public health, intellectual property, and

trade (166).

In this chapter, we explore innovations in medicines in three different ways. First is a discussion of innovative models of research and development, illustrated by India’s promising Open Source Drug Discovery initiative (OSDD). In section 4.3 is an analysis of how markets for generics are expanding, with a look into Brazil’s innovative generic laws. And lastly is an examination of ways to expand access to specialty medicine, exploring Thailand’s access programme targeting high-cost medicines.

4.2 Towards innovative R&D models

Innovations in research and development (R&D) are needed to develop new products for neglected diseases (e.g. Dengue, Chagas, river blindness) and newly emerging diseases (e.g. pandemic influenza) – both of which disproportionately affect people in LMICs. Innovations on new formulations of existing medicines appropriate for LMIC populations (e.g. paediatric formulations of HIV/AIDS treatments; heat-stable products) are also required. Traditional R&D models based on protecting intellectual property rights have failed to bring necessary technologies to market because there is often little financial profit. This is a critical friction to resolve: impoverished populations – who suffer from diseases they often cannot afford to treat – lack both the political voice and the economic means to afford new medicines. How can industry’s profit motive be effectively balanced with essential treatment needs?

Creating incentives for pharmaceutical R&D is not only an urgent issue for LMICs, but increasingly, for the rest of the world. A major global R&D challenge is the development of new antibiotics, since many bacteria have developed resistance to frequently-used antibiotics. No matter how judiciously antibiotics are prescribed, their use will inevitably generate resistant organisms, rendering novel antibiotics

Overcoming challenges in medicines availability requires innovation to identify new diagnostics and therapies for many diseases and populations around the world.

Box 4.1: Innovative push and pull R&D Strategies

“Push” strategies can be used to subsidize research inputs – using funds to spur, for instance, the discovery of new medicines. These strategies, which often devote public funds to R&D in the private sector, include: public-private partnerships such as the GAVI Alliance (168) and the GSK Diseases for the Developing World Research Centre (169); targeted research grants programmes such as the Drugs for Neglected Disease Initiative (170); and tax credits for R&D spending (169). “Pull” strategies, on the other hand, reward research output, providing an incentive to make the results available to its intended population (171). Innovative pull strategies include: prize funds (163), priority review vouchers (169), transferable patent exclusivity (169), and advance market commitments, in which governments or donors commit to buying a quantity of a drug to drive R&D (163, 172). Other strategies to incentivize priority R&D include orphan drug legislation, open source drug discovery, patent pools and regulatory harmonization (173).

less effective over time. Further complicating the matter is market logic: restricted use of antibiotics will limit sales and impede the cost recovery of drug development, providing little incentive for pharmaceutical companies to develop new antibiotics. Even if R&D for antibiotics could be sufficiently stimulated with public or private subsidies, the current business model that links revenue and profit to sales volumes will lead to marketing strategies that encourage overuse and drug resistance. Thus, innovative business models are needed to delink revenue from usage.

Alternative R&D models do exist and more are currently under development. These involve a wider range of actors and innovative collaborations to “share resources, risks, and rewards”. (167) These novel R&D approaches seek to delink sales revenue and R&D costs through push mechanisms – payments for R&D inputs by, for example, supporting the conduct of clinical trials – and through pull mechanisms such as prizes for R&D that brings successful inventions to market.

Innovative product development partnerships

(PDPs) (174, 175) have increased the number of medicines in development for neglected diseases (176). PDPs are non-profit R&D partnerships between industry and non-profit organizations with major external funding (notably by the Bill and Melinda Gates Foundation). Examples of major PDPs include the Programme for Appropriate Technology in Health (PATH), the International AIDS Vaccine Initiative (IAVI), the Medicines for Malaria Venture (MMV), the Global Alliance for TB Drug Development, and the Aeras Global TB Vaccine Foundation. In 2012, these organizations collectively accounted for two-thirds of the more than US\$ 375 million funding for PDP research (almost 12% of all global funding for research) on medicines for neglected diseases (176).

PDPs are beginning to generate products. In 2007, the Drugs for Neglected Diseases Initiative (DNDi) developed the first ever anti-malarial resulting from a PDP (177). ASAQ, a fixed-dose combination of *artesunate* and *amodiaquine* for uncomplicated malaria, is a non-exclusive and non-patented drug for adults and children in sub-Saharan Africa; it is a quality, heat-stable product that is dosed

Creating incentives for pharmaceutical R&D is not only an urgent issue for LMICs, but increasingly, for the rest of the world.

once a day (178). The drug is sold at a “no-profit, no-loss” maximum price of US\$ 1 per adult treatment to national health services and nongovernmental organizations in endemic countries. So far, ASAQ has been registered in more than 30 countries and more than 200 million treatments have been distributed (179). Using a tiered-pricing approach, the company sells the fixed-dose combination in private sector markets and contributes 3% of net private sector earnings over seven years to DNDi to further lower the public sector sales price.

Another key issue lies in the fact that restricted access to proprietary data can slow or even prevent drug discovery. India launched the Open Source Drug Discovery (OSDD) Initiative (180) to identify urgently needed medicines by combining open source innovation and product development partnerships (see section 4.2.1.). This new initiative draws upon the lessons of open-source innovation in information technology and is strategically positioned because of the Council on Scientific and Industrial Research’s history of translating its findings for the Indian generic industry.

Innovative open-access development has also begun with medicines to treat common chronic diseases affecting patients in high-income countries (181). Similar to the European Union’s Innovative Medicines Initiative (182), the Accelerating Medicines Partnership (AMP) is a new venture between the United States’ National Institutes of Health, ten biopharmaceutical companies and several non-profit organizations to transform the current model for developing new diagnostics and treatments by jointly identifying and validating promising biological targets of disease (183). To do so, the NIH and industry partners have committed to a (roughly equal) contribution towards an initial five-year budget of US\$ 230 million for up to five pilot projects in four disease areas:

Alzheimer’s disease, type 2 diabetes, rheumatoid arthritis, and systemic lupus erythematosus (183). AMP data and analyses will be made available to the entire biomedical community, with the goal of shortening the time to bring new therapies to the market.

4.2.1 India’s Open Source Drug Discovery initiative (OSDD)

In 2008, India’s Council on Scientific and Industrial Research (CSIR) piloted the OSDD to develop new medicines for those diseases that drug discovery and development processes had thus far neglected. This first targeted tuberculosis and later broadened its scope to malaria, filariasis and leishmaniasis (184). The initiative seeks to reengineer the means by which new drugs are brought to market. By sharing resources, risks and rewards, OSDD engages a community of students, scientists, clinicians, academicians, and institutions, which collaborate through an online platform and offline lab work, in partnership with companies, to develop new treatments free from monopoly rents. By publicly financing the costs of R&D, OSDD can work with generic manufacturers to produce the treatments at close-to-marginal cost, thereby ensuring greater affordability for those in need (185).

OSDD shares resources through an online collaborative platform that operates through a “clickwrap license” in which participants agree not to remove knowledge generated from the online commons for proprietary gain. So far, the platform has over 7600 registered participants from 130 countries, 13 engaged CSIR labs, 39 academic institutions and 14 industry partners. OSDD has connected with major product development partnerships, including the DNDi, the TB Alliance, and MMV. The OSDD hosts over 240 projects, both online and offline, led by over 180 principal investigators. At any given time, up to 20% of the

By sharing resources, risks, and rewards, and involving scientists around the world, OSDD exemplifies a new culture of R&D and is developing a publicly-owned pipeline for bringing new products to markets.

registered participants actively contribute.

Online collaborators work on diverse projects, focusing, for example, on identifying gene targets for therapy and understanding toxicities of pre-clinical compounds. The initiative also maintains publicly accessible databases, including an integrative genomics map of *Mycobacterium tuberculosis* (185). Engaging its online community, OSDD recently ran a *YouTube* Video competition on “The Need for New Drugs for TB.” One product from the OSDD network has already involved network volunteers, who re-annotated the entire *M. tuberculosis* genome, telescoping 300 person years of effort into four months (186-188).

The OSDD Initiative has also sought to line up the infrastructure to translate early-stage discoveries into the first in-human trials, facilitating the transfer from basic research scientists to those who might translate this work into a drug candidate. Biological resources are available through such collections as a library of plant-derived, anti-infective compounds for screening, and an open-access repository of *M. tuberculosis* clones. The initiative has also assembled a diverse small molecule repository, synthesized by a community of about 80 synthetic chemists from 35 institutions.

The OSDD Initiative’s models share both risks and rewards. Funding is both public and private, including US\$ 12 million funding from the Indian government, private-sector donations and in-kind Information Technology support from companies such as Infosys, and grants from foundations such as the Sir Dorabji Tata Trust. Funding is, in turn, released to projects, both as awards to principal investigators or as projects commissioned and coordinated by OSDD itself.

The OSDD initiative also shares financial and

non-financial rewards, both at the individual and collective levels. Individual rewards have ranged from activities encouraging women scientists to small prizes in the form of credit for phone usage and Internet access. Largely supported by the Indian government, scientists and students alike contribute voluntarily to the network’s activities. The OSDD’s collaborative platform tracks those contributing significantly to the online community project, and rewards those individuals in various ways, including authorship and acknowledgement in subsequent publications. Moreover, the best performers in the OSDD community have leveraged their participation into competitive applications for fellowship training in programmes abroad.

By publicly financing the R&D of novel antibiotics, OSDD seeks fair returns from this investment by keeping drug costs affordable through generic licensing.

To advance its virtual R&D pipeline, OSDD engages partners in such undertakings in two ways: it contracts service providers on a “work for hire” basis; and it collaborates with partners who donate their services, with the resulting intellectual property belonging to the OSDD community. Along these lines, OSDD has secured a non-exclusive right to TB drug candidate PA-824 from the TB Alliance for testing this drug in a new combination regimen (*pyrazinamide* + *moxifloxacin* + PA-824) in Phase IIB clinical trials. The combination has the potential of shortening TB treatment from six to two months.

OSDD’s non-hierarchical structure carries over to its governance. A Science Support Group – comprised of seven core members and people drawn from the OSDD community, with the leadership of Chief Mentor Dr. S. K. Brahmachari – guides the direction of the OSDD initiative and makes decisions on

policies governing its open-access repositories. Though the vision and mission of OSDD is to improve innovation for neglected diseases and provide affordable health care to all, its efforts have also inspired a generation of young minds.

By sharing resources, risks, and rewards, and involving scientists around the world, OSDD exemplifies a new culture of R&D and is developing a publicly-owned pipeline for bringing new products to markets.

4.3 Innovation in expanding markets for high-quality generic products

Quality generic medicines can greatly improve a population's access to medicines (189) – but producing generics and marketing them are not on their own sufficient to achieve this. Introducing generics requires addressing market forces and challenges in public perception, and in creating incentives for their preferential use. Until this occurs, the utilization of generics and the realization of potential savings from generic utilization, will remain variable across countries at all income levels.

Most medicines on national essential medicines lists are available as generic products – defined here as products that are intended to be clinically equivalent, lower-cost versions of the molecules of their originator brand counterparts, manufactured without a license from the originator and marketed after the expiry date of the patent or other exclusive rights. (189, 190).

The highest volumes of generic utilization and resultant medicines expenditure savings have been reported for the United States of America (USA), which has successfully addressed both market forces and the challenges of public perception (191). The United States Food and Drug Administration (FDA) approves generic products if there is evidence to show that

their active ingredient is absorbed at the same rate and to the same extent as the originator product – i.e. that they are “bioequivalent”. Studies on “bioequivalence” (199) and clinical equivalence (200) have shown that most originator and generic products in the USA are, in fact, equivalent. The FDA also enforces the same rigorous standards for quality assurance (current Good Manufacturing Processes) (192) for generics as for originator medicines. Quality assurance is one of several important steps to overcome the almost universal perception that generic products are of lower efficacy or quality than originator products.

Generic products play a crucial role in the US health system. In 2011, nearly 80% of the 4 billion prescriptions written in the USA were dispensed using generic products (193). Generics were dispensed 94% of the time when both a generic and an originator brand counterpart were available (194). Use of generics is facilitated by state-level generic substitution regulations, which, in most states, mandate pharmacists to substitute an interchangeable generic product for a prescribed originator product unless otherwise indicated by the prescriber (195). Health insurance schemes incentivize generic use through tiered pharmacy benefit policies, which have lowest patient co-payments for generic products (196).

The high use of generics has resulted in major medicine expenditure savings in the USA, where generic prices are typically a fraction of originator brand prices. Once a second generic product enters the market, the average generic price falls to half the price of the originator counterpart; additional generic competition reduces the cost further, to 20% or less (197). Without safe, high-quality generics, the USA would have spent US\$ 500 billion instead of US\$ 320 billion on medicines in 2011 (197). Between 2002 and 2011, the use of generics is estimated to have saved the US health care

Innovation required to promote generic medicines include the development of multi-pronged strategies to ensure that low-cost, high-quality generics are available, prescribed, dispensed, and used in ways that fit local contexts

system US\$ 1,070 billion (207). In addition, compared to patients who were dispensed brand-name products, those who were given prescriptions for generic products were more likely to adhere to their chronic disease treatment regimens since they incurred lower co-payments (198).

Generic products can reduce health care expenditures provided that quality generic products cost much less than their originator counterparts. Some European countries have been less successful than the USA in realizing the full savings potential from the use of generics, due to a prevailing model of administrative price regulation that caps reimbursement for generic medicines at a threshold derived from the originator price, rather than letting the market determine the price – as in the USA. When all generics are reimbursed at the same price, the incentive for price competition is lost. This is why several European countries have re-introduced elements of competition in their generics reimbursement policies. Recommendations to increase the use of generics in Europe include, among others: accelerating market authorization, pricing and reimbursement decisions for generic products; increasing prescribing through the use of electronic generic prescribing tools coupled with financial incentives; expansion of generic substitution policies; and incentives for pharmacists to preferentially dispense generics (199, 200).

If LMICs increased their use of high-quality, lower-cost generic products, they could realize substantial savings (201). Switching to generics, however, poses considerable challenges. In some LMICs, generics remain relatively expensive because of regulations that do not encourage price competition and a strong domestic generic industry that benefits from keeping prices relatively high and does not favour pro-competition reforms. In Brazil, for instance, generic prices are set at 65% of the

prices of originator brand counterparts, thus limiting price competition. In addition, the Brazilian public health care system – Sistema Único de Saúde (SUS) – does not currently apply procurement or financing levers to incentivize generic use. Other barriers to wider generic use in many countries include mistrust from both providers and patients of the quality of generic products, pharmaceutical sector policies that incentivize the use of high-cost brand name products, and lack of regulation on generic substitutions (202).

For LMICs to increase their use of generic products, several factors must be addressed:

- ▶ the availability of less expensive, high-quality generic products;
- ▶ the low levels of public trust in the quality of available generics; and
- ▶ the incentives for prescribers, dispensers, and patients to preferentially use generics.

The principal innovation required to meet the above factors include the development of multi-pronged strategies to ensure that low-cost, high-quality generics are available, prescribed, dispensed, and used in ways that fit local contexts. Local contexts will require balancing the goals of the health sector – i.e. the availability of low-cost, high-quality generic products – with those of other sectors – e.g. maximizing local generic industry profits – through public and professional education, enforced regulation, active management, and value-based financing policies.

In section 4.3.1, we describe several approaches undertaken by the government and other stakeholders in Brazil to increase the availability and use of high-quality generics.

4.3.1 The evolution of Brazil's approach to generic medicines

Access to medicines has been a constitutional right in Brazil since 1998. The societal and political environments in 1998 were favourable for the necessary technical and regulatory changes, and the government launched a multi-pronged strategy to facilitate access to high-quality, affordable generic medicines (203). Highly-publicized uses of counterfeit products (204) had encouraged social mobilization (of patient organizations, advocacy groups and the media) to improve the safety and quality of medicines. In 1999, the Brazilian Health Surveillance Agency (ANVISA) (205) was created to protect and promote the health of the population.

One of ANVISA's first actions was to develop the Brazilian Generics Law, which is one instrument in the 1999 National Medicines Policy (206). The goals of the Generics Law were to stimulate competition by increasing the number of products on the market, to improve the quality of medicines, and to facilitate access to medicines. Following international standards (206), the Brazilian Generics Law established criteria for production, bioequivalence, bioavailability, registration, prescription and dispensing of generic medicines. In 2000, Brazil's first six generic products were registered (207). Then, in January 2001, a new regulation – with Resolution 10 replacing Resolution 391 – provided greater flexibility in the registration process for generic medicines, thus accelerating the availability of generics in the market. The new regulation added information, revised points of the original resolution, and filled regulatory gaps (206).

The 1999 National Medicines Policy regulates generics, along with medicine production, procurement, prescribing, dispensing, and use. To encourage effective implementation, different

actors were engaged at the policy development stage, including various arms of the government (the Ministry of Health and ANVISA), local and multinational pharmaceutical companies, private retail pharmacies, professional organizations of doctors and pharmacists, and the general population. In 2002, to further engage multiple stakeholders, the Ministry of Health launched campaigns to educate consumers (208-210), prescribers, and dispensers about the value of generic medicines, often communicating through social media (218). The educational campaigns seem to have contributed to public awareness of generics: in 2007, 95.7% of the sampled population had heard of generic products, and 68.1% could even define "generic medication" (211).

Since the National Medicines Policy was implemented, Brazil has had three types of medicines. The first are originator brand products. The second are generics that meet clinical equivalence criteria, are commercialized under the international non-proprietary name (212) of the active ingredient in packages marked with a yellow stripe, (along with a large letter "G" and the inscription *Generic Medicines*), and which are considered interchangeable with the respective originator brand products (213). The third are "similares" or non-originator brand-name products which do not have to meet equivalence criteria, and which are marketed under a trade name.

Since 2000, regulations aimed at assuring the quality of medicines in the market have been implemented. In 2002, Resolution RDC 157 established the requirements for pharmaceutical equivalence studies for "similares". In 2003, Resolutions RDC 133 and RDC 134 required "similares" to undergo, by 2014, the same relative bioavailability and pharmaceutical equivalence tests required for generic products.

Regulated market entry of quality-assured generic products was one strategy adopted by the Brazilian government to increase the availability of high-quality medicines.

Within Brazil's public Unified Health System (SUS), prescribers must use generic names. In private practices, prescribers may use generic or brand names, but may choose to restrict the substitution of branded medicines with generics (214). Notably, the procurement of generic products is not mandatory in the SUS; rather, quality standards, product specific characteristics, and lowest price are the principal criteria for selecting a supplier and product for SUS (215). "Similares" are thus more available than generics in the public sector (214, 216).

Regulated market entry of quality-assured generic products was one strategy adopted by the Brazilian government to increase the availability of high-quality medicines. To make generics more affordable, the Brazilian Government set the maximum generic end-user product prices at 35% below the innovator brand product prices (217). On average, in 2006, generic medicines were priced 40% lower than their innovator counterparts (218).

The introduction of the 1999 Generics Law likely contributed to the growth of the domestic pharmaceutical industry. In 2003, only one Brazilian firm was among the 12 companies controlling close to half of the Brazilian market, but by 2012, 5 of the top 12 companies – with a 49% market share – were Brazilian (219). In 2002, generics made up 4.8% of the market volume, but this grew to 18% by 2008. Market share in value increased from about 4% in 2002 to about 15% in 2008 and 27% in 2013 (220). While additional policy measures are available, a multi-pronged strategy of ongoing adaptation of legislation, the government's enforcement of regulations, and its involvement in educating the public through social marketing have increased access to quality assured generic medicines at more affordable prices in Brazil (207).

4.4 Innovation in expanding access to specialty medicines

The majority of new medicines coming to market target complex diseases that require specialist treatment. Many of these diseases are increasingly prevalent across the globe, including cancer (221) and hepatitis; others, such as cystic fibrosis, affect relatively few patients, with most of these in high-income countries. Frequently, new medicines are biological agents – complex macromolecules produced by recombinant DNA technology – that come to market at prices that are orders of magnitude higher than those of small-molecule products. Biological agents are expected to represent about 20% of the world's pharmaceutical market by 2017 (222). Reasons behind the high prices for biological agents include: the challenge of establishing bioequivalence for follow-on biologics, or biosimilars; the extended data exclusivity offered to biologics (12 years in USA); and the complexity of manufacturing some biologics.

Providing access to novel cancer therapies and other specialty medicines poses enormous challenges. Innovation is required to ensure that specialty medicines reach only the patients for whom they are indicated; that they are administered in the specialty settings required for safe and effective care; that they are priced and financed in ways that individuals, households, and systems can afford; and that they maintain incentives for different actors to continue the R&D of innovative products.

Pharmaceutical companies, governments, payers, philanthropists, clinicians and professional societies, nongovernmental organizations, patient groups, academics and others have roles in improving access to valuable new specialty medicines. To make new treatments more affordable, these groups should engage in constructive dialogue about which medicines are

clinically beneficial and economically affordable, and how products should be priced to reflect their medically-proven and cost-effective value (223).

Companies can offer highly discounted prices for valuable medicines to LMICs, with tiered-pricing schemes targeting different in-country populations, patient assistance programmes for the poor, risk-sharing programmes with LMIC governments and insurance schemes, and voluntary licenses to – and partnerships with – generics manufacturers (224).

