UNDERSTANDING ACCESS TO MEDICINES IN LOW- AND MIDDLE-INCOME COUNTRIES THROUGH THE USE OF PRICE AND AVAILABILITY INDICATORS

Alexandra Cameron
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Understanding access to medicines in low- and middle-income countries through the use of price and availability indicators

Toegang tot geneesmiddelen in lage en midden inkomenslanden en het gebruik van indicatoren voor prijs en beschikbaarheid (met een samenvatting in het Nederlands)

Proefschrift

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Chapter 1

General introduction

Access to medicines in low- and middle-income countries

It is generally understood that large sections of the population in low- and middle-income countries (LMICs) lack access to medicines. The World Health Organization (WHO) has previously estimated that one-third of the world's population lacked access to essential medicines (1). While access to medicines is promoted by many international health organizations and is included as an objective of national medicines policies, it is a difficult concept to define and measure. Access to medicines has previously been defined as "having medicines continuously available and affordable at public or private health facilities or medicine outlets that are within one hour's walk from the homes of the population" (2). Given its complexity, an overall picture of the degree of access to essential medicines can only be generated using a range of proxy indicators that provide data on medicine availability and price in both the public and the private sectors, in combination with key policy indicators (3). The availability and price of medicines are reported by WHO, the United Nations (UN) and others as key measures of medicine access. Affordability is also reported as an extension of price, and while difficult to conceptualize and measure, may be more directly linked to access than price alone. Despite recent advances to expand health insurance coverage in the developing world, the majority of LMIC populations still lack access to social health insurance with a medicines benefit (4). As a result, up to 90% of people purchase medicines through out-of-pocket payments (5), making medicines the largest family expenditure item after food. High medicine prices and poor affordability can therefore act as a barrier to access to medicines. For this reason, WHO has designated affordable prices as a determinant of access to medicines, together with rational selection and use, sustainable financing, and reliable health and supply systems (6).

Efforts to measure the price, availability and affordability of medicines as key indicators of access

Prior to 2001, very little empirical evidence was available on medicine availability, and particularly price, in LMICs. Only a few small studies had been conducted in these settings to measure medicine prices and make international comparisons (7-10). These studies lacked a consistent, reproducible methodology which limited the ability to make comparisons across countries or draw general conclusions (11). In 2001, a resolution endorsed by Member States of WHO called for the development of a standardised method

for measuring medicine prices (12), which resulted in the launch of the WHO/Health Action International (HAI) Project on Medicine Prices and Availability. To address the lack of evidence on medicine availability and prices in LMICs, the project has focussed primarily on the development and application of a standard survey methodology for measuring medicine prices, availability, affordability and price components.

In studies conducted using the WHO/HAI survey methodology, the prices and availability of approximately 50 medicines is collected in a sample of facilities in sectors that serve as important medicines dispensing points (13). This includes the public sector (primary health care facilities and hospital outpatient services), the private sector (private pharmacies and drug stores), and other sectors such as non-governmental organizations (NGOs) or mission hospitals or dispensing doctors. Price data is also collected for public procurement, usually at the central level but sometimes at the facility level if procurement is decentralized. Finally, the survey methodology includes an assessment of the add-on costs that are applied through the supply and distribution chain ("price components") to determine the make-up of final price. Data is collected on a smaller number (5-7) of tracer medicines by tracking them through the supply chain and identifying the add-on costs that get applied at each stage (e.g. wholesaler, retailer). This aspect of the survey is particularly important in designing appropriate interventions to lower prices. Following a stringent quality control procedure, the results of individual WHO/HAI surveys are made publicly available through an online searchable database (14).

The WHO/HAI survey methodology has now been applied in over 70 countries. Its primary use is for investigating availability, price and affordability at the national level with the intention of identifying specific issues that may require policy or programmatic intervention in order to improve access. While numerous surveys have been conducted, there are fewer examples of resulting policy interventions to improve availability and/or lower prices. In particular, intervening in the area of pharmaceutical prices is a contentious area with numerous challenges, not least of which are the varying political and commercial interests at play (15,16). Another key challenge is the lack of evidence on effective interventions; the majority of studies that exist are descriptive in nature, even those from high-income countries (17-19). However, there are still a number of examples of the WHO/HAI survey results being used to effect positive policy change at country level. In Lebanon, for example, following the 2004 survey the Lebanese Government undertook a review of procurement and patient prices, comparing these with prices in Jordan and Saudi Arabia. This resulted in the lowering of prices for a large number of medicines. The Government also implemented regressive margins for importers, wholesalers and retailers; improved transparency by publishing patient prices; and increased the budget for purchasing cancer, HIV and other specialized medicines (20). In Tajikistan, following a 2005 survey, the Government abolished the 20% value-

added tax (VAT) on medicines (20). In United Arab Emirates, following the 2006 survey and subsequent price review, the price of many originator brands and generics were substantially reduced. Margins for chronic disease medicines have also been reduced, resulting in a further 10% reduction in patient prices (20). In Yemen, following their 2006 survey, the Government of Yemen re-introduced price-setting, limited wholesaler "bonusing" of free stock to 10% and reduced medicine prices (in some cases by up to 50%) (20).