Governments can facilitate access through regulations that increase the speed and efficiency of clinical trials for promising products. They can ensure that only valuable specialty medicines are appropriately used by improving health care delivery and informatics infrastructures and through financing policies that remove provider and patient incentives that unintentionally lead to the misuse of high-cost medicines. Governments can allocate resources, engage in innovative financing arrangements with companies, and coordinate different funding sources – e.g. the private sector, philanthropic agencies, and third-party payers – of specialty medicines for different populations in their systems.

Generic production of biosimilars, and subsequently, competition among products, are expected to make biologic compounds less expensive and more accessible. Different from small-molecule medicines, however, for which approval generally indicates interchangeability with the originator product, governments need to define requirements for approving a biosimilar. To date, regulations on the licensing and interchangeability of biosimilar products vary by jurisdiction and remain in flux (225, 226).

Governments also have the option to use compulsory licensing provisions under the

TRIPS agreement, with such licensing allowing governments to import or produce a generic version of a patented product without the consent of the patent holder (227-228). However, compulsory licensing is highly controversial and its use can lead to political pressure and potentially negative consequences for trade in other, unrelated sectors. Compulsory licensing is also time- and resource-consuming as it usually has to be applied product-by-product and company-by-company and may involve lengthy, confrontational negotiations. However, some countries (for example Brazil, India, and Thailand) have used the credible threat of applying TRIPS flexibilities to strengthen their negotiating position with innovator companies and to incentivize the development of creative solutions for better access to novel medicines with high public health impact.

Payers can collaborate on the review of new technologies, in light of new disease priorities, available budgets, and the values underlying decisions about benefit packages in their settings. They can engage with other stakeholders on the values underlying different decisions and communicate coverage decisions transparently (Chapter 3); they can also negotiate risk-sharing agreements with companies, incentivize appropriate use of products, and implement strict monitoring systems to track the spending on and use of specialty medicines (229).

Funders can contribute resources to the treatment of poor patients suffering from cancer and other complex diseases. Clinicians must push for novel therapies with substantial clinical benefits, and prescribe and dispense specialty medicines only to patients for whom the products are indicated, with strict continued clinical monitoring and support to ensure safe use in severely ill patients. Academics can contribute evidence for decision-making by evaluating the impacts of different strategies to

In most countries, high-cost specialty medicines pose a major challenge to the health system.

make specialty medicines accessible to those who need them.

Section 4.4.1. below describes a range of policy approaches used by different stakeholders in Thailand to facilitate access to selected high-cost specialty medicines (230).

4.4.1 The E2 Access programme for high-cost specialty medicines in Thailand

The National List of Essential Medicines (NLEM) has been an important part of the Thai national medicines policy since it was first published in 1981 (231). The NLEM is the basis for the mandatory payment of medicines costs by the three major Thai health insurance schemes – the Civil Servant Medical Benefit Scheme (CSMBS), the Social Security Scheme (SSS) and the Universal Coverage (UC) Scheme – which together enrol nearly all Thai people. Insured patients under these schemes do not pay for medicines on the NLEM.

As in most countries, high-cost specialty medicines pose a major challenge to the health system in Thailand. The government addressed this challenge in 2008 through a multi-pronged strategy known as the E2 access programme (232).³ The programme initially targeted ten very costly medicines (*botulinum A toxin, docetaxel, erythropoietin alfa, erythropoietin beta, letrozole, leuprorelin acetate, liposomal amphotericin B, human normal immunoglobulin intravenous, imatinib, and verteporfin*) for 21 relatively rare conditions, which require specific diagnostic and treatment monitoring approaches (232).

E2 programme medicines were listed in the newly-created NLEM E2 medicines category, which then mandated insurance schemes to pay for these high-cost medicines for patients meeting specific clinical eligibility criteria. However, unlike for other medicines in the

NLEM, insurance schemes were given time to implement coverage of E2 medicines to allow them to identify ways to address the resulting budget impact. The National Health Security Office (NHSO) began covering E2 medicines for UC scheme patients in January 2009, with the Social Welfare Office (SWO) following suit three years later (July 2012). Enrollees in the CSMBS scheme continued to receive the medicines without charge under their fee-for-service benefit (233).

Following the announcement of the E2 access programme, government, payers, and companies facilitated its implementation through strategies focused on system affordability of the regulatory coverage mandate. These strategies differed by medicine, manufacturer, and payer. For example, the government considered the use of compulsory licences for three E2 anti-cancer medicines, *letrozole, docetaxel, and imatinib* (234, 235). The Thai government allowed patent holders to negotiate before resorting to compulsory licencing. In 2008, Novartis Pharma AG agreed to provide the anti-cancer drug *imatinib* free of charge by expanding its patient access programme to all patients under the UC Scheme – in lieu of a compulsory license – facilitating the NHSO implementation of the E2 policy for this drug. For *letrozole* and *docetaxel*, the government instituted compulsory licences in January 2008 – applying this policy instrument for the first time to non-AIDS medicines – to reduce the prices of these anti-cancer medicines. Payers in turn implemented the E2 programme-mandated coverage for these medicines. In addition, the NHSO collaborated with the Government Pharmaceutical Organization (GPO), introducing in 2009 central procurement (instead of individual hospital-based procurement) for all

3. In Thailand, medicines on the National Essential Medicines List are classified in 6 groups from A to E2. The E2 category includes “high risk costly drugs to be used by a senior specialist”.

E2 products used for UC patients in hospitals. Pooled procurement resulted in lower prices of medicines, saving the government the equivalent of millions of dollars annually (236).

Operationally, the GPO distributes E2 products for UC-insured patients directly to hospitals via the so-called vendor-managed inventory system. On behalf of hospitals, the SWO engaged with the pharmaceutical manufacturer, negotiating a 50% price reduction for *imatinib*, while also completely covering the drug for social security patients as of 2012. In January 2013, the SWO transferred its budget to NHSO to participate in the central procurement and delivery of E2 medicines for SSS patients. Recently, the list of E2 medicines has been expanded and in 2013 includes 16 products indicated for 27 conditions (232).

The Thai E2 strategy illustrates aspects of a system-oriented approach to benefit policy design that combines government regulatory, managerial, and economic measures with stakeholder cooperation in order to balance equitable access to and appropriate use of medicines with their affordability – along with the development of viable markets for industry. Given an increasing number of novel, high-cost treatments available and the resulting expansion of the E2 access programme, questions about its present and future economic impacts on the health system must be raised. In addition, effects of the programme on the health of individuals who receive E2 category medicines and on the overall population's health are currently unknown.

4.5 Innovation and ethics in medicines decision-making

The increasing availability of novel but expensive medicines and health technologies heightens some ethical decision-making dilemmas – particularly around priority setting and resource allocation in health policy and

financing. These dilemmas affect countries at all income levels, although LMICs are likely to face greater constraints in re-allocating funds from other public needs to health financing. Health technology assessments – as implemented for example by NICE in the UK (237) – can contribute technical information on cost-effectiveness but importantly do not ensure that a policy decision meets ethical goals. Political battles in many countries (238, 239) and legal challenges to reimbursement decisions, mostly in those Latin American countries with a constitutional right to health (240), are illustrative of contentions in rationing health care resources. Controversies among different stakeholders are likely to become more prevalent, given that most drugs in development pipelines are biotechnology-based, will come to market with high prices, and will need to be evaluated for potential coverage by expanding health insurance schemes.

There is no easy solution to fundamental conflicts in which “reasonable people will have moral disagreements about choices that create winners and losers – often with life at stake.” (241) At a basic level, decisions on priority setting and resource allocation processes should be made in a way deemed “fair”. Generally speaking, this will require these processes to be transparent and inclusive. In addition, decisions should be deliberative and reasonable, with attention paid to appropriate scientific evidence as well as to the perceptions, interests, and values of different stakeholders affected by such decision-making.

4.6 Conclusions and recommendations

Innovation to bring urgently needed medicines to market requires novel partnerships among health system stakeholders. LMICs must find a combination of approaches that integrate the interests of these stakeholders and matches the needs of different constituencies in

Innovation to bring urgently needed medicines to market requires novel partnerships among health system stakeholders.

pluralistic financing and care systems.

The intended and potentially unintended impacts of innovations in bringing medicines to markets must be better and more systematically assessed. We do know that bringing needed medicines to markets generate prime learning opportunities for national and global systems. At this point, monitoring and evaluation of the impacts of innovative regulatory, financing, supply and delivery mechanisms on medicines access, affordability, and use are crucial – not to “take advantage of these opportunities condemns us to rediscover at great cost what is already known or to repeat past mistakes” (242). It is also critically important to consider how innovations could be optimized given the constantly changing environments of LMIC health systems, and how innovations have adapted to local contexts and implementation challenges.



5

MAKING HEALTH
MARKET SYSTEMS
WORK FOR MEDICINES

KEY MESSAGES

- ▶ Improving access to and ensuring the appropriate use of medicines requires an understanding of health market systems. In recent years, these markets have expanded dramatically in LMICs, yet policy-makers have not given them sufficient attention.
- ▶ Poorly-organized health market systems fail in many dimensions, resulting in unneeded or harmful treatments, excessive and impoverishing costs, counterfeit and substandard products, and antibiotic resistance.
- ▶ In and of themselves, the training of health-care providers and providing better, more targeted information to health system stakeholders are not enough to improve the access and appropriate use of medicines.
- ▶ Successful interventions aimed at improving health system markets and correcting market failures require continuous revision; they engage multiple stakeholders, apply a balance of incentives, controls, and capacity building, and use data to monitor the intended and unintended consequences and to enhance accountability.

5.1 The growing role of health care markets in access to medicines

Market factors are now critical to the health systems of LMICs. They are especially important in the development of medicines and other diagnostic and therapeutic technologies, as well as in the delivery of health-related goods and services. However, although markets have come to play such an important role in health systems over the last few decades, governments have not created adequate regulatory developments to provide effective market oversight (243, 244).

Most countries have highly pluralistic health care delivery systems, with health providers ranging from itinerant drug sellers, small shops and private pharmacies, private clinics, not-for-profit and government hospitals, public sector multi-specialty hospitals, and different types of provider networks. These health providers have different levels of knowledge, training, and qualifications, various types of legal and professional standing, and different mechanisms for formal and informal payment (245, 246). In most LMICs, medicines are more likely to be purchased from shops, private pharmacies, and informally-trained private providers than through government health facilities. Yet many governments and international agencies have long neglected the role of the private sector in the supply of medicines.

Health markets are highly segmented. Often, those who are well-off can afford higher-quality professional care and have better protection through privileged financing arrangements – such as private health insurance – while the poor rely on underfunded public systems and low-cost, informally-trained providers (e.g. village doctors or traditional health providers). This segmentation is further subdivided on the basis of patient preferences and social needs, their particular health condition, as well as

their understanding of disease, an assessment of provider reputation, the effectiveness of medicines, and their purchasing power (244).

Although there are many debates around the best way to organize health systems, there is a widespread consensus that markets on their own do not produce efficient or equitable health systems. Both the causes and symptoms of market failures in the health sector are well documented (247), and include information asymmetry between providers and clients that make clients vulnerable to the abuse of provider power, resulting in excessive health costs, and unneeded or ineffective treatment. This can also lead to shortages of public health and preventive services, underinsurance against major health expenditures, an inability to control health care costs, and the inequitable distribution of health services and medicines (245, 247, 248).

A variety of measures exist in most countries to counteract these market failures. These include the government provision of health services, public regulation and laws, and professional self-regulation based on adherence to rules and standards. In LMICs, many of these formal institutions are weak, and the arrangements to create market order tend to be more informal and local, such as through provider referral networks or consumer word-of-mouth (249). Active interventions in informal markets can be effective, however, and tend to require multi-component strategies that balance incentives, controls, and education and involve multiple stakeholders (250). This was demonstrated in a series of studies in Thailand and Viet Nam, where poor case management and dispensing practices at private pharmacies were improved through regulation, education, and peer support (251, 252).

The public sector in health often fails too. In LMICs, shopkeepers who sell drugs,

Although markets have come to play such an important role in health systems over the last few decades, governments have not created adequate regulatory developments to provide effective market oversight.

Active interventions in informal markets can be effective, and tend to require multi-component strategies that balance incentives, controls, and education and involve multiple stakeholders.

The public and private health sectors are clearly interconnected since the factors that threaten government systems also affect the performance of private markets. The ability of institutions to enforce agreed-upon rules specifying expectations and behavioural norms are critical to the performance of both the public and private health sectors (249, 258).

informally-trained providers, and public sector health workers who take supplemental payments or hold additional private-sector jobs – all of this operates outside the formal legal framework, leaving governments with little capacity to enforce existing regulations (253, 254). Government health services can also fail to deliver due to under-funding and weak management systems, or because of recurrent shocks to the system from civil conflict, natural disasters, and economic crises. Analyses of public-sector failure in LMICs find that government employees may be influenced by financial incentives, or political and patronage relationships, and may not act in the general interests of the population (255, 256). Some informal payments may be considered “fair” in the context of low public-sector pay, while others may be considered exploitive. Interventions that do not consider the reality of conditions for public providers and regulators may create negative, unintended consequences (257).

The public and private health sectors are clearly interconnected since the factors that threaten government systems also affect the performance of private markets. The ability of institutions to enforce agreed-upon rules specifying expectations and behavioural norms are critical to the performance of both the public and private health sectors (249, 258). The inability to provide such institutions may contribute to growing problems with substandard and counterfeit medicines, the excessive use of antibiotics, the poor quality of medical care, and excessive costs. Pharmaceuticals markets have also been harmed by unethical drug promotion practices, including misleading or false claims about a drug, non-disclosure of side effects, and sales representatives who influence doctor’s prescribing practices by offering financial incentives and gifts (250).

5.2 A systems approach to analysing health care markets

Given the interconnectedness of stakeholders in the health sector and pervasiveness of market transactions, analysing the public and private sectors separately jars with the reality of how LMIC health systems actually work, and limits the options for intervention. Instead, it can be helpful to consider health market systems, with supply and demand – or the service transactions among providers and clients in both the publicly- and privately-owned health facilities – at their core (as shown in Figure 5.1). These provider-client transactions are influenced by formal and informal sets of rules, which are established and enforced by a wide range of market actors, each of whom is influenced by many other factors. Supporting functions for providers and users in a health market include those that provide infrastructure, equipment, training and human resource management, monitoring and evaluation, coordination and management support, and financing services. These supporting functions create an environment that either enhances or constrains the market actors, reflecting the norms, values, and regulatory actions for the suppliers and users of health care and medicines (244).

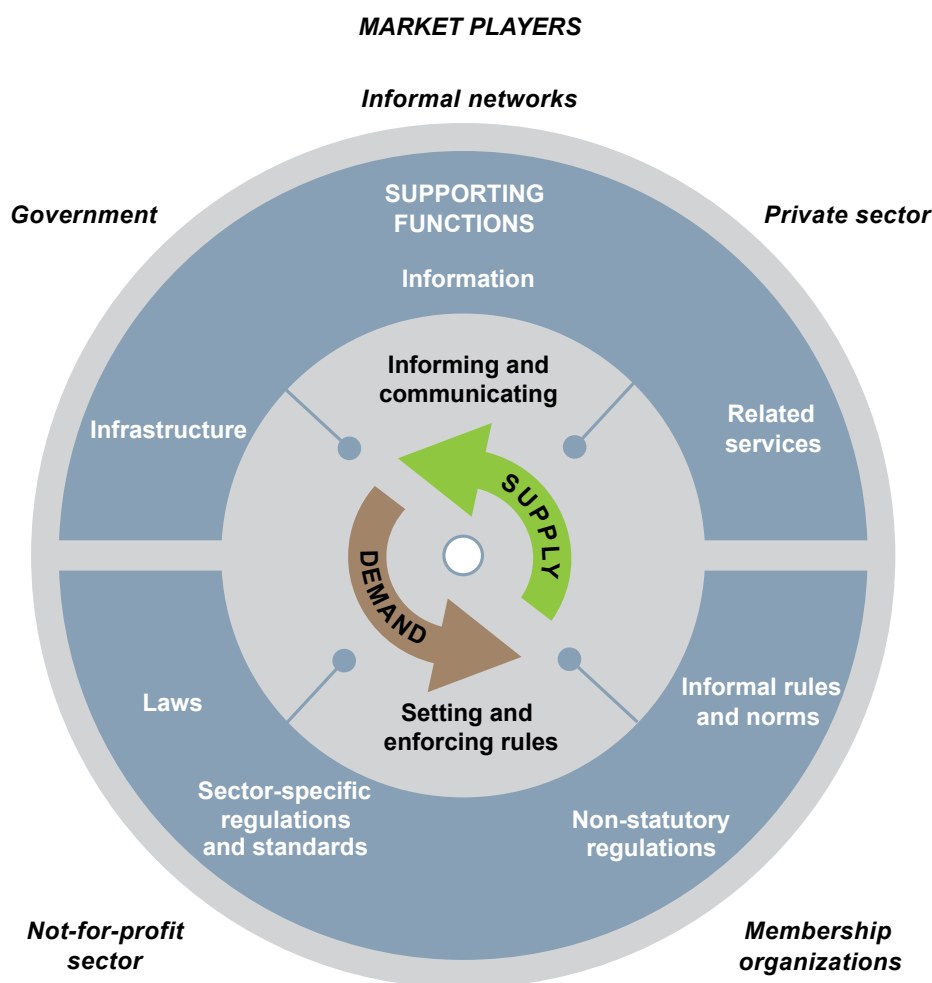
The wide number of stakeholders and interactions confers a complexity to health market systems. As in other complex systems, interventions that focus too narrowly on a specific aspect – such as strengthening the management of a single organization – are likely to fail (259). A review of interventions on informal private providers (260) found that training alone had little impact on performance – unless combined with reinforcing measures that change incentives to improve prescribing practices.

In any complex system, unintended consequences are common, and many different health system interventions, whether initiated through public or private providers, can affect medicines access, affordability, and use. One reason for this lies in the self-organizing behaviour of the different market actors, as they react to each other, test and learn new ways of acting, and create new structures and institutional arrangements. Thus, interventions that are flexible in design, and use data and feedback to adapt are more likely to succeed

(261). A systematic review of health-provider performance in LMICs (262) found that many interventions can be effective, though results are highly variable across different contexts, and that multi-component strategies with system-oriented problem-solving approaches are more likely to improve performance.

Interventions in health markets are often examined through a narrow perspective, typically only addressing their intended effects. However, to understand the wider effects on the critical stakeholders, it is essential to use

Figure 5.1: Framework for understanding health market systems adapted from Bloom et al (254)



In any complex system, unintended consequences are common, and many different health system interventions, whether initiated through public or private providers, can affect medicines access, affordability, and use.

a systems approach. This will provide a better understanding of how interventions change over time, indicate why they may succeed or fail, and point towards systemic elements that would benefit from routine monitoring and evaluation measures. Ultimately, this approach can provide insights that will inform key stakeholders in ways that can bring increased order to health market systems, which in turn will contribute to a transformation of the medicines situation in LMICs.

5.3 Case-studies of interventions addressing market failures in LMICs

Four country case-studies analyse different interventions designed to improve health markets and to address market failures in LMICs. These case-studies also highlight the role of important market players and how the intervention managed to channel their contributions towards improved medicines access.

The first case from the United Republic of Tanzania documents the development of accredited drug dispensing outlets, created in response to a weak supply chain and failing market, with the intention of providing essential medicines to the rural poor. It was designed through engagement with multiple stakeholders, with strong government leadership, and was adapted as the program became more decentralized. The participation and buy-in of drug shop owners, a neglected market player in the health systems of LMICs, was an important component of its success.

The second case – the *MoPoTsyo* programme in Cambodia – addressed a market failure that left diabetes patients without care. It did this by creating an innovative and effective network for highly sought-after services that rotated around a new market player – a peer educator.

The third case-study – Thailand's Antibiotic

Smart Use project – was a response to market failure involving the over-prescription, inappropriate demand, and subsequent growth of treatment resistance to antibiotics. It reveals how many different stakeholders were involved in the design and implementation of the programme, which required concerted efforts to align competing interests and incentives.

The final case-study, from Kenya, is a recent social business innovation, *Familia Nawiri*, designed to increase access to generic medicines for poor populations. It also aims to build a sustainable enterprise that meets both social goals for the population and a level of profitability to continue operations. It also highlights the use of "systems dynamics" research methods to understand how this type of intervention can achieve its intended objectives in a complex environment.

These case-studies combine a review of published and grey literature, complemented by direct or indirect information collected in the field through an analysis of monitoring data, internal or external evaluation reports, discussions with key informants, and access to unpublished data. Full case-studies are available in the web annex.

5.3.1 The United Republic of Tanzania: accredited drug-dispensing outlets

Private medicine retailers are key players in supplying medicines in LMICs (263-265), yet their role tends to be ignored in devising health policies, strategies, and monitoring and evaluation approaches. In rural areas of the United Republic of Tanzania, most people depend on *duka la dawa baridi* (DLDBs) or private medicines outlets for essential medicines, since most of the country's pharmacies and formal health facilities are in urban areas (266). Whereas these outlets are only authorized to sell over-the-counter medicines or

non-prescription medicines, they frequently sell prescription medicines illegally. They typically have poorly-trained staff, inadequate drug storage facilities, and low-quality drugs.

In 2003, the accredited drug-dispensing outlets (ADDO) programme was launched in the United Republic of Tanzania's Ruvuma region to train and accredit DLDBs with the aim of improving access to quality medicines and increasing consumer demand for appropriate medicines. Intended as a partnership between public and private actors, the programme set out to improve government oversight of standards for training, operations, and quality control. Capacity building was a strong focus of the programme, training shop owners in effective business practices – e.g. monitoring sales, stock expiry, profit management, and training dispensers in treatment guidelines and stock management. Taken together, this pushed training far beyond any previous interventions (267). The programme also rolled out a public information campaign.