While the WHO/HAI survey method was primarily designed to inform country-level policies and programs, it also has utility in improving our understanding of access to medicines on a broader level, for example by identifying trends across countries and individual disease areas. This information can be used to support evidence-based advocacy and policy-making at both supra national and national levels.

The need to better understand global and regional trends in access to medicines to drive international efforts

Major advances for life expectancy and health status of the poor depend on access to essential drugs that are inexpensive and easily available on the global market (15). It is therefore not surprising that many global stakeholders are interested in improving access to medicines in low- and middle-income countries, from donors to UN agencies to NGOs such as HAI (21), OXFAM (22) and Médecins Sans Frontières (23). Improving access to medicines is also a target of the Millennium Development Goals (MDGs): "in cooperation with pharmaceutical companies, provide access to affordable, essential drugs in developing countries" (3). However, as previously mentioned data on levels of access to medicines upon which to base advocacy, funding and programmatic decisions has been somewhat sparse. While country-level data is useful in working towards national solutions tailored to the individual country context, those working in the international health arena require an understanding of general trends to be able to garner support for efforts to improve access to medicines more generally.

Various aspects of access to medicines have recently been explored using the medicine purchase transactions of international donors (24). This body of work is highly useful in understanding which donor medicine purchasing policies and practices are most effective and how donor funds can be optimized. However donor funds are limited primarily to the "big three" diseases, namely HIV/AIDS, tuberculosis (TB) and malaria. The majority of essential medicines outside these three diseases are purchased at the national

level (and even for TB and malaria medicines are also purchased using domestic funds). To gain a comprehensive view of access to medicines, it is imperative to have an understanding of these medicines in addition to those which are donor-funded. However, while donor reporting requires data on medicine product information, volumes and prices to be reported, thereby offering a rich data source for analysis (24), no such data source is available for other essential medicines. While in the past 10 years numerous national, regional and international medicine price reporting websites have emerged (25), the types of information reported varies substantially. For example, some sources report manufacturer list prices, others report reimbursement prices, while others report government procurement prices (25). Further, lack of descriptive information on the prices provided limits their comparability, for example, whether a reported price includes VAT or not is often impossible to determine (25).

While the WHO/HAI surveys have been designed primarily for use at the national level, once a critical mass of survey data was available from a large number of countries, it generated an opportunity to use this data to report on access to medicines at the global level. Several international health data sources have begun to report international country results, including both the WHO World Health Statistics Report (26) and the MDG Gap Task Force Report (3,27-29) and MDG database (30). The database of prices and availability of medicines collected through the WHO/HAI method is therefore a key source of data for access to medicines in low- and middle-income countries with clear utility at the global level as well as at the national level. This data source offers several advantages for global reporting. Firstly, the methodology has been validated (31) and is standardized across survey to improve comparability. In addition, data quality control is undertaken at multiple points throughout the data collection, entry and analysis process, thereby limiting the potential for incorrect data (13). Further, data is available for a large number of low- and middle-income countries from all geographic regions, thereby allowing for global and regional analyses. Finally, while the medicines surveyed in each country varies according to local specificities, data is available for a subset of commonly available medicines for all surveys, thereby allowing direct comparisons across individual products and groups of identical products. As such, the WHO/HAI dataset is a comprehensive and reliable source of publicly-available data on facility-level availability and price of medicines.

Goals and objectives of this thesis

While donor reporting requirements are shedding light on medicine prices and other market indicators for HIV/AIDS, TB and malaria, similar information on other essential medicines is badly needed to inform the access to medicines debate at the global level and inform global funding, advocacy and programmatic efforts. Through the WHO/HAI project, a rich data source exists on the price and availability of a wide range of medicines in a large number of countries around the world. While country-level results have been used in international reports and fora as evidence that availability is poor and prices are high, this thesis attempts to determine whether additional, more nuanced results can be obtained. Specifically, this thesis will examine whether data on medicine prices and availability obtained through WHO/HAI surveys can be used to elucidate various facets of access to medicines through the application of different method and analyses. Given the heterogeneity of the other sectors surveyed in different countries, this thesis is limited to the data from public and private sectors which are more directly comparable across countries. In summary, the hypothesis of the thesis is that national medicine price and availability data can be analysed in a variety of ways that can contribute to our global understanding of access to medicines in low- and middle-income countries, and can support evidence-based advocacy and policy-making.