Following two years of assessment, consultation and design, the ADDO programme was launched by the Tanzania Food & Drugs Authority (TFDA), the Ministry of Health and Social Welfare (MOHSW), DLDB owners and Management Sciences for Health (MSH) – an international NGO that was initially funded to perform this work by the Bill and Melinda Gates Foundation. A 2004 law required all DLDBs to practice the ADDO set of accreditation standards and code of ethics, established through consultation with government officials, medical officers and DLDB owners.

The ADDO programme began with 210 outlets in one region (Ruvuma), with credit assistance provided to the DLDB owners to pay for the physical upgrades needed to meet accreditation standards. Early in the programme, a high-profile government study visit to the

region resulted in the MOHSW describing the programme as a “key MOHSW programme” and not a “donor-funded project,” then allocating government funds for the further expansion of the programme. After a 2006 independent evaluation of the pilot, the programme was rolled-out by central authorities to three more regions. By 2007, it was clear that a centralized management approach was taking too long, was too expensive, and had overstretched their ability to inspect and support DLDBs. A decentralized approach was then taken through the training of trainers and local inspectors, along with greater involvement of local governments, including local government financial contributions. This was successful, cutting the cost of rolling-out in half, and the time reduced from 18 to 12 months per region, with more regions launching the programme in parallel.

The government took a number of actions to institutionalize the programme. In 2007, Tanzania's National Health Insurance fund incorporated the ADDOs into its scheme. The government also revised the legal framework to mandate local government planning and budgeting (2008), to update the standards to allow local inspection and the phase-out of unaccredited DLDBs (2009), and to clarify ADDO programme oversight.

In 2010, at the initiation of ADDO owners, the NGO MSH facilitated the creation of a new ADDO provider/dispenser professional association to give them a stronger voice in dealing with regulatory authorities and local governments. It enabled the joint procurement of drugs to reduce purchasing prices, and provided savings and credit opportunities to members.

By 2013, ADDOs were found in every region of the country, in both rural and urban areas. There were 5,500 ADDOs representing over

Private medicine retailers are key players in supplying medicines in LMICs (263-265), yet their role tends to be ignored in devising health policies, strategies, and monitoring and evaluation approaches.

“Expert patients” are trained to carry out pre-defined clinical tasks and community outreach, and establish a link between the community and health services. In some cases, their contribution to minimizing stigma and achieving greater involvement of communities in health care delivery and treatment programmes is also recognized.

60% of all drug outlets in the country, and the programme trained more than 13,000 dispensers and 3,200 local inspectors. The quality of services continues to improve. For example, in Ruvuma, patients receiving recommended malaria treatment rose from 6% in 2003 to 24% in 2004 and 63% in 2010.

The availability and quality of products has already improved. No unregistered products were found in 2010 compared to 2% in 2004 and 26% in 2001. The availability of antibiotics in Ruvuma in 2010 was 70% compared with 79% in 2004 and 53% at 2001. Less is known about how well the programme is reaching the poor; reports suggest that ADDOs are still not found in the most inaccessible parts of the country where households are especially impoverished, as it would be difficult for them to be profitable.

Although international donors largely financed the original programme-development costs, roll-out costs soon came to be shouldered by ADDO owners. Unsurprisingly, in all regions, prices increased after accreditation since the costs of upgrading shops and stocks, and training dispensers, needed to be recouped in some way. Yet these increases have been marginal; a 10-year evaluation of the pilot ADDOs found that antibiotics cost 15% above median prices in 2004 and 16% in 2010, according to the International Drug Price Indicator Guide.

Other African countries such as Uganda and Liberia have set up similar programmes. The engagement of stakeholders, including a supportive regulatory environment created by these national governments, attention to technical support, available financing, demand generation, linkages to community health initiatives, and use of information and evaluation to guide changes will be critical factors in their success.

5.3.2 Cambodia: task shifting to expert patients for diabetes care

Many health interventions consider patients as recipients of care, without paying attention to how they might play an active role in their own treatment. This second case-study from Cambodia illustrates the importance of “expert patients” – individuals who are suitably educated about their own disease so that they can not only effectively contribute to their own treatment, but provide support to others. Health care delivery through “expert patients” has been tested as an innovative approach to expand HIV treatment and care to counteract shortages of health staff in resource-limited settings. “Expert patients” are trained to carry out pre-defined clinical tasks and community outreach, and establish a link between the community and health services. In some cases, their contribution to minimizing stigma and achieving greater involvement of communities in health care delivery and treatment programmes is also recognized. Such task shifting could be especially important for chronic diseases that require long-term care: in many LMICs, the burden of NCDs is rising (268, 269), yet the capacity of health systems to provide that care remains sharply limited.

In Cambodia, 3.1% of the adult population (roughly 44,000 out of 1.4 million) have diabetes. *MoPoTsyo* is a Cambodian NGO established in 2004 to empower people living with diabetes to self-manage their condition by creating networks of community-based diabetes peer educators. It originated out of both a market and a state failure to provide diabetes care and medicines in urban slums. Over time, both the scale and scope of services has expanded, and the growing network of peer educators has become more tightly linked to other market players, such as pharmacies, laboratories, and public and private sector health providers – though it has been less successful

in connecting to the Ministry of Health.

The NGO uses expert patients as peer educators. They receive training, basic equipment and supplies, and host weekly patient gatherings and education sessions in their homes, which act as patient information centres. Their activities (on average three half-days per week) focus on providing people living with diabetes with reliable information on nutrition and exercise and basic skills such as self-measurement of glucose levels. The peer educators are trained to do blood glucose tests and general follow-up work, and if the patient does not show up for follow-up, the peer educator will visit the patient at home to motivate them to continue treatment. The educators receive financial incentives for service and performance, including incentives for activities such as screening, monitoring, patient gatherings, and a travel reimbursement. The average monthly incentive is around US\$ 30 a month; as a comparison, garment factory workers earn US\$ 75 a month. Occasionally, incentives have led to conflicts of interests, including one instance where the number of urine glucose self-test results recorded by a peer educator exceeded the amount of urine strips she had received – but fortunately, these seem rare.

By the end of 2013, with a growing membership and a weak public health system, *MoPoTsyo* started to become more engaged with service delivery aspects. For example, when the NGO started to roll-out activities in rural areas, they found that there were no doctors trained in diabetes care and no consultation services available for patients at either health centres or district referral hospitals. The organisation hired a number of doctors from diabetes clinics in Phnom Penh to carry out diabetes consultations and to train local doctors.

In 2006, the NGO decided to address the protracted problem of inadequate access to

diabetes and chronic disease medicines through a revolving drug fund. It established contracts with local pharmacies to sell certain generic medicines, procured in bulk internationally, at a fixed price to *MoPoTsyo* members. The pharmacies, mostly private, are allowed a 15% profit margin. The pharmacies were chosen in close collaboration with district health authorities, looking predominantly at their proximity to network coverage area, but also at the reputation of the people running them. Pharmacy receipts given to patients are collected by the peer educators, allowing the NGO to monitor both the performance of the pharmacies and patient adherence. Until recently, most contracted pharmacies were private, but the NGO is now also working with pharmacy outlets in public facilities.

In early 2010, *MoPoTsyo* started to develop its own capacity to carry out laboratory tests, again in response to a service gap. At the referral hospitals these tests were either unavailable or unaffordable; *MoPoTsyo* charges less than half the price of public hospitals. Blood samples are taken in the community and transported to a central laboratory, and the test results are sent to the peer educator, who explains them to the patient. The programme now includes other services relevant to diabetes, with peer educators also addressing hypertension or organising eye screening in collaboration with private non-profit clinics.

By the end of 2012, over 12,000 people were registered patients with *MoPoTsyo*, with nearly 500,000 adults having been screened for diabetes. An external evaluation in 2011 (270) showed that the programme had seen major successes. There were significant improvements in fasting blood glucose levels and both systolic and diastolic blood pressure in a randomly-selected group of patients who were in the programme for at least two years, with about one-third of patients reaching

Financial and non-financial incentives in place for physicians and pharmacists may be misaligned with appropriate drug use.

treatment targets for fasting blood glucose and two-thirds for blood-pressure levels. More than two-thirds of patients reported improvement (“better” or “much better”) in terms of their perceived health, ability to control their condition, and adherence to both medication and lifestyle adjustments when compared to their situation before joining the programme.

There have also been several unintended consequences of the scheme. For example, many patients incorrectly view peer educators as doctors, relying on them for disease management. Although the aim of the networks is to help patients self-manage, many patients remain passive. It is not always clear whether the peer is reluctant to pass certain tasks to the patients or whether the patients do not want to take on responsibility. Some peer educators do take on roles beyond their training, such as giving advice on which medicines to take or how to adjust dosage. Peer educators have in many cases become gatekeepers to other health services; when patients encounter a health problem, many turn to them for non-diabetes related questions for which they are ill equipped to provide referral advice. Given the high unmet demand for health services and the lack of professional providers in this market, peer educators, who are trusted and available, have filled some of this gap.

The success of the network has led the Ministry of Health to plan on absorbing it, but this plan presents several unresolved issues. Inherently, the effectiveness of a network that operates largely outside the formal health system creates strong concerns for the health system. And indeed, despite the low capacities of the Cambodian government to offer diabetes care, Ministry of Health officials have condemned the vertical approach of the networks – questioning the sustainability of a system reliant on donor funds and which has organised access to medicines and delivery of services in

parallel to the public health system.

Senior Ministry of Health officials and physicians believe that diabetes care, including laboratory services, consultation and medicine supply, must be accessed through the formal health system. Similarly, the Ministry of Health opposed the Revolving Drug Fund, since it goes against official government policy that medicines should be provided for free. However, there is no alternative vision on how to ensure a constant supply of affordable medicines and laboratory supplies for chronic conditions without patient contributions and the type of innovation that has been developed by MoPoTsyo.

5.3.3 Thailand: Antibiotic Smart Use Initiative

The third case-study uses traditional stakeholders – physicians and pharmacists – as the entry point for an intervention designed to improve the use of antibiotics. The misuse of antibiotics, for instance, is rampant in Thailand and has serious health effects; in 2010, antimicrobial resistance in the country caused at least 3.2 million extra hospitalization days and 38,481 deaths (271). This case-study shows that the financial and non-financial incentives in place for physicians and pharmacists may be misaligned with appropriate drug use. This has resulted in the underuse, overuse, or misuse of medicines, which in the case of antibiotics, can drive resistance – a growing global threat producing untreatable or expensive infections.

In Thailand, there is no divide between prescription and dispensing systems: physicians may dispense medicines, and pharmacists may prescribe them. Both directly benefit from dispensing more antibiotics under a fee-for-service system. This situation is further exacerbated by the fact that the country has strong consumer-demand for antibiotics, irrespective of the cause of infection. Thailand’s Drug Act

classifies antibiotics as drugs with potentially serious side effects or *ya-an-talai*, which translates to “dangerous drugs”. Colloquially, however, antibiotics are sometimes called *ya-gae-ug-sep*, which means “drugs that counter inflammation”. This reinforces the layperson’s belief that all inflammatory symptoms can be cured with antibiotics, whether or not the cause is bacterial.

Thailand’s Antibiotics Smart Use (ASU) Initiative was established by the Thai Food and Drug Agency (FDA) in 2007 to improve the rational use of these medicines by improving education on antibiotic use to address local misconceptions. The Initiative also promoted alternative treatments, such as traditional Thai herbal medicines – listed in the country’s National Essential Medicines List – for non-bacterial infections to discourage people from demanding antibiotics from their doctor (271). It targeted three conditions not requiring antibiotic treatment: upper respiratory infections, acute diarrhoea, and simple wounds. The programme focused on healthy ambulatory patients older than two years of age, and took care to exclude those who were hospitalized, diagnosed with diabetes or a compromised immune system, or suffering from serious co-morbidities.

ASU began as a network of researchers from Thailand’s Ministry of Public Health and pharmacists and doctors from Srinakharinwirot University and Chulalongkorn University. They piloted educational and training reforms to improve prescribing in 10 hospitals and 87 primary health centers in the Saraburi province, which had received seed money from WHO. During the pilot phase, the provincial health office monitored: antibiotic prescription rates; provider attitudes of effectiveness and knowledge of antibiotics; non-prescription rates in cases of non-bacterial infections; and patient health and satisfaction. Applying these same indicators, the second phase scaled-up this

intervention to 44 hospitals and 621 primary health centres in three provinces and two hospital networks. The National Health Security Office (NHSO) piloted a pay-for-performance system to realign financial incentives to prescribers and providers. Under the guidance of the FDA, local health authorities managed this initiative with additional assistance from the NHSO and the Health Systems Research Institute.

The Initiative’s third phase has seen the network grow to 22 public hospital systems in 15 provinces, with the focus on longer-term sustainability (271). The first phase of the ASU intervention offered a half-day training on clinical guidelines for physicians, nurses and pharmacists. These efforts were intended to reassure providers that antibiotics were neither appropriate nor necessary for patients with a viral infection. Health-care providers were also given posters and pamphlets to communicate better with patients, while also receiving white-light illuminators in lieu of flashlights to improve the diagnosis of sore throats.

The Initiative has a strongly decentralized approach that relies on engaging local partners from health care, government, and academia, to adapt guidelines to their own health care settings and communities. The partners included hospital directors, provincial health administrators, university researchers, medical and pharmacy students as well as local physicians, nurses and pharmacists. The ASU Initiative has encouraged ownership among local partners by enabling them to brand and design locally effective methods to improve the use of antibiotics in their communities, bolstered by regional and national support networks and educational and some financial guidance (271). The Initiative seeks to integrate these changes into local health care systems by influencing individual behaviour rather than enforcing guidelines through a heavy-handed, top-down

approach.

In Cha-lae District in Songkha Province, ASU advocates added the principles of appropriate use of antibiotics into their own local “health constitution,” and they signed memoranda of understanding with grocery store owners not to sell antibiotics over the counter. In the Muaklek District in Saraburi, the ASU network enlisted not only local hospitals, but also the community bank, which rewarded customers with reimbursements for groceries if they correctly completed a self-assessment quiz on how to care for oneself without antibiotics in the face of an upper respiratory infection, acute diarrhoea, or a simple wound. (272).

The first stage of the Initiative led to impressive declines in antibiotic prescription rates in hospitals (decreases were between 18% and 23%) and in primary health centres (between 39% and 46%) (271, 272) – a strong achievement given that the original goal aimed to reduce prescription rates by 10%. The third phase began in 2010 to ensure sustainability of these policy initiatives. Persuaded by the initial success of ASU, the National Health Security Office (NHSO) – responsible for universal health coverage for 47 million Thais – changed the capitated, pay-for-performance system to ensure greater compliance with antibiotic prescribing guidelines. It did so by moving from a process evaluation, relying on a checklist of key activities, to an output evaluation that measured the actual level of antibiotic prescriptions for upper respiratory infections and acute diarrhoeal cases.

In response to a need by providers to have other treatment options, ASU developed packages of herbal medicines for non-bacterial infections. These traditional Thai medicines were approved in the National Formulary for relieving symptoms of viral infections and were packaged in capsules similar to antibiotics.

However, herbal medicines are not without side effects, and the initiative is teaching providers that the best treatment at times may be watchful waiting.

An important goal of the Initiative was to lower consumer demand for antibiotics. It did so through an educational programme rolled out in participating pharmacies. When patients came in for prescriptions, pharmacists asked them to use a mirror to examine their own tonsils along with a tongue depressor and white light illuminator, and contrast this against side-by-side pictures of typical bacterial and viral throat infections. This allowed them to see when their symptoms did not appear to be caused by bacteria. The pharmacists also provided alternative herbal treatments to relieve the patients’ symptoms. While not totally preventing the over-the-counter purchase of antibiotics, the pilot study found that over 90% of the 998 patients fully recovered and more than 80% were satisfied with treatment outcomes (272).

These types of interventions could help address challenges in the fee-for-service model. The ASU Initiative has also looked into incentives under the Diagnosis-Related Group-based payment system and into establishing an audit system that would provide hospital-level comparisons. Where positive financial incentives may not suffice, these may, in the future, need to be complemented by negative financial incentives, or penalties.

The ASU Initiative in Thailand reveals the complex interplay between providers and patients, national guidelines and locally inspired efforts to implement them, and incentive systems and culturally mediated interventions. As it unfolded, the Initiative evolved in unanticipated ways into a network with multiple implementing partners and various sources of funding, with some agencies playing key informal

influencing roles, while others created and enforced more formal rules. The Initiative reveals the importance of local stakeholder ownership in overcoming long-held expectations and practices in a sustained way.

5.3.4 Kenya: Familia Nawiri social business initiative

This fourth case-study examines the role played by pharmaceutical companies through their social business initiatives, and the new forms of medicines supply and service provision these initiatives can create in LMIC health markets.

According to 2006 Nobel Peace Prize winner Muhammad Yunus, the two main business prototypes – organizations that seek to maximize profit and shareholder value; and not-for-profit organizations that seek to maximize social gain – are inadequate in addressing the global and systemic concerns around medicines access (273, 274). As a hybrid of both models, “social businesses” can be an effective alternative (275). Social businesses seek to maximize social good, but must also be financially profitable to cover their costs and offer a return on investment. In Yunus’ model, profit goes to those stakeholders who help fulfil the mission of these social businesses, rather than to shareholders.

This is not an easy task, however. Several businesses focusing on the world’s poor, or “bottom of the pyramid” populations, have had difficulty achieving both commercial and social value, particularly at a significant and sufficient scale (276). In the last five years, several pharmaceutical companies have begun social business or shared-value initiatives (277), including for example, a programme in China aimed at diabetes prevention and management (278) and the *Arogya Parivar* programme in India designed to increase the

availability and use of generic medicines for people living in rural India (279). While such initiatives can achieve substantial scale and generate profit – within four years, *Arogya Parivar* achieved financial sustainability by serving more than 42 million people in 31,000 villages across 10 states in India – unfortunately not much is known about how well they meet both commercial and social objectives.

Adapting the *Arogya Parivar* model from India, the company began the *Familia Nawiri* programme in 2012 in Kenya, where access to medicines is characterized by a lack of quality generics in the public sector; geographic and economic barriers that prevent access to medicines for the poor; overuse of antibiotics; and underuse of chronic disease treatment (280). In a 2009 household survey, 57% of respondents in the poorest households reported that they could not afford the medicines they need, and 48% of poor households with a chronically ill member had no medicines at home (281).

Familia Nawiri aims to provide access to needed care and selected essential medicines at affordable prices to the rural poor. The programme targets the country’s more than 600,000 individuals with incomes below US\$ 1 per day in more than 100,000 households. Health educators – community members who ideally have a degree in a health-related field – are engaged to raise awareness of basic health and social issues, and connect households with providers to receive care and medicines. The health educators are given a week’s training on key topics, including: personal and environmental hygiene; appropriate use of medicines; symptoms and treatment of respiratory infections, diarrhoea, diabetes, and hypertension; de-worming; and health insurance enrolment. Each health educator is responsible for two-to-three wards, covering about 12,000 households and 70,000 individuals, and working closely with the national

Social businesses seek to maximize social good, but must also be financially profitable to cover their costs and offer a return on investment. In Yunus’ model, profit goes to those stakeholders who help fulfil the mission of these social businesses, rather than to shareholders.

health system's community health workers to set up health camps.

The day-long health camps provide primary health care to about 300 community members at a time and are staffed by local physicians, nurses, diploma medical assistants, community health workers, and pharmaceutical technicians who either volunteer their time or are salaried employees of a contracted local private health care delivery organization. Clinical officers diagnose, prescribe, and refer to local hospitals as needed, and pharmaceutical technicians dispense medicines from the country's national essential medicines list that are procured locally from mission hospitals, the Mission for Essential Drugs Supply (MEDS), or private sector distributors. Drug prices are in line with the MEDS price guide and products are sourced from different manufacturers. Community members pay a flat KES 200 registration fee (about US\$ 2.30) for each camp visit, which covers consultations, laboratory tests, and medicines. *Familia Nawiri* covers all remaining costs. The *Familia Nawiri* initiative assumes that community members will continue to seek needed care outside of health camps, in public sector facilities or from the private providers who serve in the camps.

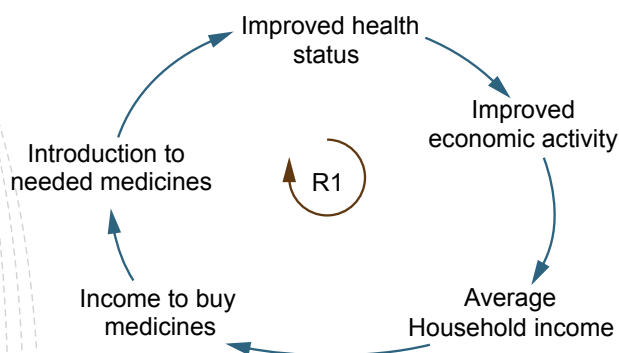
The *Familia Nawiri* programme seeks to be profitable through increased sales of generic medicines. Company representatives work with all health-care providers in the area to facilitate increased availability and prescription of the sponsoring company's products. Each representative targets between 300 and 500 clinical officers, nurses, and pharmacists.