Thesis outline and preview

The remainder of this thesis uses national data on medicine prices and availability collected using the standardized WHO/HAI method, to examine various aspects of access to medicines at a global level. In **Chapter 2**, WHO/HAI survey data on medicine price and availability is aggregated on a global level, taking several steps to improve the comparability of national results, to examine whether any overall conclusions can be drawn on medicine prices and availability in low- and middle-income countries. In **Chapter 3**, price and availability results are examined for groups of medicines in different therapeutic areas, specifically by comparing medicine availability for medicines used for acute vs. chronic conditions. In **Chapter 4**, medicine prices and availability are investigated for individual disease areas, namely cardiovascular disease (**Chapter 4.1**) and epilepsy (**Chapter 4.2**), to see if general conclusions could be drawn across countries. A fourth approach is to use medicine price data to quantify impoverishment effects of medicine purchases, described in **Chapter 5**. Finally, medicine prices are used in combination with consumption data to estimate potential savings at a population level which could arise from switching consumption from originator brands to generics (**Chapter 6**). Each of these approaches uses the same data source – facility based data on medicine prices

and availability – to elucidate various aspects of price and/or availability of medicines and draw global-level conclusions.

The concluding chapter of this thesis contains a discussion of the usefulness of national data on medicine price and availability to inform our understanding of access to medicines at the supra national level and to support evidence-based advocacy and policy-making **(Chapter 7)**. The limitations of aggregating national data on the pharmaceutical sector are described, and the policy and programmatic implications of the study findings are presented. Finally, areas for future research are identified that could improve our overall understanding of access to medicines.

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Chapter 2

Medicine prices, availability, and affordability in 36 developing and middle-income countries: a secondary analysis

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Lancet 2009;373:240–9.

Summary

Background

WHO and Health Action International (HAI) have developed a standardised method for surveying medicine prices, availability, affordability, and price components in low-income and middle-income countries. Here, we present a secondary analysis of medicine prices and availability in 45 national and subnational surveys done using the WHO/HAI methodology.

Methods

Data from 45 WHO/HAI surveys in 36 countries were adjusted for inflation or deflation and purchasing power parity. International reference prices from open international procurements for generic products were used as comparators. Results are presented for 15 medicines included in at least 80% of surveys and four individual medicines.

Findings

Average public sector availability of generic medicines ranged from 29.4% to 54.4% across WHO regions. Median government procurement prices for 15 generic medicines were 1.11 times corresponding international reference prices, although purchasing efficiency ranged from 0.09 to 5.37 times international reference prices. Low procurement prices did not always translate into low patient prices. Private sector patients paid 9–25 times international reference prices for lowest-priced generic products and over 20 times international reference prices for originator products across WHO regions. Treatments for acute and chronic illness were largely unaffordable in many countries. In the private sector, wholesale mark-ups ranged from 2% to 380%, whereas retail mark-ups ranged from 10% to 552%. In countries where value added tax was applied to medicines, the amount charged varied from 4% to 15%.

Interpretation

Overall, public and private sector prices for originator and generic medicines were substantially higher than would be expected if purchasing and distribution were efficient and mark-ups were reasonable. Policy options such as promoting generic medicines and alternative financing mechanisms are needed to increase availability, reduce prices, and improve affordability.

Introduction

Medicines account for 20–60% of health spending in developing and transitional countries (1), compared with 18% in countries of the Organisation for Economic Co-operation and Development (2). Up to 90% of the population in developing countries purchase medicines through out-of-pocket payments (3), making medicines the largest family expenditure item after food. As a result, medicines are unaffordable for large sections of the global population and are a major burden on government budgets.

The organisation of a country's pharmaceutical sector can have implications for medicine availability, price, and affordability. In fully public systems, medicines are financed, procured, and distributed by a centralised government unit; in mixed systems, public funding from central budgets or social health insurance is used to reimburse patients or private pharmacies, or medicines are supplied through government medical stores and health facilities but paid for by patient fees; in fully private systems, patients or private insurance systems pay the entire cost of medicines purchased from private pharmacies and drug sellers. Most countries use a combination of these approaches (4).

In 2001, a resolution endorsed by Member States of WHO called for the development of a standardised method for measuring medicine prices (5), which resulted in the launch of the WHO/Health Action International (HAI) Project on Medicine Prices and Availability. The project aims to contribute to target 17 of the Millennium Development Goals: "in cooperation with pharmaceutical companies, provide access to affordable, essential drugs in developing countries".

Before the WHO/HAI project, only a few small studies had been done in low-income and middle-income countries to measure medicine prices and make international comparisons (6-9). Lack of consistent or reproducible methodologies restricted the comparability of these studies, and left them open to criticism (10). As such, the WHO/HAI project's initial focus was on the development of a standardised method for measuring medicine prices, availability, affordability, and price components. After pilot testing in nine countries (11), the methodology was launched in 2003 (12).

More than 50 WHO/HAI medicine pricing surveys have been done (13-15), and results are available on the HAI website (13). Other activities have included validation studies, secondary analyses of survey data by region and disease group (16), investigations into country price variations, and development of a methodology for routine medicine price monitoring. In addition to the WHO/HAI pricing surveys, other class-specific studies of medicine prices across countries have also been done (17).

This paper presents a secondary analysis of medicine availability, price, affordability, and price components in 45 national and subnational surveys done using the WHO/HAI methodology.

Methods

WHO/HAI survey methodology

The WHO/HAI methodology has been published as a manual (12). In the typical survey, data for the availability and price of a specific list of medicines are collected in at least four geographic or administrative areas in a sample of public health facilities, registered private retail medicine outlets, and optionally in medicine outlets in other sectors (e.g. mission hospitals). Data are also collected on government procurement prices, generally at the central level. The methodology also includes estimating the add-on costs that contribute to the final price of medicines by tracking these backwards through the distribution chain. National surveys are usually undertaken, although subnational surveys are recommended in large countries.

Sampling

Medicine outlets are selected using a multistage clustered approach. Survey areas include the main urban centre plus three areas randomly selected from those that can be reached within a day's travel from the main urban centre. In each survey area, the main public hospital, plus four randomly-selected public medicine outlets reachable within 4 hours' travel from the main hospital, make up the public sector facility sample. The private sector and other sector samples are identified by selecting one medicine outlet in each sector that is geographically closest to each public outlet.

Medicines

Survey medicines include a standard list of 30 core medicines to allow international comparisons. Core medicines were selected to indicate a range of treatments for common acute and chronic conditions that cause substantial morbidity and mortality. They are recommended, usually as first-line courses of treatment, in global, regional, and national treatment guidelines; are available in standard formulations and are widely used in many countries or regions; and most are included in the WHO Model List of Essential Medicines. Medicines provided largely through donations or externally funded vertical programmes, such as antiretroviral or tuberculosis medicines, are not included because they do not indicate the typical functioning of the pharmaceutical sector. In

each survey, medicines are removed from the core list if the corresponding disease is not prevalent in the country or if the specific formulation or dosage form is not available. The surveys also include up to 20 supplementary medicines identified for their local clinical relevance. For each medicine, data are collected for both the originator brand, defined as the product that was first authorised worldwide for marketing, and the lowest-priced generic equivalent found at each medicine outlet. Generics are defined as pharmaceutical products intended to be interchangeable with the originator brand product, manufactured without a licence from the originator manufacturer, and marketed after the expiry of patent or other exclusivity rights.

Data collection and analysis

Trained data collectors visit medicine outlets and record medicine availability and price using a standardised form. Several validation and data checking steps during and after collection ensure data quality. Data are entered into a preprogrammed spreadsheet (Excel) by two people using a double entry technique. Results are cross-checked, after which a data validation programme is run which highlights outliers that need verification.

Each sector's data are analysed separately. Availability is reported as the percentage of medicine outlets where a medicine was located on the day of the survey. To facilitate international comparisons, price results are presented as median price ratios, or the ratio of a medicine's median price across outlets to the Management Sciences for Health (MSH) median inter-national reference price for the year preceding the survey (18). MSH international reference prices were selected as the most useful reference standard because they are widely available, updated frequently, and fairly stable over time. They represent actual procurement prices for medicines offered to low-income and middle-income countries by non-profit suppliers and international tender prices. Most MSH prices are for generic products, and are usually ex-works prices (the price at the purchase site that does not include insurance and freight costs) (18). Higher ratios are therefore expected for procurement prices that include insurance and freight. Survey medicines are generally off-patent and thus the generic comparator can be used as the reference price for both originator and generic products. At least four prices must be obtained for calculation of the median price ratio, except for procurement data where one price is sufficient. Affordability is estimated using the salary of the lowest-paid unskilled government worker to establish the number of days' wages needed to purchase courses of treatment for common conditions. Because chronic diseases need ongoing treatment, affordability of a 30-day supply of medicines has been used to indicate monthly medicine expenditures. An example of the data generated from the WHO/HAI survey is provided in the Appendix.