As the programme expands, it seeks to facilitate the population's enrolment in micro-savings schemes and health insurance. *Familia Nawiri* sets up partnerships with a micro-savings organization; in community meetings, representatives explain micro-savings approaches and facilitate households' enrolment in health savings plans using the m-Pesa mobile savings platform (282, 283). Future plans include facilitating enrolment in the National Hospital Insurance Fund, which covers inpatient care at government and mission hospitals and using a mobile health platform to provide health education to communities. By 2017, the *Familia Nawiri* programme is expected to have reached 7 million villagers and all private providers in the country, and to have broken even financially.

The complexity of social business initiatives for improving access to essential medicines makes an initiative like *Familia Nawiri* a good candidate for a systems dynamics' analysis. (284, 285). Based on interviews with *Familia Nawiri* social business leaders and local health systems experts, case-study authors identified key relationships between actors and their hypothesized behaviours in the system and created a hypothetical conceptual model of the *Familia Nawiri* Initiative (see web annex for the case-study and detailed explanations of the model).

The conceptual model shown in Figure 5.2 indicates that at the heart of the programme is a single reinforcing feedback loop (R1).

Figure 5.2: Reinforcing feedback loop representing the *Familia Nawiri* social business model



This illustrates the hypothesis that improving access to quality medicines for the poor improves their health status, which in turn improves economic activity and household income, thus increasing the available financial resources to purchase medicines. If the medicines purchased are products of the social business company, this feedback loop will generate profit for the company, which can be invested in expanding the programme.

This core feedback loop exists in every health care system. What sets the *Familia Nawiri* programme apart from other typical systems is the network of stakeholders involved: the use of privately-supported health educators working with local community health care workers to raise awareness about health care and financing among the rural poor, combined with privately-run health camps to facilitate their access to care and a strengthened private-sector medicines supply system. Health camps are not new in Kenya; government officials and medical schools offer health camps periodically. However, the initiative has created a reliable schedule of health camps and emphasises the provision of high-quality care

through manageable staff-to-client ratios, increased availability of laboratory testing, and selection of medicines from the national essential medicines list, through which the target patient population has easier access to initial care. Regular follow-up care may be sought in subsequent health camps and from public and private sector providers. This continuity of attention leads to a second reinforcing loop in the system, as shown in Figure 5.3 below.

In the next analytical step, additional hypotheses are incorporated into the model in the form of causal loops, to represent the hypothesized effects of: promoting treatment adherence through continued provision of medicines in the private sector; financing via health savings accounts and microfinance opportunities for poor families; improved health of the participants on their lifespan and livelihoods; and the financial returns of the social business, as seen in Figure 5.4. Note that a more detailed analysis is provided in the web annex.

The further expanded conceptual model presented in the web annex illustrates effects of private sector medicines sales. It also shows

Figure 5.3: Interventions to create a growth loop for the ongoing purchase of medicines in the *Familia Nawiri* social business model

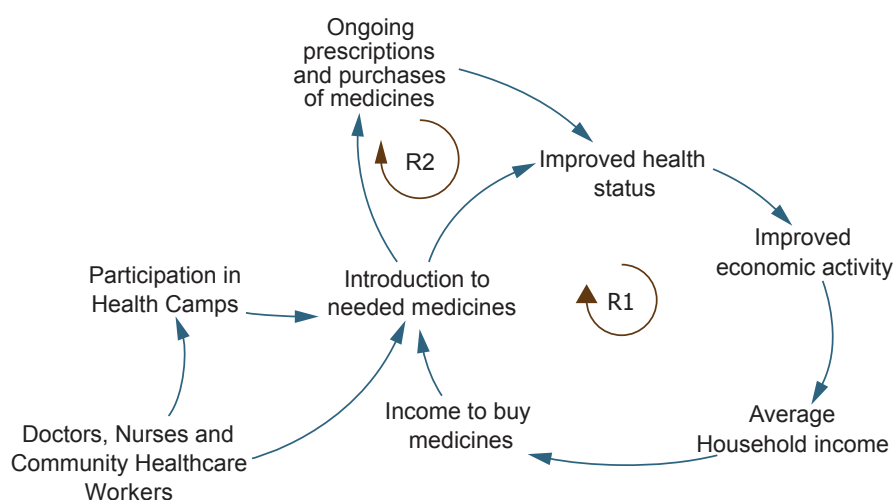
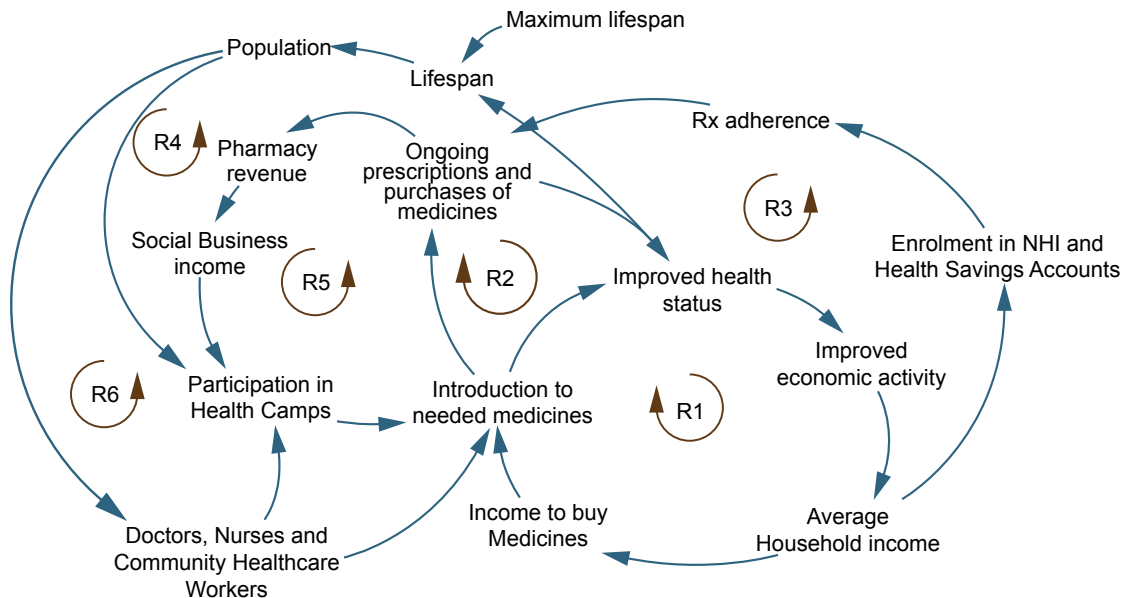


Figure 5.4: Expanded conceptual map of *Familia Nawiri*

The four case-studies described in this chapter are quite distinct, yet each highlights the need to acknowledge that many different stakeholders are central to health market systems.

that there are a number of factors that can interfere with the growth of the system, and need to be examined and managed in the programme. These include:

- ▶ Limited ability of health educators to effectively disseminate messages about prevention, health care, and accessing services through health camps to the target population;
- ▶ Community resistance to accessing health care services in health camps (e.g. due to fees, inconvenience, or poor service quality);
- ▶ Poor continuity of care due to low rates of engagement with local health workers and limited access to care in public and private sectors;
- ▶ Failure of patients to adhere to treatments, especially for chronic illnesses;
- ▶ Unnecessary use of medicines, such as antibiotics for viral infections; and

- ▶ Continued limited affordability of medicines.

5.4 Conclusions and recommendations

The four case-studies described in this chapter are quite distinct, yet each highlights the need to acknowledge that many different stakeholders are central to health market systems. The efforts captured by the case-studies were all initiated in response to a market failure involving medicines; each intervention took a different entry point in the system and followed different pathways. The main stakeholders targeted in each intervention illustrate different parts of the health market, from drug shop owners and dispensers (ADD0 case) to expert patients (*MoPoTsyo*) to physicians and pharmacists (ASU project), to a pharmaceutical-company initiated medicines supplier and health provider organization (*Familia Nawiri*).

These examples provide policy-makers with several intervention models. However, they should note that in each case, multiple

stakeholders play critical roles in both the design and implementation of the interventions. Paying attention to the demands of the population, or the intended beneficiaries of the health system, was something that each of the interventions did explicitly, and has been a critical part of their success. Beyond this, governments had other essential roles. Government agencies played a leading part in the ADDO and ASU cases, with the lead agencies having to navigate the separate interests of central and local governments. They also provided a permissive environment in the *MoPoTsyo* case and the *Familia Nawiri* case. Other characteristics of the case-studies that policy-makers should consider is that each of the cases involved external agencies, either to provide assistance to the design (ADDO case), or for evaluation and research (all cases). In each of the cases, as the enterprise grew in scale, management adapted by becoming increasingly decentralized, even if the original programmes were managed centrally.

Policy-makers and programme implementers should plan for an intervention changing over time, and to involve multiple components that address different aspects of the market system. In each of the cases discussed in this chapter, the interventions involved multiple components that evolved to adapt to the circumstances. Each of the interventions provided training, but never as the sole, or even main intervention. Finding ways to align incentives, and provide supervision and accountability has been critical in each case, but in different ways. This is because in each case, unintended consequences are a real threat (e.g. excessive drug prices in ADDO case; peer educators taking on roles beyond their abilities in the *MoPoTsyo* case; overuse of herbal medicines in the ASU case; and unaffordable prices or overuse of antibiotics in the *Familia Nawiri* case). It is important to note that none of the

interventions were implemented as originally designed. In order to better manage change, timely monitoring data has been important for frequent course corrections, while independent evaluations have also played important roles in informing these changes.

Although considerable challenges and opportunities remain, these case-studies provide a promising basis for an improved understanding of and innovative abilities to intervene in health market systems in the quest to ensure access and appropriate use of essential medicines in LMICs. The key considerations for policy-makers are that they should pursue strategies that involve the engagement of key stakeholders in both the supply and demand for essential medicines, build in flexible and multi-component interventions that are expected to change over time, pay attention to the incentives and institutions involved, and use data to examine both the intended and unintended outcomes of an intervention in an accountable way.

None of the interventions were implemented as originally designed. In order to better manage change, timely monitoring data has been important for frequent course corrections, while independent evaluations have also played important roles in informing these changes.

6

USING A SYSTEMS
PERSPECTIVE TO
INNOVATE IN ACCESS
TO MEDICINES

We must encourage and actively support decision-making that uses inclusive, multi-stakeholder processes representing the many voices and needs from across an LMIC health system.

Decision-making on medicines policies must use information and financing levers; decision-makers must routinely monitor the impacts of medicines policies and adapt strategies to continuously changing environments.

6.1 Introduction

The preceding chapters have highlighted the many challenges in ensuring equitable access, affordability and the appropriate use of medicines. In Chapter 2, we offered a historical perspective on the development of essential medicines and health systems, then identifying priority issues related to the access, affordability, and use of medicines in health systems in LMICs. The central argument in Chapter 3 framed medicines against the goals of universal health coverage and argued that an explicit focus on medicines is required to advance UHC. In Chapter 4, we highlighted innovative means for bringing new and existing medicines to people, including new public-private partnerships and efforts designed to increase the use of quality-assured generic products. Lastly, in Chapter 5, we examined the importance of health market systems in access to medicines, using four country case-studies to analyse different interventions designed to improve health markets and to address market failures in LMICs.

Taken together, the chapters illustrate the diverse and innovative ways in which LMICs have addressed key medicines challenges, while emphasizing the continued and even urgent need to find new solutions. In this chapter we summarize the key lessons from our analysis, and suggest actions to guide both the decision-making and research agenda as the field moves forward.

We believe that improving access to medicines requires three major approaches, along with an appreciation for several elements that crosscut each approach.

1. Recognizing the interconnected nature of all health system building blocks, a systems approach is crucial in improving access to medicines across LMICs. Access to medicines must be an explicit

focus in health system strengthening or universal health coverage efforts that target improved equity in health care access, quality, and financing.

Giving people access to the high-quality, affordable medicines they require can only occur within a context of stronger health systems that have reduced barriers to the full and equitable participation of populations across LMICs. In applying a systems approach to medicines – situating essential medicines against the full complexity of a health system so that we might better visualize how interventions in the pharmaceutical sector influence the rest of the health system and vice versa – we must encourage and actively support decision-making that uses inclusive, multi-stakeholder processes representing the many voices and needs from across an LMIC health system.

Within any system, there are competing policy objectives. Inevitably, these varying objectives challenge stakeholders' abilities to maximize equitable access to medicines and their appropriate use, efficiency, and (household and system) affordability. Decision-making on medicines policies must use information and financing levers; decision-makers must routinely monitor the impacts of medicines policies and adapt strategies to continuously changing environments.

2. Recognizing that access to medicines is much more than a series of interactions between patients and public health services, innovations for developing medicines and implementing medicines policies are essential to bring both novel and existing medicines to people.

In the development of novel medicines, we require innovations that engage multiple public- and private-sector partners, that build on

advances in information and communications technology, and that find sustainable ways of funding research and development that move beyond a dependency on sales revenue alone. Expanding access to novel, and often high-cost, products raises challenging clinical, ethical, economic, legal and political questions which, to be resolved, require routine multi-stakeholder engagement in fair and inclusive decision-making processes. Innovations for increasing the use of quality-assured generic products must include multi-pronged strategies that involve governments, payers, health care consumers, researchers, and the media.

3. Recognizing the many dynamics, factors and systems that influence pharmaceutical and health sector governance, it is crucial that we use the leverage of UHC and a systems-informed access to medicines approach to map, analyse and involve actors of influence, and to actively guide health market systems.

Improving the access to and appropriate use of medicines requires an understanding of the relevant actors, dynamics, factors and systems influencing pharmaceutical and health sector governance. And, as argued in Chapter 5, of crucial importance is a deeper understanding of health market systems. In recent years, these markets have expanded dramatically in LMICs, yet to date have not been given sufficient attention by policy-makers. Poorly-organized health market systems can negatively affect many aspects of health care, resulting in unneeded or harmful treatment, excessive and impoverishing costs, counterfeit and substandard products, and antibiotic resistance.

There are many potential points of innovation and intervention in a pharmaceuticals market system. Successful interventions engage multiple stakeholders, blending approaches that include training and capacity strengthening,

economic incentives, and regulatory and managerial controls. Such interventions must also take advantage of existing data to monitor both intended and unintended consequences of changes in systems in order to continuously adapt interventions – and to facilitate the accountability of different stakeholders.¹

Pharmaceutical market interventions should feature:

- ▶ the dynamic and sustained engagement of many different health system stakeholders.
- ▶ easily accessible information that can continually inform decisions on medicines policies and other interventions, while assessing their impacts and facilitating accountability.
- ▶ flexible policy and programme strategies that can adapt to continuously changing environments.

6.2 Essential cross-cutting elements: Engagement, information and adaptation

Cross-cutting each of the above approaches are three elements critical to both the decision-making and the research agenda: engaging diverse health system stakeholders, generating and using information to facilitate dialogue and inform decisions, and adapting to changing health systems. Considering each of these elements in turn creates a much more comprehensive, systems-informed vision of the way forward.

6.2.1 Engaging diverse health system stakeholders

Across the three major approaches to improving access to medicines is an overarching need

Innovations for increasing the use of quality-assured generic products must include multi-pronged strategies that involve governments, payers, health care consumers, researchers, and the media.

1. Accountability is defined here as the obligation of multiple health system stakeholders to provide information about, or justification for, their actions to others, with the possibility of sanctions for failure to comply with rules or to engage in appropriate actions (286).

Table 6.1: Examples of objectives, roles and responsibilities of key stakeholders in advancing the access, affordability and appropriate use of medicines

Stakeholders	Main objectives	Main roles and responsibilities
Central government	<ul style="list-style-type: none"> Offer political leadership Ensure national security Expand or maintain international relations and trade Ensure social and economic welfare 	<ul style="list-style-type: none"> Set, implement and enforce laws, regulations and policies Allocate resources Strategically plan and coordinate with state actors
Central ministries of health	<ul style="list-style-type: none"> Improve health of the population Strengthen health care and pharmaceutical systems Control expenditures on medicines Improve the access, affordability and appropriate use of medicines Provide a stewardship function for the health system that engages with key stakeholders 	<ul style="list-style-type: none"> Set, implement and enforce health-related laws, regulations and policies Allocate resources for health care Strategically plan and coordinate with actors in health system
Regional, district, provincial or municipal authorities	<ul style="list-style-type: none"> Maintain political leadership Ensure social and economic welfare 	<ul style="list-style-type: none"> Implement and enforce laws, regulations and policies Strategically plan and coordinate with state actors at the regional, provincial or municipal level
Regional, district, provincial or municipal health authorities	<ul style="list-style-type: none"> Ensure functioning health care system, including supply, financing, delivery and use of needed medicines 	<ul style="list-style-type: none"> Set, implement and enforce health-related laws, regulations and policies locally Allocate resources for health care locally Strategically plan and coordinate with actors in the local health system
Pharmaceutical manufacturers (local and international)	<ul style="list-style-type: none"> Sell medicines and turn a profit 	<ul style="list-style-type: none"> Produce and sell safe, high-quality essential medicines Agree to and/or engage in the generic production of medicines for LMIC use
Pharmaceutical distributors	<ul style="list-style-type: none"> Sell medicines and turn a profit 	<ul style="list-style-type: none"> Ensure timely, efficient delivery of essential needed medicines
Health care facilities (including primary, secondary, tertiary; public, private, and NGO)	<ul style="list-style-type: none"> Ensure health care service delivery operations Provide quality care Improve patients' satisfaction with care Balance income and expenditures, or make profit 	<ul style="list-style-type: none"> Implement health and medicines policies Deliver health care services Procure, stock, administer or dispense essential medicines

Stakeholders	Main objectives	Main roles and responsibilities
Health care providers (formal and informal)	Provide high-quality services Ensure patients' satisfaction with care Maintain income level or make a profit	Prescribe and dispense medicines
Patients and households	Obtain high-quality medicines at affordable prices	Pay for services and obtain medicines
Civil society	Represent interests of non-state actors Participate in strengthening the health care system Support individuals and households in their community	Advocate for the health care needs, including medicines, of the community Convene or participate in policy dialogues
Professional associations	Maintain or improve the rights and working conditions of health professionals Maintain or improve professional capacity and professional ethics	Negotiate relationships Train, license and monitor professionals
Health-financing agencies responsible for revenue collection, pooling and purchasing	Prioritize fund allocation Ensure appropriate use of funds Remain financially sustainable	Set financing rules for health care and medicines management strategies Pay for health care services and medicines
Bilateral and multilateral donors; philanthropic organizations	Contribute funding that works to strengthen health systems	Identify points within health systems that align with the medicines agenda for direct financial transfer, capacity building and other technical support

to engage diverse health system stakeholders. As different elements of systems must function in a coordinated fashion to ensure that medicines benefit lives – from the development, production, marketing, registration, selection, financing, procurement, distribution, prescribing, the dispensing and ultimately the use of medicines – the routine inclusion of multiple stakeholders is of critical importance. Patients, households, communities, researchers, service providers, procurement officers, drug distributors, local and central health system managers

and decision-makers, regulatory authorities, payers, national policy-makers in and outside the health sector, local and international pharmaceutical industries, civil society organizations (e.g. community organizations, professional associations, etc.), international funding agencies and development aid partners must all participate at various different points – and we must recognize that each has inherently different roles, values and objectives (as shown in Table 6.1).

The roles, responsibilities, interests, and constraints of key stakeholders, including their relationships and power dynamics, must be clearly understood, potentially through different situation- or stakeholder-analysis tools.

In fact, these roles, values and objectives determine their behaviours in systems. Taken together, they can enable, reinforce, or potentially undermine the goals of medicines policies and interventions (287). A crucial understanding, however, is that these stakeholders each contribute to stronger health systems in vastly different ways – without necessarily working together in harmony.

Two engagement factors are of particular importance in designing and implementing policies and interventions addressing the access, affordability and appropriate use of medicines. First, the roles, responsibilities, interests, and constraints of key stakeholders, including their relationships and power dynamics, must be clearly understood, potentially through different situation- or stakeholder-analysis tools (288, 289). To this end, Table 6.1 maps each of the major stakeholders related to the access to medicines movement in a typical health system, and outlines their main objectives and principal roles and responsibilities.

Second, inclusive dialogue built on transparent processes are vital to inform and guide decisions on policies and interventions. Given the multiplicity of actors in the health system, decisions on policies and interventions may not be able to satisfy all stakeholders – but they should meet the interests of the stakeholders crucial to the success and sustainability of those policies and interventions. The Alliance's 2009 Flagship Report on Systems Thinking presents 10 useful steps to involve system stakeholders in the design and evaluation of interventions (with the first four steps around intervention design presented in Box 6.1).

6.2.2 Generating and using information to facilitate dialogue and inform decisions

While tremendous amounts of strong data on medicines is currently collected as part of

existing health system processes, it must be collected and analysed in a more systematic way – with the particular intention of informing medicines policy and implementation decisions. At present, this data lies in a fragmented manner across different parts of a health system – with facilities, for instance monitoring use of medicines, and health financing agents monitoring medicines expenditures – leaving important observations and results often unlinked and not informing each other. This process of information gathering, synthesis and exchange must evolve, with robust linkages developed between health information and medicines, an issue we address in more detail in the subsections below.

A proposed set of core medicines indicators – along with information on data sources and collection instruments developed by WHO and other agencies – is presented in the web annex. These indicators can be used for: assessing current medicines situations; monitoring changes over time in the access, use, availability and financing of medicines; periodically evaluating the impacts of those changes; and promoting transparency through the exchange of information among major medicines stakeholders. Specific contexts will require the selection and adaptation of different indicators.

Assessing current medicines situations and routinely monitoring impacts of changes

Evaluating indicators of product quality, availability, volumes and appropriateness of medicines – including their utilization, prices, and expenditures – can highlight multiple perspectives and key issues that policy-makers may wish to address. The routine monitoring of such indicators allows for timely correction as an intervention is implemented. Data for core indicators may be collected at facilities (e.g. hospitals or dispensaries), through medicines

Inclusive dialogue built on transparent processes are vital to inform and guide decisions on medicines policies and interventions.

financing agencies (e.g. health-financing agencies), or in aggregated form at the national or sub-national levels. Data sources may include health care facility procurement and dispensing registers, payment data in health care financing organizations, national health and expenditure surveys, as well as aggregated, usually proprietary, sales volumes data.

Information on core medicines indicators based on both routine data and targeted surveys will help decision-makers understand the existing situation and identify policy targets. Routine data can be used for timely management decisions on the selection and procurement of medicines, reimbursement or cost-containment strategies, disease management, and annual planning or budgeting decisions.

While core medicines indicators can inform decision-makers about what is happening with respect to medicines at a particular point in time, they provide limited understanding or answers about why (e.g. why medicines availability is low, why out-of-pocket medicines

expenditures are high) and how these situations can improve. To understand why utilization or expenditures are at a certain level, additional information is needed to comprehend the behaviour of different system stakeholders. Core medicines indicators must be combined with quantitative and qualitative information on other health system components – such as health care financing, human resources, health service delivery, care seeking, and provider and community perceptions of medicines. Exploring the causes behind current medicines situations – from the perspective of multiple system stakeholders – must guide policy approaches and decisions.

Achieving equity in medicines access and use requires the identification of populations that are particularly neglected, under-covered, or underserved. Doing so will provide concrete guidance for decision-makers in formulating policies and designing implementation packages aimed at closing the equity gap.

In assessing equity, core medicines indicators

This process of information gathering, synthesis and exchange must evolve, with robust link-ages developed between health information and medicines

Information on core medicines indicators based on both routine data and targeted surveys will help decision-makers understand the existing situation and identify policy targets.

Box 6.1: Four steps to systems-informed intervention design (12)

In designing an intervention, the 2009 Report (12) recommends the following four steps:

- 1. Convene Stakeholders:** Identify and convene stakeholders including selected intervention designers and implementers, users of the health system, and representatives of the research community.
- 2. Collectively Brainstorm:** Collectively deliberate on possible system-wide effects of the proposed intervention.
- 3. Conceptualize Effects:** Develop a conceptual pathway mapping how the intervention will affect health and the health system through its sub-systems, and through the reaction and adaptation of health system stakeholders
- 4. Adapt and Redesign:** Adapt and redesign the proposed intervention to optimize synergies and other positive effects while avoiding or minimizing any potentially major negative effects.

In assessing equity, core medicines indicators must be measured by sub-populations defined by age, gender, socioeconomic quintiles, geographical location, ethnic groups, and other characteristics of disadvantaged or vulnerable populations.

must be measured by sub-populations defined by age, gender, socioeconomic quintiles, geographical location, ethnic groups, and other characteristics of disadvantaged or vulnerable populations. Disease-specific utilization and expenditure data are useful to understand whether patients with particular health conditions are currently neglected. Since health care and financing institutions routinely collect data, data is often only available for patients who can access services or are covered under health-financing arrangements. Understanding the lack of health care coverage and the needs of underserved populations requires reaching out to people who do not regularly use health services. This is mostly achieved through household surveys, larger population studies, or by triangulating data from multiple data sources.

Periodically evaluating the impacts of policies and interventions

Core medicines indicators can also be used for evaluating the effects of policies and interventions. To do so, they must be measured at different points in time before and after any change is implemented, and also from the perspectives of multiple stakeholders. For example, a reimbursement policy may reduce medicines expenditures by a health insurance scheme but in fact increase household out-of-pocket expenditures – which may particularly impact vulnerable populations. Gathering information regularly over time about impacts on multiple stakeholders is thus necessary to evaluate and adapt a medicines reimbursement policy.

Periodic evaluations can lead to corrective measures or the formulation of new policies and innovative interventions. They are not intended for routine management decisions but usually serve the purpose of strategic planning, broader policy reform, or new

intervention design.

Promoting transparency through the exchange of information among stakeholders

Not only does information about medicines exist in different parts of the health system, it is often under the responsibility of different stakeholders. For example, procurement agencies may have information on the sources, types, quality, and prices of the medicines they purchase, but may not have access to data on the population's need or ability to afford medicines – both of which are key factors that must inform procurement decisions. Prescribers make decisions based on clinical information including efficacy and safety, but may not know about medicines availability or prices, and the impact of those two factors on out-of-pocket expenditures.

Combining and triangulating data from multiple sources could significantly improve stakeholders' information on access, affordability and appropriate use in all parts of the system and guide decisions. Sharing data does require the full engagement of different stakeholders, and explicit agreements on governance and use of data in the system for improving access to medicines. Given that multiple stakeholders are likely to continue to be involved in the financing and provision of medicines, collating and sharing information from multiple stakeholders seems increasingly important to support system-wide management decisions, strategic planning, and broader policy reforms. Such information is also essential for working towards equity in pluralistic health care and financing systems.

6.2.3 Adapting to changing health systems

Most decision-makers are well aware of the complexity of the systems and structures for which they are responsible. They experience

challenges in implementing policies and interventions on a daily basis and intuitively know that change is not linear. That said, decision-makers must increasingly understand and plan for the shifting behaviours and responses of systems over time so that they might adapt policies and interventions accordingly. Whether in response to the unintended consequences of a policy strategy, to new challenges from emerging diseases, or to new opportunities arising from novel treatments, medicines strategies must ensure that the right incentives are in place to mitigate negative consequences and maximize positive outcomes.

While core medicines indicators are necessary to inform decision-makers and implementers of challenges and bottlenecks, or of successes essential to the replication and scaling-up of interventions, they are not sufficient on their own. Another set of indicators, referred to as “implementation outcomes variables” (11, 292) (see Table 6.2) are needed to assess how an intervention has been implemented, including the challenges faced.

Various methods are available to assess implementation outcomes, depending on the nature of the implementation problem and the needs and timeliness of decision-making. These methods draw on a wide variety of qualitative, quantitative and mixed-methods research approaches (11, 293). More importantly, this type of implementation research must be aligned with the needs of those who implement changes in systems; it should be seen as a core function of a programme or policy implementation and embedded in the programme cycle. Implementation research questions are often put forward by decision-makers or implementers who face challenges and ask relevant questions to solve them. Implementation research can be a powerful tool in facing implementation challenges and overcoming them through concrete assistance to decision-makers in applying both evidence and experience in their decisions (11, 293).

Whether in response to the unintended consequences of a policy, to new challenges from emerging diseases, or to new opportunities arising from novel treatments, medicines strategies must ensure that the right incentives are in place to mitigate negative consequences and maximize positive outcomes.

Box 6.2: Factors influencing the implementation of policy decisions or specific interventions

Damschroder et al. (292) outline the key factors that influence the implementation of policy decisions and/or specific interventions. These factors include:

- ▶ the underlying characteristics of policy decisions or interventions – i.e. whether they are flexible and adaptable, and whether they are based on an active process to engage stakeholders.
- ▶ the stakeholders involved, and their agency, choices, power relations, and predictable and unpredictable reactions.
- ▶ the implementation process itself, and whether it includes the use of data and feedback for active course correction.
- ▶ the inner and outer settings of the policy or implementation, including local contexts as well wider economic, social and political contexts.

6.3 A framework for moving forward

As discussed throughout this report, some of the key factors for improving the access to, affordability and appropriate use of medicines in LMICs are:

- ▶ the dynamic engagement of multiple stakeholders from across the health system, with particular reference to both the supply and demand sides of the pharmaceutical sector.
- ▶ the increased access to the types of information needed both to support decisions and to examine the intended and unintended outcomes of changes or interventions across the health system.
- ▶ multi-component and flexible interventions that are expected to change over time, and that are aligned with relevant stakeholders, incentives and institutions.

Table 6.2: Intervention implementation outcomes adapted from Peters et al (11, 293)

Implementation outcomes	Definition	Outcomes
Acceptability	Perception among stakeholders that an intervention is acceptable	User satisfaction with the intervention
Adoption	Intention, initial decision, or actions in employing an intervention	Utilization of services by users and utilization of processes or techniques by providers or managers
Appropriateness	Relevance of the intervention in a particular setting or for a particular target audience	Compatibility of intervention with other interventions in place, suitability to local context
Feasibility	The extent to which an intervention can be carried out in a particular setting	Practicality of intervention in everyday use
Fidelity	The degree to which an intervention is implemented according to original design	Adherence to original design and quality of implementation
Cost	Total cost of implementation as well as the incremental cost of the implementation strategy	Total cost and marginal cost
Coverage	The degree to which the target population receives the intervention	Effective coverage and penetration
Sustainability	The extent to which an intervention is maintained or institutionalized in a given setting	Continuation, institutionalization, and integration of the intervention

We propose the following three actions as a way forward:

1. Include access to medicines and their appropriate use as an explicit focus in health system strengthening and efforts towards universal health coverage. Approaches to improve equity in health care access, quality, and financing must address access to medicines. This includes ensuring that:

- ▶ diverse stakeholders related to access to medicines are a part of discussions and plans to strengthen health systems, promoting transparent decision processes, and accountability in the design and implementation of strategies – with a particular focus on equity.
- ▶ principles around the availability of quality-assured products, equitable access to medicines, and their appropriate and efficient use, and household and system affordability, are incorporated into the objectives of institutions that design and manage changes in the health system.
- ▶ core medicines indicators are included in metrics for assessing health systems performance.
- ▶ equitable medicines access, appropriate medicines use, and affordability of medicines are explicit principles underlying and informing UHC strategies. Decision-makers can take advantage of the convening power of the UHC agenda to develop multi-pronged pharmaceutical policy strategies when addressing financing, human resource development, service delivery, governance, health information system development, public education, and other aspects of system change that collectively lead towards UHC. Decision-makers can also bring together key actors involved in the medicines value chain, and link them

with those in other areas of the health system. Monitoring the approaches towards UHC should include the monitoring of medicines quality, availability, access, use, and affordability for different populations.

2. Recognize the needs for transparency and governance in the medicines sector within and across health systems, and then strengthen governance capacities.

Effective medicines stewardship should include all relevant stakeholders – including the informal sector, the public service-delivery sector, or the pharmaceutical industry – and requires ongoing innovation in institutional arrangements, and potentially a change in social norms and values (without which previously marginalized actors may remain so). Effectively organized, regulated and governed health market systems can, for instance, control medicines costs, reduce counterfeit and substandard products, respond to antibiotic resistance, and improve general levels of treatment.

Crucially, pluralistic health systems – encompassing the public and private sectors, private health markets, the informal health sector, and externally-driven, vertical approaches to treating disease – require a different, more innovative form of governance than those required for governing public health care delivery alone. *For essential medicines in any LMIC health system, there is more than one authority, more than one governance structure.* We must begin with acknowledging that this inherent diversity may be beneficial to achieving health system goals and advancing UHC. Following this acceptance, we can determine the stakeholders to involve in governance processes – in dialogue and engagement, for instance – the capacity strengthening and economic incentives required, the type of information that can routinely inform decisions on medicines policies and other interventions

For essential medicines in any LMIC health system, there is more than one authority, more than one governance structure.

(while assessing their impacts and facilitating accountability), and the needed regulatory and managerial controls.

3. Build more robust connections between information, medicines and decision-making. The need for connected and robust information processes cuts across the above two actions. Recognizing that vital information related to medicines lies in a fragmented manner across a health system – and that this information is central to a systems-oriented approach to medicines – there is an urgent need to develop innovative means for connecting not only information and medicines, but the stakeholders who gather, shape, control and make decisions based upon that information. One solution could be the creation of dynamic platforms to connect, share and discuss issues related to access to medicines. Ranging from the local to the global level, such platforms could include networks, communities of practice, knowledge translation platforms, and health system observatories – entities dedicated to sharing information and evidence on medicines, including experiences and other tacit knowledge from the field, as well as the formal or synthesized findings of health systems research and implementation research on medicines. Such platforms will ensure continuous learning and allow innovations to adapt to changes in systems over time.

Further innovation could include the adoption of an implementation research agenda, while also strengthening the capacity of researchers and decision-makers to generate and use information and evidence for sound medicines-related decision-making. This should include strengthening the capacity to monitor medicines indicators in order to move beyond routine monitoring to examine implementation challenges and promote a wide exchange of information that allows health systems to

engage in a continuous learning process.

As population needs and the health systems to meet those needs continue to evolve in an increasingly connected world, old challenges will persist and new ones will arise. No one stakeholder or single approach will suffice to ensure that medicines contribute to improving individual and population health and well-being. The emerging synergies between efforts to improve health equity, to strengthen health systems, and to provide universal health coverage, offer unprecedented opportunities to make appropriately-used medicines accessible and affordable across LMICs.

The time is now – for communities, for nations, for our community of nations – to act upon these synergies, and respond to the pressing medicines needs in LMICs.

Box 6.3: Medicines in health systems: An agenda for action

To take forward many of the recommendations made throughout this report – and ultimately create better health outcomes – health system decision-makers should:

- 1.** Incorporate policy-making principles that advance the availability of quality-assured products, the equitable access to medicines, their appropriate and efficient use, and ensure household and system affordability;

- 2.** Include a diverse set of medicines stakeholders in medicines policy and program design, implementation, monitoring and evaluation;

- 3.** Implement innovative stewardship arrangements for the multiple private and public channels through which medicines reach people;

- 4.** Use the convening power of UHC to integrate multi-pronged medicines policies and pharmaceutical management strategies into health care delivery and financing systems;

- 5.** Connect fragmented information on medicines, and also the stakeholders who collect and use this information;

- 6.** Include core medicines-focused indicators in assessments of health systems and UHC performance; and

- 7.** Enable continuous learning of the health system through implementation research on changes concerning medicines in systems.

REFERENCES

1. Essential medicines. Geneva: World Health Organization (http://www.who.int/medicines/services/essmedicines_def/en/, accessed 20 June 2014).
2. Hogerzeil HV, Mirza Z. Access to essential medicines as part of the right to health. In: *The world medicines situation 2011*. Geneva: World Health Organization; 2011 (<http://apps.who.int/medicinedocs/en/m/abstract/Js18772en/>, accessed 14 August 2014).
3. What is universal health coverage? In: Universal health coverage [website]. Geneva: World Health Organization (http://www.who.int/universal_health_coverage/en/index.html, accessed 28 January 2014).
4. Leadership priorities. Geneva: World Health Organization (http://www.who.int/about/who_reform/change_at_who/leadership_priorities/en/#.UzAE9PldVDA, accessed 20 June 2014).
5. Hogerzeil HV, Samson M, Casanovas JV, Rahmani-Ocra L. Is access to essential medicines as part of the fulfilment of the right to health enforceable through the courts? *Lancet*. 2006;368(9532):305–11. [http://dx.doi.org/10.1016/S0140-6736\(06\)69076-4](http://dx.doi.org/10.1016/S0140-6736(06)69076-4) PMID:16860700
6. Millennium Development Goals and beyond 2015. Goal 8: Develop a global partnership for development. Target 8.E. New York: United Nations (<http://www.un.org/millenniumgoals/global.shtml>, accessed 28 January 2014).
7. Hogerzeil HV. Essential medicines and human rights: what can they learn from each other? *Bull World Health Organ*. 2006;84(5):371–5. <http://dx.doi.org/10.2471/BLT.06.031153> PMID:16710546
8. Daniels N, Teagarden JR, Sabin JE. An ethical template for pharmacy benefits. *Health Aff (Millwood)*. 2003;22(1):125–37. <http://dx.doi.org/10.1377/hlthaff.22.1.125> PMID:12528844
9. Daniels N, Valencia-Mendoza A, Gelpi A, Avila MH, Bertozzi S. The art of public health: pneumococcal vaccine coverage in Mexico. *Lancet*. 2010;375(9709):114–5. [http://dx.doi.org/10.1016/S0140-6736\(10\)60037-2](http://dx.doi.org/10.1016/S0140-6736(10)60037-2) PMID:20109878
10. UHC-Medicines. Universal coverage and medicines: starting a dialogue (<http://uhc-medicines.org/1st-conference-washington-dc/>, accessed 19 August 2014).
11. Peters DH, Tran N, Adam T. Implementation research in health: a practical guide. Geneva: Alliance for Health Policy and Systems Research, World Health Organization; 2013.
12. De Savigny D, Adam T. Systems thinking for health systems strengthening. Geneva: Alliance for Health Policy and Systems Research, World Health Organization; 2009.
13. Laing R, Waning B, Gray A, Ford N, 't Hoen E. 25 years of the WHO essential medicines lists: progress and challenges. *Lancet*. 2003;361(9370):1723–9. [http://dx.doi.org/10.1016/S0140-6736\(03\)13375-2](http://dx.doi.org/10.1016/S0140-6736(03)13375-2) PMID:12767751
14. Health topics: essential medicines. Geneva: World Health Organization (http://www.who.int/topics/essential_medicines/en/, accessed 28 January 2014).
15. Resolution A/RES/66/2. Political declaration of the High-level Meeting of the General Assembly on the Prevention and Control of Non-communicable Diseases. New York: United Nations General Assembly; 2011 (http://www.un.org/ga/search/view_doc.asp?symbol=A/RES/66/2, accessed 19 August 2014).
16. Summary theme 8. International Conference on Improving the Use of Medicines, Antalya, Turkey, November 2011 (<http://www.inrud.org/icium2011-documents/upload/ICIUM2011-Theme-Summaries-16APRIL2012.pdf>, accessed 28 January 2014).
17. Hogerzeil HV, Liberman J, Wirtz VJ, Kishore SP, Selvaraj S, Kiddell-Monroe R, et al.; Lancet NCD Action Group. Promotion of access to essential medicines for non-communicable diseases: practical implications of the UN political declaration. *Lancet*. 2013;381(9867):680–9. [http://dx.doi.org/10.1016/S0140-6736\(12\)62128-X](http://dx.doi.org/10.1016/S0140-6736(12)62128-X) PMID:23410612
18. Cameron A, Ewen M, Ross-Degnan D, Ball D, Laing R. Medicine prices, availability, and affordability in 36 developing and middle-income countries: a secondary analysis. *Lancet*. 2009;373(9659):240–9. [http://dx.doi.org/10.1016/S0140-6736\(08\)61762-6](http://dx.doi.org/10.1016/S0140-6736(08)61762-6) PMID:19042012
19. Niëns LM, Cameron A, Van de Poel E, Ewen M, Brouwer WBF, Laing R. Quantifying the impoverishing effects of purchasing medicines: a cross-country comparison of the affordability of medicines in the developing world. *PLoS Med*. 2010;7(8):e1000333. <http://dx.doi.org/10.1371/journal.pmed.1000333> PMID:20824175
20. Wagner AK, Graves AJ, Reiss SK, Lecates R, Zhang F, Ross-Degnan D. Access to care and medicines, burden of health care expenditures, and risk protection: results from the World Health Survey. *Health Policy*. 2011;100(2-3):151–8. <http://dx.doi.org/10.1016/j.healthpol.2010.08.004> PMID:20828854
21. Reddy SR, Ross-Degnan D, Zaslavsky AM, Soumerai SB, Wagner AK. Health care payments in the Asia Pacific: validation of five survey measures of economic burden. *Int J Equity Health*. 2013;12(1):49. <http://dx.doi.org/10.1186/1475-9276-12-49> PMID:23822552
22. Lu Y, Hernandez P, Abegunde D, Edejer T. Medicine expenditures. In: *The world medicines situation 2011*. Geneva: World Health Organization; 2011 (<http://apps.who.int/medicinedocs/documents/s18767en/s18767en.pdf>, accessed 28 January 2014).
23. 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. Geneva: World Health Organization; 2012 (http://www.who.int/medicines/areas/rational_use/en, accessed 28 January 2014).
24. The rational use of drugs. Report of the conference of experts. Nairobi, Kenya, 25–29 November 1985. Geneva: World Health Organization. 1987 (<http://apps.who.int/medicinedocs/documents/s17054e/s17054e.pdf>, accessed 28 January 2014).
25. International Network on Rational Use of Drugs (<http://www.inrud.org/About-INRUD/index.cfm>, accessed 28 January 2014).
26. International Conference on Improving the Use of medicines, Antalya, Turkey, November 2011 (<http://www.icium.org/index.htm>, accessed 28 January 2014).
27. Everybody's business: strengthening health systems to improve health outcomes. Geneva: World Health Organization; 2007 http://www.who.int/healthsystems/strategy/everybodys_business.pdf, accessed 18 August 2014).
28. Equitable access to essential medicines: a framework for collective action. Geneva: World Health Organization; 2004 (WHO Policy Perspectives on Medicines, No. 8):1–6 (http://whqlibdoc.who.int/hq/2004/WHO_EDM_2004.4.pdf, accessed 28 January 2014).
29. Bigdeli M, Jacobs B, Tomson G, Laing R, Ghaffar A, Dujardin B, et al. Access to medicines from a health system perspective. *Health Policy Plan.* 2013;28(7):692–704. <http://dx.doi.org/10.1093/heapol/czs108> PMID:23174879
30. Anderson RA, McDaniel RR Jr. Managing health care organizations: where professionalism meets complexity science. *Health Care Manage Rev.* 2000;25(1):83–92. <http://dx.doi.org/10.1097/00004010-200001000-00010> PMID:10710732
31. Plsek PE, Wilson T. Complexity, leadership, and management in healthcare organisations. *BMJ.* 2001;323(7315):746–9. <http://dx.doi.org/10.1136/bmj.323.7315.746> PMID:11576986
32. Plsek PE, Greenhalgh T. Complexity science: The challenge of complexity in health care. *BMJ.* 2001;323(7313):625–8. <http://dx.doi.org/10.1136/bmj.323.7313.625> PMID:11557716
33. Kannampallil TG, Schauer GF, Cohen T, Patel VL. Considering complexity in healthcare systems. *J Biomed Inform.* 2011;44(6):943–7. <http://dx.doi.org/10.1016/j.jbi.2011.06.006> PMID:21763459
34. Sheikh K, Gilson L, Agyepong IA, Hanson K, Ssengooba F, Bennett S. Building the field of health policy and systems research: framing the questions. *PLoS Med.* 2011;8(8):e1001073. <http://dx.doi.org/10.1371/journal.pmed.1001073> PMID:21857809
35. Lall S, Bibile S. The political economy of controlling transnationals: the pharmaceutical industry in Sri Lanka (1972–1976). *World Dev.* 1977;5(8):677–97. [http://dx.doi.org/10.1016/0305-750X\(77\)90085-7](http://dx.doi.org/10.1016/0305-750X(77)90085-7)
36. Greene JA. Making medicines essential: the emergent centrality of pharmaceuticals in global health. *Biosocieties.* 2011;6(1):10–33. <http://dx.doi.org/10.1057/biosoc.2010.39>
37. Laing R, Waning B, Gray A, Ford N, 't Hoen E. 25 years of the WHO essential medicines lists: progress and challenges. *Lancet.* 2003;361(9370):1723–9. [http://dx.doi.org/10.1016/S0140-6736\(03\)13375-2](http://dx.doi.org/10.1016/S0140-6736(03)13375-2) PMID:12767751
38. Managing access to medicines and health technologies (MDS-3). Arlington (VA): Management Sciences for Health; 2012 (<http://www.msh.org/news-events/press-room/managing-drug-supply-third-edition-now-available-online>, accessed 20 June 2014).
39. Prequalification programme. Geneva: World Health Organization (<http://apps.who.int/prequal/>, accessed 29 July 2014)
40. Medicines prices: a new approach to measurement. Geneva: World Health Organization and Health Action International; 2003 (<http://www.haiweb.org/medicineprices/news/31122008/Medicine%20Prices%20Manual%202003.pdf>, accessed 20 June 2014).
41. Medicines Transparency Alliance (MeTA) core tools ([http://www.medicines Transparency Alliance \(MeTA\) core tools](http://www.medicines Transparency Alliance (MeTA) core tools), accessed 20 June 2014).
42. van Olmen J, Marchal B, Van Damme W, Kegels G, Hill PS. Health systems frameworks in their political context: framing divergent agendas. *BMC Public Health.* 2012;12(1):774. <http://dx.doi.org/10.1186/1471-2458-12-774> PMID:22971107
43. Rowden R. The ghosts of user fees past: exploring accountability for victims of a 30-year economic policy mistake. *Health Hum Rights.* 2013;15(1):E175–85. PMID:25006085
44. The world health report. Health systems: improving performance. Geneva: World Health Organization; 2000 (<http://www.who.int/whr/2000/en/>, accessed 18 August 2014).
45. WHA58.33. Sustainable health financing, universal coverage and social health insurance. In: Fifty-eighth World Health Assembly, Geneva, 16–25 May 2005. Resolutions and decisions, annex. Geneva: World Health Organization; 2005:124–6 (http://apps.who.int/gb/ebwha/pdf_files/WHA58-REC1/english/A58_2005_REC1-en.pdf, accessed 19 August 2014).
46. The world health report. Health systems financing: the path to universal coverage. Geneva: World Health Organization; 2010 (<http://www.who.int/whr/2010/en/>, accessed 18 August 2014).
47. World development report 1993: investing in health. Washington (DC): World Bank; 1993 (<https://openknowledge.worldbank.org/handle/10986/5976>, accessed 20 June 2014).
48. Jamison DT, Summers LH, Alleyne G, Arrow KJ, Berkley S, Binagwaho A, et al. Global health 2035: a world converging

- within a generation. *Lancet*. 2013;382(9908):1898–955. [http://dx.doi.org/10.1016/S0140-6736\(13\)62105-4](http://dx.doi.org/10.1016/S0140-6736(13)62105-4) PMID:24309475
49. Macroeconomics and health: investing in health for economic development. Report of the Commission on Macroeconomics and Health. Geneva: World Health Organization; 2001 (<http://whqlibdoc.who.int/publications/2001/924154550x.pdf>, accessed 20 June 2014).
50. Das P, Samarasekera U. The Commission on Macroeconomics and Health: 10 years on. *Lancet*. 2011;378(9807):1907–8. [http://dx.doi.org/10.1016/S0140-6736\(11\)61828-X](http://dx.doi.org/10.1016/S0140-6736(11)61828-X) PMID:22145166
51. Hoen E, Berger J, Calmy A, Moon S. Driving a decade of change: HIV/AIDS, patents and access to medicines for all. *J Int AIDS Soc*. 2011;14(1):15. <http://dx.doi.org/10.1186/1758-2652-14-15> PMID:21439089
52. Bond P. Globalization, pharmaceutical pricing, and South African health policy: managing confrontation with U.S. firms and politicians. *Int J Health Serv*. 1999;29(4):765–92. <http://dx.doi.org/10.2190/4MA6-53E3-LE1X-C1YY> PMID:10615573
53. Clinton Foundation Health Access Initiative (<http://www.clintonfoundation.org/our-work/clinton-health-access-initiative>, accessed 20 June 2014).
54. Global Fund to Fight AIDS, Tuberculosis and Malaria (<http://www.theglobalfund.org/en/about/>, accessed 20 June 2014).
55. United States President's Emergency Plan for AIDS Relief (<http://www.pepfar.gov/press/c19573.htm>, accessed 20 June 2014).
56. UNITAID: innovative financing to shape markets for HIV/AIDS, malaria and tuberculosis (<http://www.unitaid.eu/en/>, accessed 20 June 2014).
57. Krishna RJ, Whalen J. Novartis loses Glivec patent battle in India. *Wall Street Journal*. 1 April 2013 (<http://online.wsj.com/news/articles/SB10001424127887323296504578395672582230106>, accessed 20 June 2014).
58. Securing IP and access to medicine: is oncology the next HIV? Danbury (CT): IMS Consulting Group; 2013 (http://www.imshealth.com/deployedfiles/imshealth/Global/Content/Home%20Page%20Content/High-Growth%20Markets/Securing_IP_and_Access_to_Medicine_in_Emerging%20Markets.pdf, accessed 20 June 2014).
59. Rabkin M, El-Sadr WM. Why reinvent the wheel? Leveraging the lessons of HIV scale-up to confront non-communicable diseases. *Glob Public Health*. 2011;6(3):247–56. <http://dx.doi.org/10.1080/17441692.2011.552068> PMID:21390970
60. Chronic care of HIV and noncommunicable diseases: how to leverage the HIV experience. Geneva: Joint United Nations Programme on HIV/AIDS; 2011 (UNAIDS/JC2145E; http://www.unaids.org/en/media/unaids/contentassets/documents/unaidspublication/2011/20110526_JC2145_Chronic_care_of_HIV.pdf, accessed 19 August 2014).
61. MDG Gap Task Force Report 2013. Millennium Development Goal 8: the global partnership for development: the challenge we face. New York: United Nations (http://www.un.org/en/development/desa/policy/mdg_gap/mdg_gap2013/mdg_report_2013_en.pdf, accessed 20 June 2014).
62. Cameron A, Roubos I, Ewen M, Mantel-Teeuwisse AK, Leufkens HGM, Laing RO. Differences in the availability of medicines for chronic and acute conditions in the public and private sectors of developing countries. *Bull World Health Organ*. 2011;89(6):412–21. <http://dx.doi.org/10.2471/BLT.10.084327> PMID:21673857
63. From access to adherence: the challenges of antiretroviral treatment. Studies from Botswana, Tanzania and Uganda. University of Amsterdam, World Health Organization and Royal Tropical Institute; 2006 (<http://apps.who.int/medicinedocs/en/d/Js13400e/>, accessed 20 June 2014).
64. Knaul FM, Wong R, Arreola-Ornelas H, Méndez O; Network on Health Financing and Social Protection in Latin America and the Caribbean (LANET). Household catastrophic health expenditures: a comparative analysis of twelve Latin American and Caribbean Countries. *Salud Publica Mex*. 2011;53 Suppl 2:s85–95. PMID:21877097
65. Yadav P, Lega Tata H, Babaley M. Storage and supply chain management. In: The world medicines situation. Geneva: World Health Organization; 2011 (<http://apps.who.int/medicinedocs/documents/s20037en/s20037en.pdf>, accessed 20 June 2014).
66. Summary, theme 7. International Conference on Improving the Use of Medicines, Antalya, Turkey, November 2011 (<http://www.inrud.org/icium2011-documents/upload/ICIUM2011-Theme-Summaries-16APRIL2012.pdf>, accessed 20 June 2014).
67. Faden L, Vialle-Valentin C, Ross-Degnan D, Wagner A. Active pharmaceutical management strategies of health insurance systems to improve cost-effective use of medicines in low- and middle-income countries: a systematic review of current evidence. *Health Policy*. 2011;100(2-3):134–43. <http://dx.doi.org/10.1016/j.healthpol.2010.10.020> PMID:21185616
68. Summary, theme 14. International Conference on Improving the Use of Medicines, Antalya, Turkey, November 2011 (<http://www.inrud.org/icium2011-documents/upload/ICIUM2011-Theme-Summaries-16APRIL2012.pdf>, accessed 20 June 2014).
69. Holloway K, van Dijk L. Rational use of medicines. In: The world medicines situation. Geneva: World Health Organization; 2011 (<http://apps.who.int/medicinedocs/documents/s18064en/s18064en.pdf>, accessed 20 June 2014).
70. 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. Geneva: World Health Organization; 2012 (http://apps.who.int/iris/bitstream/10665/75828/1/WHO_EMP_MAR_2012.3_eng.pdf, accessed 20 June 2014).
71. Aitken M, Gorokhovich L. Advancing the responsible use of

- medicines: applying levers for change. IMS Institute for Healthcare Informatics; 2012 (http://www.imshealth.com/ims/Global/Content/Insights/IMS%20Institute%20for%20Healthcare%20Informatics/Responsible%20Use%20of%20Medicines/IHII_Advancing_Responsible_Use_of_Meds_Report.pdf, accessed 20 June 2014).
72. World Health Organization. The benefits and risks of self-medication. WHO Drug Information. 2000;14:1–2.
73. Connelly P, Rosen S. Treatment of HIV/AIDS at South Africa's largest employers: myth and reality. *S Afr Med J*. 2006;96(2):128–33. PMID:16532081
74. Patel A, Gauld R, Norris P, Rades T. "This body does not want free medicines": South African consumer perceptions of drug quality. *Health Policy Plan*. 2010;25(1):61–9. <http://dx.doi.org/10.1093/heapol/czp039> PMID:19726560
75. Wagner AK, Graves AJ, Fan Z, Walker S, Zhang F, Ross-Degnan D. Need for and access to health care and medicines: are there gender inequities? *PLoS ONE*. 2013;8(3):e57228. <http://dx.doi.org/10.1371/journal.pone.0057228> PMID:23505420
76. Stephens P, Ross-Degnan D, Wagner AK. Does access to medicines differ by gender? Evidence from 15 low and middle income countries. *Health Policy*. 2013;110(1):60–6. <http://dx.doi.org/10.1016/j.healthpol.2013.01.016> PMID:23422029
77. National policy on traditional medicine and regulation of herbal medicines: report of a WHO Global Survey. Geneva: World Health Organization; 2005 (<http://apps.who.int/medicinedocs/en/d/Js7916e/2.html#Js7916e.2>, accessed 20 June 2014).
78. Attaran A, Barry D, Basheer S, Bate R, Benton D, Chauvin J, et al. How to achieve international action on falsified and sub-standard medicines. *BMJ*. 2012;345 nov13 22:e7381. <http://dx.doi.org/10.1136/bmj.e7381> PMID:23149211
79. Burki T. The real cost of counterfeit medicines. *Lancet Infect Dis*. 2010;10(9):585–6. [http://dx.doi.org/10.1016/S1473-3099\(10\)70173-0](http://dx.doi.org/10.1016/S1473-3099(10)70173-0) PMID:20815112
80. Newton PN, Amin AA, Bird C, Passmore P, Dukes G, Tomson G, et al. The primacy of public health considerations in defining poor quality medicines. *PLoS Med*. 2011;8(12):e1001139. <http://dx.doi.org/10.1371/journal.pmed.1001139> PMID:22162953
81. Summary, theme 2. International Conference on Improving the Use of Medicines, Antalya, Turkey, November 2011 (<http://www.inrud.org/icium2011-documents/upload/ICIUM2011-Theme-Summaries-16APRIL2012.pdf>, accessed 20 June 2014).
82. QUAMED: quality medicines for all (<http://www.quamed.org/en/home.aspx>, accessed 20 June 2014).
83. Trouiller P, Oliaro P, Torreele E, Orbinski J, Laing R, Ford N. Drug development for neglected diseases: a deficient market and a public-health policy failure. *Lancet*. 2002;359(9324):2188–94. [http://dx.doi.org/10.1016/S0140-6736\(02\)09096-7](http://dx.doi.org/10.1016/S0140-6736(02)09096-7) PMID:12090998
84. Report of the third partners' meeting on better medicines for children. Geneva: World Health Organization; 2011 (http://www.who.int/childmedicines/progress/3rd_partners_meeting.pdf, accessed 20 June 2014).
85. Correa C, Matthews D. Discussion paper: the DOHA declaration ten years on and its impact on access to medicines and the right to health. New York: United Nations Development Programme, Bureau for Development Policy; 2011 (http://www.undp.org/content/dam/undp/library/hiv/aids/Discussion_Paper_Doha_Declaration_Public_Health.pdf, accessed 20 June 2014).
86. Stop TB partnership (<http://www.stoptb.org/gdf/>, accessed 20 June 2014).
87. Reddy M, Gill SS, Kalkar SR, Wu W, Anderson PJ, Rochon PA. Oral drug therapy for multiple neglected tropical diseases: a systematic review. *JAMA*. 2007;298(16):1911–24. <http://dx.doi.org/10.1001/jama.298.16.1911> PMID:17954542
88. Pedrique B, Strub-Wourgaft N, Some C, Oliaro P, Trouiller P, Ford N, et al. The drug and vaccine landscape for neglected diseases (2000–11): a systematic assessment. *Lancet Glob Health*. 2013;1(6):e371–9. [http://dx.doi.org/10.1016/S2214-109X\(13\)70078-0](http://dx.doi.org/10.1016/S2214-109X(13)70078-0) PMID:25104602
89. Leisinger KM, Garabedian LF, Wagner AK. Improving access to medicines in low and middle income countries: corporate responsibilities in context. *South Med Rev*. 2012;5(2):3–8. PMID:23535994
90. Summary, theme 17 International Conference on Improving the Use of Medicines, Antalya, Turkey, November 2011 (<http://www.inrud.org/icium2011-documents/upload/ICIUM2011-Theme-Summaries-16APRIL2012.pdf>, accessed 20 June 2014).
91. Haupt S, Krämer A. Bringing medicines to low income markets. A guide to creating inclusive business models. Berlin: German Federal Ministry for Economic Cooperation and Development (BMZ); 2012 (<http://www.giz.de/Wirtschaft/de/downloads/giz2012-0025en-medicines-low-income-markets.pdf>, accessed 20 June 2014).
92. Access to medicines index: what is the index? (<http://www.accessmedicineindex.org/what-index>, accessed 18 August 2014).
93. Hogerzeil HV. Big Pharma and social responsibility – the access to medicine index. *N Engl J Med*. 2013;369(10):896–9. <http://dx.doi.org/10.1056/NEJMp1303723> PMID:24004116
94. O'Connell T, Rasanathan K, Chopra M. What does universal health coverage mean? *Lancet*. 2014;383(9913):277–9. [http://dx.doi.org/10.1016/S0140-6736\(13\)60955-1](http://dx.doi.org/10.1016/S0140-6736(13)60955-1) PMID:23953765
95. Resolution A/RES/67/81. Global health and foreign policy. New York: United Nations General Assembly; 2013 (http://apps.who.int/gb/ebwha/pdf_files/WHA58-REC1/english/A58_2005_REC1-en.pdf, accessed 19 August 2014).

96. The world health report. Research for universal health coverage. Geneva: World Health Organization; 2013 (http://apps.who.int/iris/bitstream/10665/85761/2/9789240690837_eng.pdf, accessed 18 August 2014).
97. Brearly L, Marten R, O'Connell T. Universal health coverage: a commitment to close the gap. New York (NY): Rockefeller Foundation, Save the Children, United Nations Children's Fund, World Health Organization; 2013 (<http://www.rockefellerfoundation.org/uploads/files/57e8a407-b2fc-4a68-95db-b6da680d8b1f.pdf>, accessed 18 August 2014).
98. Averill C. Universal health coverage: why health insurance schemes are leaving the poor behind. Oxford: Oxfam; 2013 (Oxfam Briefing Paper 176) (http://www.oxfam.org/sites/www.oxfam.org/files/bp176-universal-health-coverage-091013-sum-en_.pdf, accessed 20 June 2014).
99. World Health Report 2013: Research for universal health coverage. Dr Margaret Chan, Director-General of the World Health Organization, Remarks at the launch of the World Health Report 2013, Beijing, China, 15 August 2013 (http://www.who.int/dg/speeches/2013/whr_20130815/en/, accessed 20 June 2014).
100. Holloway KA, Ivanovska V, Wagner AK, Vialle-Valentin C, Ross-Degnan D. Have we improved use of medicines in developing and transitional countries and do we know how to? Two decades of evidence. *Trop Med Int Health*. 2013;18(6):656–64. <http://dx.doi.org/10.1111/tmi.12123> PMID:23648177
101. Holloway KA, Ivanovska V, Wagner AK, Vialle-Valentin C, Ross-Degnan D. Prescribing for acute childhood infections in developing and transitional countries, 1990–2009. *Paediatr Int Child Health*. 2014;Feb 6:2046905514Y0000000115. [Epub ahead of print]
102. The global use of medicines: outlook through 2017. IMS Institute for Healthcare informatics; 2013 (http://www.imshealth.com/deployedfiles/imshealth/Global/Content/Corporate/IMS%20Health%20Institute/Reports/Global_Use_of_Meds_Outlook_2017/IIHI_Global_Use_of_Meds_Report_2013.pdf, accessed 20 June 2014).
103. Mendis S, Fukino K, Cameron A, Laing R, Filipe A Jr, Khatib O, et al. The availability and affordability of selected essential medicines for chronic diseases in six low- and middle-income countries. *Bull World Health Organ*. 2007;85(4):279–88. <http://dx.doi.org/10.2471/BLT.06.033647> PMID:17546309
104. Medicines use in primary care in developing and transitional countries: fact book summarizing results from studies reported between 1990 and 2006. Geneva: World Health Organization; 2009.
105. Laxminarayan R, Duse A, Wattal C, Zaidi AK, Wertheim HF, Sumpradit N, et al. Antibiotic resistance – the need for global solutions. *Lancet Infect Dis*. 2013;13(12):1057–98. [http://dx.doi.org/10.1016/S1473-3099\(13\)70318-9](http://dx.doi.org/10.1016/S1473-3099(13)70318-9) PMID:24252483
106. Yusuf S, Islam S, Chow CK, Rangarajan S, Dagenais G, Diaz R, et al.; Prospective Urban Rural Epidemiology (PURE) Study Investigators. Use of secondary prevention drugs for cardiovascular disease in the community in high-income, middle-income, and low-income countries (the PURE Study): a prospective epidemiological survey. *Lancet*. 2011;378(9798):1231–43. [http://dx.doi.org/10.1016/S0140-6736\(11\)61215-4](http://dx.doi.org/10.1016/S0140-6736(11)61215-4) PMID:21872920
107. Bowry AD, Shrank WH, Lee JL, Stedman M, Choudhry NK. A systematic review of adherence to cardiovascular medications in resource-limited settings. *J Gen Intern Med*. 2011;26(12):1479–91. <http://dx.doi.org/10.1007/s11606-011-1825-3> PMID:21858602
108. Shahrawat R, Rao KD. Insured yet vulnerable: out-of-pocket payments and India's poor. *Health Policy Plan*. 2012;27(3):213–21. <http://dx.doi.org/10.1093/heapol/czr029> PMID:21486910
109. Yip W, Hsiao WC. Non-evidence-based policy: how effective is China's new cooperative medical scheme in reducing medical impoverishment? *Soc Sci Med*. 2009;68(2):201–9. <http://dx.doi.org/10.1016/j.socscimed.2008.09.066> PMID:19019519
110. UN Commission on Life-Saving Commodities for Women and Children. Commissioner's Report September 2012. New York: United Nations; 2012 (http://www.unicef.org/media/files/UN_Commission_Report_September_2012_Final.pdf, accessed 1 June 2013).
111. Piette JD, Heisler M, Wagner TH. Problems paying out-of-pocket medication costs among older adults with diabetes. *Diabetes Care*. 2004;27(2):384–91. <http://dx.doi.org/10.2337/diacare.27.2.384> PMID:14747218
112. Global Health Observatory. Geneva: World Health Organization; 2013 (<http://www.who.int/gho/en/>, accessed 20 June 2014).
113. Cancer Mondial. Lyon: International Agency for Research on Cancer; 2013 (<http://www-dep.iarc.fr>, accessed 20 June 2014).
114. Clinical guidelines 2013. London: National Institute for Health and Care Excellence; 2013 (<http://www.nice.org.uk/guidance>, accessed 20 June 2014).
115. Simoens S. Health economic assessment: a methodological primer. *Int J Environ Res Public Health*. 2009;6(12):2950–66. <http://dx.doi.org/10.3390/ijerph6122950> PMID:20049237
116. Medical devices: health technology assessment. Geneva: World Health Organization (http://www.who.int/medical_devices/assessment/en/, accessed 20 August 2014).
117. Donaldson C, Bate A, Brambley P, Waldner H. Moving forward on rationing: an economic view. *BMJ*. 2008;337:a1872. <http://dx.doi.org/10.1136/bmj.a1872> PMID:18845596
118. Quality assurance and safety of medicines: challenges and strategic directions. Geneva: World Health Organization; 2013 (http://www.who.int/medicines/about/qsm_strategy/en/,

accessed 20 June 2014).

119. Laing R, Hogerzeil H, Ross-Degnan D. Ten recommendations to improve use of medicines in developing countries. *Health Policy Plan.* 2001;16(1):13–20. PMID: 11238425

120. Drugs and therapeutics committees: a practical guide. Geneva: World Health Organization; 2003 (<http://apps.who.int/medicinedocs/pdf/s4882e/s4882e.pdf>, accessed 20 August 2014).

121. Aaserud M, Dahlgren AT, Kösters JP, Oxman AD, Ramsay C, Sturm H. Pharmaceutical policies: effects of reference pricing, other pricing, and purchasing policies. *Cochrane Database Syst Rev.* 2006;(2):CD005979. PMID:16625648

122. Austvoll-Dahlgren A, Aaserud M, Vist G, Ramsay C, Oxman AD, Sturm H, et al. Pharmaceutical policies: effects of cap and co-payment on rational drug use. *Cochrane Database Syst Rev.* 2008;(1):CD007017. PMID:18254125

123. Sturm H, Austvoll-Dahlgren A, Aaserud M, Oxman AD, Ramsay C, Vernby A, et al. Pharmaceutical policies: effects of financial incentives for prescribers. *Cochrane Database Syst Rev.* 2007;(3):CD006731. PMID:17636851

124. Lu CY, Ross-Degnan D, Soumerai SB, Pearson S-A. Interventions designed to improve the quality and efficiency of medication use in managed care: a critical review of the literature – 2001–2007. *BMC Health Serv Res.* 2008;8(1):75. <http://dx.doi.org/10.1186/1472-6963-8-75> PMID:18394200

125. Carapinha JL, Ross-Degnan D, Desta AT, Wagner AK. Health insurance systems in five sub-Saharan African countries: medicine benefits and data for decision making. *Health Policy.* 2011;99(3):193–202. <http://dx.doi.org/10.1016/j.healthpol.2010.11.009> PMID:21167619

126. Chu X, Chen Q, Fang X. Can national health insurance programs improve health outcomes? Re-examining the case of the new cooperative medical scheme in rural China. Joint Annual Meeting Agricultural and Applied Economics Association (AAEA) & Canadian Agricultural Economics Society (CAES), Washington (DC), 4–6 August 2013 (http://ageconsearch.umn.edu/bitstream/150488/2/AAEA_2013_Chen%20%288%29.pdf, accessed 13 July 2014).

127. UHC Forward. Indonesia (<http://uhcforward.org/content/Indonesia>, accessed 20 June 2014).

128. Harimurti P, Pambudi E, Pigazzini A, Tandon A. The nuts and bolts of Jamkesmas: Indonesia's government-financed health coverage programme. Washington (DC): World Bank; 2013.

129. National Health Insurance Scheme. Annual report 2011. Accra: National Health Insurance Authority; 2011 (<http://www.nhis.gov.gh/files/annualreport2011.pdf>, accessed 20 June 2014).

130. Popular S. Mexico, one of the few countries that achieved universal health coverage. Mexico DF: Comisión Nacional de Protección Social en Salud; 2012.

131. Gutierrez JP, Hernandez-Avila M, Lee GM. Cobertura universal en salud: los retos del monitoreo y la afiliación en jóvenes. Cuernavaca: Instituto Nacional de Salud Pública; 2012 (<http://ensanut.insp.mx/doctos/analiticos/CoberturaUniversal.pdf>, accessed 19 August 2014).

132. Fang Y, Wagner AK, Yang S, Jiang M, Zhang F, Ross-Degnan D. Access to affordable medicines after health reform: evidence from two cross-sectional surveys in Shaanxi Province, western China. *Lancet Glob Health.* 2013;1(4):e227–37. [http://dx.doi.org/10.1016/S2214-109X\(13\)70072-X](http://dx.doi.org/10.1016/S2214-109X(13)70072-X) PMID:25104348

133. Yip WC, Hsiao WC, Chen W, Hu S, Ma J, Maynard A. Early appraisal of China's huge and complex health-care reforms. *Lancet.* 2012;379(9818):833–42. [http://dx.doi.org/10.1016/S0140-6736\(11\)61880-1](http://dx.doi.org/10.1016/S0140-6736(11)61880-1) PMID:22386036

134. Witter S, Garshong B. Something old or something new? Social health insurance in Ghana. *BMC Int Health Hum Rights.* 2009;9(1):20. <http://dx.doi.org/10.1186/1472-698X-9-20> PMID:19715583

135. Blanchet NJ, Fink G, Osei-Akoto I. The effect of Ghana's National Health Insurance Scheme on health care utilisation. *Ghana Med J.* 2012;46(2):76–84. PMID:22942455

136. Barimah KB, Mensah J. Ghana's National Health Insurance Scheme: insights from members, administrators and health care providers. *J Health Care Poor Under-served.* 2013;24(3):1378–90. <http://dx.doi.org/10.1353/hpu.2013.0144> PMID:23974406

137. Roberts MJ, Reich MR. Case study J: drug coverage in Ghana's National Health Insurance Scheme. In: Roberts MJ, Reich MR, editors. *Pharmaceutical reform, a guide to improving performance and equity.* Washington (DC): World Bank; 2011.

138. King G, Gakidou E, Imai K, Lakin J, Moore RT, Nall C, et al. Public policy for the poor? A randomised assessment of the Mexican universal health insurance programme. *Lancet.* 2009;373(9673):1447–54. [http://dx.doi.org/10.1016/S0140-6736\(09\)60239-7](http://dx.doi.org/10.1016/S0140-6736(09)60239-7) PMID:19359034

139. Wirtz VJ, Santa-Ana-Tellez Y, Servan-Mori E, Avila-Burgos L. Heterogeneous effects of health insurance on out-of-pocket expenditure on medicines in Mexico. *Value Health.* 2012;15(5):593–603. <http://dx.doi.org/10.1016/j.jval.2012.01.006> PMID:22867767

140. Mensah S, Acheampong OB. Analysis of top 100 drugs by cost and utilization: first quarter 2009. Accra: National Health Insurance Authority; 2009.

141. Backliwal A, Mani S. Navigating the new Thailand. Bangkok: IMS Asia Pacific Insight. 2011;1(1):12–14 (http://www.imshealth.com/deployedfiles/ims/Global/Asia%20Pacific/2011_Magazine_Asia_softcopy%20FINAL.pdf, accessed 18 August 2014).

142. Stern D, Reissman D. Specialty pharmacy cost management strategies of private health care payers. *J Manag Care Pharm.* 2006;12(9):736–44. PMID:17249906

143. Seiter A, Gyansa-Lutterodt M. Policy note: the pharmaceutical sector in Ghana. Washington (DC): World Bank; 2009 (<http://apps.who.int/medicinedocs/documents/s16765e/s16765e.pdf>, accessed 23 August 2013).
144. Whitehead M. The concepts and principles of equity and health. *Int J Health Serv.* 1992;22(3):429–45. <http://dx.doi.org/10.2190/986L-LHQ6-2VTE-YRRN> PMID:1644507
145. Sen A. Inequality reexamined. Cambridge (MA): Harvard University Press; 1992.
146. Anand P, Santos C, Smith R. The measurement of capabilities. In: Basu K, Kanbur R, editors. *Arguments for a better world: essays in honor of Amartya Sen.* Oxford: Oxford University Press; 2009.
147. Sen A. The idea of justice. Cambridge (MA): Harvard University Press; 2009.
148. Farmer P. To repair the world: Paul Farmer speaks to the next generation. Berkeley: University of California Press; 2013.
149. Martin DK, Gibson JL, Singer PA. Priority setting. In: Singer PA, Viens AM, editors. *The Cambridge textbook of bioethics.* Cambridge: Cambridge University Press; 2008:251–6.
150. Making fair choices on the path to universal health coverage. Final report of the WHO Consultative Working Group on Equity and Universal Health Coverage. Geneva: World Health Organization; 2014 (http://www.who.int/choice/documents/making_fair_choices/en/, accessed 29 July 2014).
151. Schlander M. NICE accountability for reasonableness: a qualitative study of its appraisal of treatments for attention-deficit/hyperactivity disorder (ADHD). *Curr Med Res Opin.* 2007;23(1):207–22. <http://dx.doi.org/10.1185/030079906X159461> PMID:17261237
152. Daniels N. Accountability for reasonableness: an update. *BMJ.* 2008;9:337:a1850. doi: 10.1136/bmj.a1850.
153. Maluka S, Kamuzora P, Sansebastián M, Byskov J, Ndawi B, Olsen ØE, et al. Implementing accountability for reasonableness framework at district level in Tanzania: a realist evaluation. *Implement Sci.* 2011;6(11):11. <http://dx.doi.org/10.1186/1748-5908-6-11> PMID:21310021
154. Kwon S, Oh J, Jung Y, Heo J. Citizen Council for health insurance policy-making. *Korean J Health Econ Policy.* 2012;18(3):103–19.
155. Gibson JL, Martin DK, Singer PA. Priority setting in hospitals: fairness, inclusiveness, and the problem of institutional power differences. *Soc Sci Med.* 2005;61(11):2355–62. <http://dx.doi.org/10.1016/j.socscimed.2005.04.037> PMID:15950347
156. Daniels N, Sabin JE. Setting limits fairly: learning to share resources for health. Oxford: Oxford University Press; 2008.
157. Quality assurance and safety of medicines: challenges and strategic directions. Geneva: World Health Organization; 2013 (http://www.who.int/medicines/about/qsm_strategy/en/, accessed 20 June 2014).
158. Ozar D, Berg J, Werhane PH, Emanuel L, for the National Working Group on Health Care Organizational Ethics. *Organizational ethics in health care: toward a model for ethical decision making by provider organizations.* Washington (DC): American Medical Association; 2000:5–6.
159. Managing access to medicines and health technologies (MDS-3). Arlington (VA): Management Sciences for Health; 2012 (<http://www.msh.org/sites/msh.org/files/mds3-jan2014.pdf>, accessed 18 August 2014)
160. Sabin JE, Director, Harvard Pilgrim's Ethics Advisory Group (EAG). Personal communication, 2013.
161. Development of country profiles and monitoring of the pharmaceutical situation in countries. Geneva: World Health Organization (http://www.who.int/medicines/areas/coordination/coordination_assessment/en/, accessed 20 June 2014).
162. Innovating and empowering people for health. Geneva: World Health Organization; 2012.
163. Report of the Consultative Expert Working Group on Research and Development. Financing and coordination. Geneva: World Health Organization; 2012 (http://www.who.int/phi/CEWG_Report_5_April_2012.pdf, accessed 20 June 2014).
164. Frost LJ, Reich MR. Access: how do good health technologies get to poor people in poor countries. Boston (MA): Harvard Center for Population and Development Studies; 2008.
165. About the Center for Health Market Innovations (CHMI) (<http://healthmarketinnovations.org/about>, accessed 18 August 2014).
166. World Trade Organization, World Intellectual Property Organization, World Health Organization. Promoting access to medical technologies and innovations. Intersections between public health, intellectual property and trade. Geneva: WTO Secretariat; 2012 (http://www.wto.org/english/res_e/publications_e/who-wipo-wto_2013_e.htm, accessed 20 June 2014).
167. So AD, Ruiz-Esparza Q, Gupta N, Cars O. 3Rs for innovating novel antibiotics: sharing resources, risks, and rewards. *BMJ.* 2012;344:e1782. <http://dx.doi.org/10.1136/bmj.e1782> PMID:22491076
168. GAVI Alliance. Vaccine investment strategy (<http://www.gavialliance.org/about/strategy/vaccine-investment-strategy/>, accessed 20 June 2014).
169. Bird T. Big pharma a catalyst for change. US Chamber of Commerce, Washington (DC): Free Enterprise; 2009 (<http://www.freeenterprise.com/2009/03/big-pharma-a-catalyst-for-change>, accessed 20 June 2014).
170. Drugs for neglected diseases initiative (DNDi) (<http://www.dndi.org>, accessed 18 August 2014).

171. Ridley DB, Grabowski HG, Moe JL. Developing drugs for developing countries. *Health Aff (Millwood)*. 2006;25(2):313–24. <http://dx.doi.org/10.1377/hlthaff.25.2.313> PMID:16522573
172. Bill and Melinda Gates Foundation: What we do (<http://www.gatesfoundation.org/What-We-Do/Global-Development/Vaccine-Delivery>, accessed 18 August 2014).
173. Villa S, Compagni A, Reich MR. Orphan drug legislation: lessons for neglected tropical diseases. *Int J Health Plann Manage*. 2009;24(1):27–42. <http://dx.doi.org/10.1002/hpm.930> PMID:18435430
174. PATH's drug development global programme (<http://sites.path.org/drugdevelopment/>, accessed 20 June 2014).
175. Coster H. Can non-profit drug companies cure diseases of poverty? *Forbes*. 12 January 2011 (<http://www.forbes.com/sites/helencoster/2011/01/12/can-non-profit-drug-companies-cure-diseases-of-poverty/>, accessed 20 June 2014).
176. Moran M, Guzman J, Chapman N, Abela-Oversteegen L, Howard R, Farrell P. Neglected disease research and development. The public divide. G-Finder, Policy Cures; 2013 (http://www.policycures.org/downloads/GF_report13_all_web.pdf, accessed 20 June 2014).
177. Drugs for Neglected Diseases Initiative (DNDi): disease portfolio (<http://www.dndi.org/diseases-projects/portfolio/asaq.html>, accessed 20 June 2014).
178. Pecoul B, Sevcik A-M, Amuasi J, Diap G, Kiechel J-R. The story of ASAQ: the first antimalarial product development success. Geneva: Health Partnership Review, Global Forum for Health Research; 2008:77–83 (http://www.dndi.org/images/stories/pdf_scientific_pub/2008/Pecoul_The_story_of_ASAQ_HPR_2008.pdf, accessed 20 June 2014).
179. Drugs for neglected diseases initiative (DNDi): treatments (<http://www.dndi.org/treatments/asaq.html>, accessed 20 June 2014).
180. Open source drug discovery (<http://www.osdd.net/home>, accessed 18 August 2014).
181. Editorial. Accelerating drug discovery. *Lancet*. 2014;383(9917):575. doi: 10.1016/S0140-6736(14)60202-6. PMID: 24529455.
182. Innovative Medicines Initiative (<http://www.imi.europa.eu>, accessed 20 June 2014).
183. National Institutes of Health: Accelerating Medicines Partnership (<http://www.nih.gov/science/amp/>, accessed 20 June 2014).
184. Bhardwaj A, Scaria V, Raghava GP, Lynn AM, Chandra N, Banerjee S, et al.; Open Source Drug Discovery Consortium. Open source drug discovery – a new paradigm of collaborative research in tuberculosis drug development. *Tuberculosis (Edinb)*. 2011;91(5):479–86. PMID:21782516
185. Bhardwaj A, Bhartiya D, Kumar N, Scaria V; Open Source Drug Discovery Consortium. TBrowse: an integrative genomics map of *Mycobacterium tuberculosis*. *Tuberculosis (Edinb)*. 2009;89(5):386–7. <http://dx.doi.org/10.1016/j.tube.2009.07.005> PMID:19683474
186. Vashisht R, Bhardwaj A, Brahmachari SK; OSDD Consortium. Social networks to biological networks: systems biology of *Mycobacterium tuberculosis*. *Mol Biosyst*. 2013;9(7):1584–93. <http://dx.doi.org/10.1039/c3mb25546h> PMID:23629487
187. Vashisht R, Mondal AK, Jain A, Shah A, Vishnoi P, Priyadarshini P, et al.; OSDD Consortium. Crowd sourcing a new paradigm for interactome driven drug target identification in *Mycobacterium tuberculosis*. *PLoS ONE*. 2012;7(7):e39808. <http://dx.doi.org/10.1371/journal.pone.0039808> PMID:22808064
188. Anand P, Sankaran S, Mukherjee S, Yeturu K, Laskowski R, Bhardwaj A, et al.; OSDD Consortium. Structural annotation of *Mycobacterium tuberculosis* proteome. *PLoS ONE*. 2011;6(10):e27044. <http://dx.doi.org/10.1371/journal.pone.0027044> PMID:22073123
189. Generic drugs. Geneva: World Health Organization. (<http://www.who.int/trade/glossary/story034/en/> accessed 29 July 2014).
190. Kaplan WA, Wirtz VJ, Stephens P. The market dynamics of generic medicines in the private sector of 19 low and middle income countries between 2001 and 2011: a descriptive time series analysis. *PLoS ONE*. 2013;8(9):e74399. <http://dx.doi.org/10.1371/journal.pone.0074399> PMID:24098644
191. Davit BM, Nwakama PE, Buehler GJ, Conner DP, Haidar SH, Patel DT, et al. Comparing generic and innovator drugs: a review of 12 years of bioequivalence data from the United States Food and Drug Administration. *Ann Pharmacother*. 2009;43(10):1583–97. <http://dx.doi.org/10.1345/aph.1M141> PMID:19776300
192. United States Food and Drug Administration. Facts about current good manufacturing practices (cGMPs) (<http://www.fda.gov/drugs/developmentapprovalprocess/manufacturing/ucm169105.htm>, accessed 20 June 2014).
193. Generic drug savings in the US. Washington: Generics Pharmaceutical Association; 2012 (<http://www.gphaonline.org/media/cms/IMSStudyAug2012WEB.pdf>, accessed 20 June 2014).
194. The use of medicines in the United States: review of 2011. Parsippany (NJ): IMS Institute for Healthcare Informatics; 2012 (http://www.imshealth.com/ims/Global/Content/Insights/IMS%20Institute%20for%20Healthcare%20Informatics/IHII_Medicines_in_U.S_Report_2011.pdf, accessed 20 June 2014).
195. Vivian JC. Generic-substitution laws. *US Pharm*. 2008;33(6):30–4 (<http://www.uspharmacist.com/content/s/44/c/9787/>, accessed 20 June 2014).
196. Academy of Managed Care Pharmacy. Formulary management (<http://www.amcp.org/WorkArea/DownloadAsset>.

- aspx?id=9298, accessed 20 June 2014).
197. United States Food and Drug Administration. Generic competition and drug prices (<http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm129385.htm>, accessed 20 June 2014).
 198. Shrank WH, Hoang T, Ettner SL, Glassman PA, Nair K, DeLapp D, et al. The implications of choice: prescribing generic or preferred pharmaceuticals improves medication adherence for chronic conditions. *Arch Intern Med*. 2006;166(3):332–7. <http://dx.doi.org/10.1001/archinte.166.3.332> PMID:16476874
 199. Carone G, Schwierz C, Xavier A. Cost-containment policies in public pharmaceutical spending in the EU. Brussels: European Commission; 2012(European Economy Economic Papers 461). (http://ec.europa.eu/economy_finance/publications/economic_paper/2012/pdf/ecp_461_en.pdf, accessed 20 June 2014).
 200. Simoens S. Sustainable provision of generic medicines in Europe. Report for the European Generic Medicines Association; 2013 (http://www.generikusegyesulet.hu/contents/uploads/documents/document_1371468848_620.pdf, accessed, 18 August 2014).
 201. Cameron A, Mantel-Teeuwisse AK, Leufkens HG, Laing RO. Switching from originator brand medicines to generic equivalents in selected developing countries: how much could be saved? *Value Health*. 2012;15(5):664–73. <http://dx.doi.org/10.1016/j.jval.2012.04.004> PMID:22867775
 202. Kaplan WA, Ritz LS, Vitello M, Wirtz VJ. Policies to promote use of generic medicines in low and middle income countries: a review of published literature, 2000–2010. *Health Policy*. 2012;106(3):211–24. <http://dx.doi.org/10.1016/j.healthpol.2012.04.015> PMID:22694970
 203. National drug policy. Brasília; Brazil Ministry of Health; 2001.
 204. Cardoso R, Mezarobba G, Ferraz S, Fran R, Paiva E, Brasil S, et al. [The paradise of counterfeit drugs]. *Revista Veja*; 1998 (http://veja.abril.com.br/080798/p_040.html, accessed 10 February 2014) (in Portuguese).
 205. ANVISA: Brazilian Health Surveillance Agency (<http://portal.anvisa.gov.br/wps/portal/anvisa-ingles>, accessed 7 February 2014).
 206. Araújo LU, Albuquerque KT, Kato KC, Silveira GS, Maciel NR, Spósito PA, et al. [Generic drugs in Brazil: historical overview and legislation]. *Rev Panam Salud Publica*. 2010;28(6):480–92. PMID:21308175 (in Portuguese).
 207. Dias CRC, Romano-Lieber NS. [Process of implementation of the generic drug policy implementation in Brazil]. *Cad Saude Publica*. 2006;22(8):1661–9 (in Portuguese). <http://dx.doi.org/10.1590/S0102-311X2006000800014> PMID:16832537
 208. Government of Brazil. Educational videos: medicines (<https://www.youtube.com/user/TVNBR/search?query=ANVISA+gen%C3%A9ricos>, accessed 20 August 2014).
 209. Brazilian social media channel (<http://www.youtube.com/user/CanalPortalBrasil>, accessed 7 February 2014).
 210. Facebook inc. [Ministry of Health Brazil] Facebook page (in Portuguese) (https://www.facebook.com/minsaude?ref=br_tf, accessed 20 June 2014).
 211. Rocha CE da, Barros JAC de, Silva MDP. Levantamento de dados sobre o conhecimento e informação acerca dos medicamentos genéricos em uma população de pacientes do serviço de saúde ambulatorial do Recife, Pernambuco, Brasil [Survey on knowledge and information about generic drugs in a population of patients in the outpatient health service of Recife, Pernambuco, Brazil]. *Cad Saude Publica*. 2007;23:1141–50.
 212. International nonproprietary names: guidance. Geneva: World Health Organization; 1997 (<http://www.who.int/medicines/services/inn/en/>, accessed 7 February 2014).
 213. ANVISA: Brazilian Health Surveillance Agency. [Generic drugs: orientation]. Brasília: Distrito Federal; 2002 (in Portuguese) (http://portal.anvisa.gov.br/wps/wcm/connect/a09ae180483c0adca421af0d8b4275ce/genericos_cartilha.pdf?MOD=AJPERES, accessed 19 August 2014).
 214. Miranda ES, Pinto CB, dos Reis AL de A, Emmerick IC, Campos MR, Luiza VL, et al. [Availability of generic drugs in the public sector and prices in the private sector in different regions of Brazil]. *Cad Saude Publica*. 2009;25(10):2147–58 (in Portuguese). <http://dx.doi.org/10.1590/S0102-311X2009001000006> PMID:19851615
 215. Luiza VL, Castro CG, Nunes JM. [Pharmaceutical procurement by the public sector: the quality/cost relationship]. *Cad Saude Publica*. 1999;15(4):769–76 (in Portuguese). <http://dx.doi.org/10.1590/S0102-311X1999000400011> PMID:10633199
 216. Bertoldi AD, Helfer AP, Camargo AL, Tavares NUL, Kanavos P. Is the Brazilian pharmaceutical policy ensuring population access to essential medicines? *Global Health*. 2012;8(1):6. <http://dx.doi.org/10.1186/1744-8603-8-6> PMID:22436555
 217. ANVISA Brazilian Health Surveillance Agency. [Effects of CMED Resolution No. 02/04 in price analysis of new medicines]. Brasília: Gerência de Avaliação Econômica de Novas Tecnologias; 2013 (in Portuguese).
 218. Vieira FS, Zucchi P. [Price differences between generic and innovator medicines in Brazil]. *Rev Saude Publica*. 2006;40(3):444–9 (in Portuguese). <http://dx.doi.org/10.1590/S0034-89102006000300012> PMID:16810368
 219. Santos EC, Ferreira MA. [Pharmaceutical industry and the introduction of generic drugs on Brazilian market]. *Rev Nexos Econômicos*. 2014;7(2):95–120.
 220. ProGenericos (<http://www.progenericos.org.br/index.php/mercado>, accessed 20 June 2014).
 221. Global burden of diseases, injuries and risk factors study series. *Lancet* (<http://www.thelancet.com/themed/global-burden-of-disease>, accessed 20 August 2014).

222. Global spending on medicines. IMS Institute for Healthcare Informatics. (http://www.imshealth.com/deployedfiles/imshealth/Global/Content/Corporate/IMS%20Health%20Institute/Reports/Global_Use_of_Meds_Outlook_2017/Biologics_Market.pdf, accessed 20 August 2014).
223. Kantarjian HM, Fojo T, Mathisen M, Zwelling LA. Cancer drugs in the United States: Justum Pretium—the just price. *J Clin Oncol*. 2013;31(28):3600–4. <http://dx.doi.org/10.1200/JCO.2013.49.1845> PMID:23650428
224. Shankar R, Kinsey E, Thomas P, Hooper J, Tejani S. Securing IP and access to medicine: is oncology the next HIV? IMS Consulting Group white paper on compulsory licensing and other risks to intellectual property rights in oncology. IMS Consulting Group; 2013 (http://www.imshealth.com/deployedfiles/imshealth/Global/Content/Home%20Page%20Content/High-Growth%20Markets/Securing_IP_and_Access_to_Medicine_in_Emerging%20Markets.pdf, accessed 20 June 2014).
225. FDA issues draft guidance on biosimilar product development. United States Food and Drug Administration. 9 February 2012 (<http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm291232.htm>, accessed 20 June 2014).
226. Tóthfalusi L, Endrőnyi L, Chow SC. Statistical and regulatory considerations in assessments of interchangeability of biological drug products. *Eur J Health Econ*. 2014;15(S1) Suppl 1:S5–11. <http://dx.doi.org/10.1007/s10198-014-0589-1> PMID:24832831
227. World Trade Organization. Compulsory licensing of pharmaceuticals and TRIPS. Geneva: Information and Media Relations Division of the WTO Secretariat; 2006 (http://www.wto.org/english/tratop_e/trips_e/public_health_fa_q_e.htm, accessed 19 August 2014).
228. Public Citizen's Global Access to Medicines Program. Compulsory licensing and government use of patents for pharmaceuticals (<http://www.citizen.org/access>, accessed 20 June 2014).
229. Understanding specialty pharmacy management and cost control. Plano (TX): Pharmaceutical Strategies Group; 2010 (http://www.psgconsults.com/Understanding_Specialty_Pharmacy_Management_and_Cost_Control_FINAL.pdf, accessed 20 June 2014).
230. Yamabhai I, Mohara A, Tantivess S, Chaisiri K, Teerawattananon Y. Government use licenses in Thailand: an assessment of the health and economic impacts. *Global Health*. 2011;7(1):28. <http://dx.doi.org/10.1186/1744-8603-7-28> PMID:21838926
231. Yoongthong W, Hu S, Whitty JA, Wibulpolprasert S, Sukantho K, Thientawee W, et al. National drug policies to local formulary decisions in Thailand, China, and Australia: drug listing changes and opportunities. *Value Health*. 2012;15(1) Suppl:S126–31. <http://dx.doi.org/10.1016/j.jval.2011.11.003> PMID:22265059
232. National Drug Committee. National list of essential medicines 2008. Nonthaburi: The Thai Food and Drug Administration; 2008 (<http://drug.fda.moph.go.th:81/nlem.in.th/medicine/essential/list>, accessed 20 June 2014).
- (233) Turongkaravee S, Rattanavipapong W, Khampang R, Leelahavarong P, Teerawattananon Y, Tantivess S. Evaluation of high-cost medicine scheme (Category E2) under the 2008 national list of essential medicines. Nonthaburi: Health Intervention and Technology Assessment Program; 2012.
234. The Ministry of Public Health and the National Health Security Office Thailand. The 10 burning questions on the government use of patents on the four anti-cancer drugs in Thailand. Nonthaburi: Ministry of Public Health; 2008.
235. Wibulpolprasert S, Chokevivat V, Oh C, Yamabhai I. Government use licenses in Thailand: the power of evidence, civil movement and political leadership. *Global Health*. 2011;7(7):32. <http://dx.doi.org/10.1186/1744-8603-7-32> PMID:21910864
236. National Health Security Office. Annual report 2012. Bangkok: National Health Security Office; 2012.
237. About technology appraisals. National Institute for Health and Clinical Excellence. (http://www.nice.org.uk/aboutnice/whatwedo/abouttechnologyappraisals/about_technology_appraisals.jsp, accessed 20 June 2014).
238. Roughead EE, Gilbert AL, Vitry AI. The Australian funding debate on quadrivalent HPV vaccine: a case study for the national pharmaceutical policy. *Health Policy*. 2008;88(2–3):250–7. <http://dx.doi.org/10.1016/j.healthpol.2008.03.012> PMID:18468714
239. Linley WG, Hughes DA. Societal views on NICE, cancer drugs fund and value-based pricing criteria for prioritising medicines: a cross-sectional survey of 4118 adults in Great Britain. *Health Econ*. 2013;22(8):948–64. <http://dx.doi.org/10.1002/hec.2872> PMID:22961976
240. Reveiz L, Chapman E, Torres R, Fitzgerald JF, Mendoza A, Bolis M, et al. [Right-to-health litigation in three Latin American countries: a systematic literature review]. *Rev Panam Salud Publica*. 2013;33(3):213–22 (in Spanish). <http://dx.doi.org/10.1590/S1020-49892013000300008> PMID:23698141
241. Daniels N, Sabin J. Setting limits fairly: learning to share resources for health. Oxford: Oxford University Press; 2008:193.
242. Frenk J. The global health system: strengthening national health systems as the next step for global progress. *PLoS Med*. 2010;7(1):e1000089. <http://dx.doi.org/10.1371/journal.pmed.1000089> PMID:20069038
243. Mackintosh M, Koivusalo M. Health systems and commercialization: in search of good sense. In: Mackintosh M, Koivusalo M, editors. Commercialization of health care: global and local dynamics and policy responses. Basingstoke: Palgrave Macmillan; 2005.
244. Bloom G, Kanjilal B, Lucas H, Peters DH, editors. Trans-

- forming health markets in Asia and Africa: improving quality and access for the poor. London: Routledge; 2013.
245. Bennett S, McPake B, Mills A. Private health providers in developing countries: serving the public interest? London: Zed Press; 1997.
246. Bloom G, Standing H. Pluralism and marketisation in the health sector: meeting health needs in contexts of social change in low and middle income countries. Brighton: Institute for Development Studies; 2001:136.
247. Peters DH, Bloom G. Developing world: bring order to unregulated health markets. *Nature*. 2012;487(7406):163–5. <http://dx.doi.org/10.1038/487163a> PMID:22785295
248. Arrow KJ. Uncertainty and the welfare economics of healthcare. *Am Econ Rev*. 1963;13(5):941–73.
249. Chang HJ. Understanding the relationship between institutions and economic development: some key theoretical issues. In: Chang HJ, editor. Institutional change and economic development. London: Anthem Press; 2007.
250. Shah NM, Brieger WR, Peters DH. Can interventions improve health services from informal private providers in low and middle-income countries? A comprehensive review of the literature. *Health Policy Plan*. 2011;26(4):275–87. <http://dx.doi.org/10.1093/heapol/czq074> PMID:21097784
251. Chalker J, Chuc NTK, Falkenberg T, Tomson G. Private pharmacies in Hanoi, Vietnam: a randomized trial of a 2-year multi-component intervention on knowledge and stated practice regarding ARI, STD and antibiotic/steroid requests. *Trop Med Int Health*. 2002;7(9):803–10. <http://dx.doi.org/10.1046/j.1365-3156.2002.00934.x> PMID:12225513
252. Chalker J, Ratanawijitrasin S, Chuc NTK, Petzold M, Tomson G. Effectiveness of a multi-component intervention on dispensing practices at private pharmacies in Vietnam and Thailand – a randomized controlled trial. *Soc Sci Med*. 2005;60(1):131–41. <http://dx.doi.org/10.1016/j.socs-cimed.2004.04.019> PMID:15482873
253. Ensor T, Weinzierl S. A review of regulation in the health sector in low and middle income countries: signposts to more effective states. Brighton: Institute of Development Studies; 2006.
254. Bloom G, Henson S, Peters DH. Innovation in regulation of rapidly changing health markets. *Global Health*. 2014;10(1):53. <http://dx.doi.org/10.1186/1744-8603-10-53> PMID:24961602
255. Lewis N. Governance and corruption in public health care systems. Washington (DC): Center for Global Development; 2006 (Center for Global Development working paper 76).
256. Vian T. Review of corruption in the health sector: theory, methods and interventions. *Health Policy Plan*. 2008;23(2):83–94. <http://dx.doi.org/10.1093/heapol/czm048> PMID:18281310
257. Pritchett L, Woolcock M. Solutions when the solution is the problem: arraying the disarray in development. *World Dev*. 2004;32(2):191–212. <http://dx.doi.org/10.1016/j.world-dev.2003.08.009>
258. North DC. Institutions, institutional change and economic performance. New York: Cambridge University Press; 1990.
259. Elliot D, Gibson A, Hitchins R. Making markets work for the poor: rationale and practice. *Enterprise Dev Microfinance*. 2008;19(2):101–19. <http://dx.doi.org/10.3362/1755-1986.2008.011>
260. Norris P, Herxheimer A, Lexchin J, Mansfield P. Drug promotion: what we know, what we have yet to learn. Reviews of materials in the WHO/HAI database on drug promotion. Geneva: World Health Organization and Health Action International; 2005.
261. Peters DH, El-Saharty S, Siadat B, Janovsky K, Vujcic M, editors. Improving health services in developing countries: from evidence to action. Washington (DC): The World Bank; 2009.
262. Rowe AK, Rowe SY, Peters DH, Holloway KA, Chalker J, Ross-Degnan D. Preliminary results of a systematic review of the effectiveness of strategies to improve health worker performance in low- and middle-income countries (abstract). American Society for Tropical Medicine and Hygiene (abstract book), 2013; 89(5 suppl):25 (http://www.astmh.org/AM/Template.cfm?Section=Abstracts_and_Education1&Template=/CM/ContentDisplay.cfm&ContentID=5373, accessed 20 June 2014).
263. Wafula FN, Miriti EM, Goodman CA. Examining characteristics, knowledge and regulatory practices of specialized drug shops in sub-Saharan Africa: a systematic review of the literature. *BMC Health Serv Res*. 2012;12(1):223. <http://dx.doi.org/10.1186/1472-6963-12-223> PMID:22838649
264. Brieger WR, Osamor PE, Salami KK, Oladepo O, Otusanya SA. Interactions between patent medicine vendors and customers in urban and rural Nigeria. *Health Policy Plan*. 2004;19(3):177–82. <http://dx.doi.org/10.1093/heapol/czh021> PMID:15070866
265. Smith F. The quality of private pharmacy services in low and middle-income countries: a systematic review. *Pharm World Sci*. 2009;31(3):351–61. <http://dx.doi.org/10.1007/s11096-009-9294-z> PMID:19343530
266. Review of the accredited drug dispensing outlets (ADDO) roll out programme in Tanzania. Reet: Health Research for Action (HERA); 2006.
267. Goodman C, Kachur SP, Abdulla S, Bloland P, Mills A. Drug shop regulation and malaria treatment in Tanzania – why do shops break the rules, and does it matter? *Health Policy Plan*. 2007;22(6):393–403. <http://dx.doi.org/10.1093/heapol/czm033> PMID:17921151
268. Cambodia Health Service Delivery Profile. Manila: WHO Regional Office for the Western Pacific; 2012 (http://www.wpro.who.int/health_services/service_delivery_profile_cambodia.pdf, accessed 20 June 2014).

269. Grundy J, Khut QY, Oum S, Annear P, Ky V. Health system strengthening in Cambodia – a case study of health policy response to social transition. *Health Policy*. 2009;92(2-3):107–15. <http://dx.doi.org/10.1016/j.healthpol.2009.05.001> PMID:19501425
270. Eggermont N. Evaluation of a peer-education program for diabetes and hypertension in rural Cambodia. Ghent: University of Ghent; 2011 (<http://ebookbrowse.com/thesis-natalie-mopotsyo-evaluation-pdf-d352080109>, accessed 20 June 2014).
271. Sumpradit N, Chongtrakul P, Anuwong K, Puntong S, Kongsomboon K, Butdeemee P, et al. Antibiotics Smart Use: a workable model for promoting the rational use of medicines in Thailand. *Bull World Health Organ*. 2012;90(12):905–13. PMID:23284196
272. Sumpradit N. Food and Drug Administration, Ministry of Public Health, Thailand, personal communication, 2013.
273. Yunus M, Weber K. Creating a world without poverty: social business and the future of capitalism. New York (NY): Public Affairs; 2009.
274. Yunus M, Weber K. Building social business: the new kind of capitalism that serves humanity's most pressing needs. New York (NY): Public Affairs; 2010.
275. Yunus M, Moingeon B, Lehmann-Ortega L. Building social business models: lessons from the Grameen experience. *Long Range Plann*. 2010;43(2-3):308–25. <http://dx.doi.org/10.1016/j.lrp.2009.12.005>
276. Rangan K, Chu M, Petkoski D. Segmenting the base of the pyramid. *Harvard Business Review* June 2011:113–7 (<http://hbr.org/2011/06/the-globe-segmenting-the-base-of-the-pyramid/ar/1>, accessed 19 August 2014).
277. Peterson K, Rehrig M, Stamp M, Kim S. How pharmaceutical and medical device companies create shared value in global health. *FSG*; 2012 (<http://www.fsg.org/tabid/191/ArticleId/557/Default.aspx?srpush=true>, accessed 20 June 2014).
278. Changing diabetes in China. Novo Nordisk blueprint for change programme; 2011 (<http://www.novonordisk.com/images/Sustainability/PDFs/Blueprint%20for%20change%20-%20China.pdf>, accessed 20 June 2014).
279. Pasrija A. Arogya Parivar: Commercial innovation to improve healthcare access at the bottom of the pyramid in rural India. Poster presented at the Third International Conference for Improving Use of Medicines, Antalya, Turkey, November 2011.
280. Kenya pharmaceutical country profile. Nairobi: Ministry of Medical Services in collaboration with the World Health Organization; 2010 (http://www.who.int/medicines/areas/coordination/kenya_pharmaceuticalprofile_december2010.pdf, accessed 20 June 2014).
281. Access to essential medicines in Kenya: a household survey. Nairobi: Ministry of Medical Services and Ministry of Public Health & Sanitation; 2009 (<http://apps.who.int/medicinedocs/documents/s18696en/s18696en.pdf>, accessed 20 June 2014).
282. Merritt C. Mobile money transfer services: The next phase in the evolution of person-to-person payments. *J Payments Strategy Systems*. 2011;5(2):143–60.
283. Mas I, Raddcliffe D. Mobile payments go viral: M-PESA in Kenya. *SciTech Lawyer*. 2013;9(3) (http://www.americanbar.org/content/dam/aba/events/science_technology/merritt.authcheckdam.pdf, accessed 20 August 2014).
284. Randers J, editor. Elements of the system dynamics method. Cambridge: MIT Press; 1980.
285. Sterman JD. Business dynamics: systems thinking and modeling for a complex world. Boston: Irwin/McGraw-Hill; 2000.
286. Brinkerhoff DW. Accountability and health systems: toward conceptual clarity and policy relevance. *Health Policy Plan*. 2004;19(6):371–9. <http://dx.doi.org/10.1093/heapol/czh052> PMID:15459162
287. Kamuzora P, Gilson L. Factors influencing implementation of the community health fund in Tanzania. *Health Policy Plan*. 2007;22(2):95–102. <http://dx.doi.org/10.1093/heapol/czm001> PMID:17299023
288. Leisinger KM. Poverty, disease and medicines in low- and middle-income countries: the roles and responsibilities of pharmaceutical corporations. *Bus Prof Ethics J*. 2012;31(1):135–85. <http://dx.doi.org/10.5840/bpej20123116>
289. Gilson L, Erasmus E, Borghi J, Macha J, Kamuzora P, Mtei G. Using stakeholder analysis to support moves towards universal coverage: lessons from the SHIELD project. *Health Policy Plan*. 2012;27 Suppl 1:i64–76. <http://dx.doi.org/10.1093/heapol/czs007> PMID:22388502
290. Campbell S. The knowledge translation curriculum. Ottawa: Canadian Coalition for Global Health Research; 2012 (<http://ccghr.ca/resources/knowledge-translation/>).
291. Damschroder LJ, Aron DC, Keith RE, Kirsh SR, Alexander JA, Lowery JC. Fostering implementation of health services research findings into practice: a consolidated framework for advancing implementation science. *Implement Sci*. 2009;4(1):50. <http://dx.doi.org/10.1186/1748-5908-4-50> PMID:19664226
292. Peters DH, Adam T, Alonge O, Agyepong IA, Tran N. Implementation research: what it is and how to do it. *BMJ*. 2013;347:f6753. PMID:24259324

A systems approach allows us to situate medicines against the full complexity of a health system. This creates a deeper understanding of how interventions in the medicines sector influence the rest of the health system and vice versa. In applying a systems approach, crucial connections become visible: improving access to medicines can promote health equity, and contribute to both stronger health systems and the goals of universal health coverage. Based on case-studies of medicines situations across low- and middle-income countries, this report concludes with three core arguments for the medicines agenda:

- ▶ Include access to medicines and their appropriate use as an explicit focus in health system strengthening and efforts towards universal health coverage;
- ▶ Recognize the needs for transparency and governance in the medicines sector within and across health systems, and then strengthen governance capacities;
- ▶ Build more robust connections between information, medicines and decision-making.



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