Methodology of the secondary analysis

Data for the secondary analysis were obtained from the HAI global database of survey results (13). Composite data (eg, median price ratio, % availability) were obtained for individual medicines summarised across medicine outlets.

Survey inclusion criteria

All national and subnational surveys that were completed, verified, and included in the HAI database at the time of data extraction (May, 2008) were included in the analysis (table 1). Where repeat surveys were undertaken in a country, the most recent data set was used. Data from the pilot surveys were included where the methodology was consistent with subsequent surveys. Of the 45 surveys included, five were pilot surveys and 14 were subnational surveys.

Medicine selection

A preliminary analysis showed that eight medicines were included in at least 90% of the 45 surveys, 15 in 80% of surveys, and 20 in 70% of surveys. To increase comparability of the findings, summary results are presented for 15 medicines included in at least 80% of surveys, irrespective of their actual availability at individual facilities (table 2). Results are also presented individually for four commonly used medicines: amoxicillin 250 mg capsule or tablet, ciprofloxacin 500 mg capsule or tablet, glibenclamide 5 mg capsule or tablet, and salbutamol 200-dose inhaler 0.1 mg/dose. These medicines indicate how well summary data represent results for individual medicines, and could illustrate differences between treatments for chronic and acute conditions.

All surveys were standardised to the year 2004, using MSH 2003 international reference prices. 2004 was chosen as the base year since most surveys (26 of 45) were done that year. For those countries that did not use MSH 2003 international reference prices in their survey, some differences between original country results and the adjusted results are expected due to fluctuations in MSH prices over time. These fluctuations are small for older multisource medicines (eg, glibenclamide, salbutamol inhaler) but can be larger for medicines with few suppliers or those recently off patent (eg, ranitidine) (19).

Patient price data were corrected for inflation or deflation between the survey year and the base year (using the consumer price index) and also adjusted for the purchasing power parity of the national currency (20). Despite debate on its relation to medicine price inflation, the consumer price index was used after consensus from consulted health economists, since it remains the most widely accepted inflator and deflator for internationally procured pharmaceutical prices and is available for all countries. Procurement

data were adjusted for inflation or deflation and corrected for the exchange rates used in the surveys to standardise local prices to constant dollars. These were not adjusted for purchasing power parity, since most public sector procurements are made through competitive international tenders, and thus should be able to achieve comparable purchase prices irrespective of the purchasing power of the local currency.

Data analysis

Data were analysed by WHO Region: Africa, Americas, eastern Mediterranean, Europe, southeast Asia, and western Pacific (table 2). These regions were selected because WHO Regional offices have previously expressed interest in taking action on issues of medicine price and availability (21). To investigate whether trends exist across countries of similar economic status, data were also analysed by World Bank income group: low-income countries, lower-middle income countries, and upper-middle income countries (22). In the former analysis by World Bank income group, the high-income category was not included, since only two surveys (Kuwait and United Arab Emirates) fell into this category. Indian survey results are reported separately, because of the unique nature of the Indian pharmaceutical market.

Mean percent availability across WHO regions and World Bank income groups was calculated for the four commonly used individual medicines mentioned above as well as for the basket of 15 medicines in each country. Mean median price ratios were also calculated across WHO regions.

In each country and within World Bank income groups, the mean percent differences in price between originator brands and lowest-priced generics (the brand premium) were calculated for medicines available as both product types. The number of medicine pairs available in each survey ranged from seven to nine in India, one to 14 in low-income countries, three to 13 in lower-middle income countries, and nine to 12 in upper-middle income countries.

Field data for the actual mark-ups and other add-on costs that occur in the public and private sector distribution chains are reported by country. Limited data are available, since many countries did not undertake this aspect of the survey. Other countries only reported official fees and mark-ups, which were not included because their application in practice could not be verified.

Results

In the public sector, the availability of the basket of 15 generic medicines was low, ranging from 9.7% in Yemen to 79.2% in Mongolia (table 3). Regional availability ranged from 29.4% in Africa to 54.4% in the Americas; mean availability in the public sector was lower than in the private sector in all regions.

Even in the private sector, availability of generics was low, ranging from 50.1% in the western Pacific to 75.1% in southeast Asia. High private sector availability of generics was recorded in Syria (97.5%) and Chennai, India (91.8%), whereas low availability was seen in Chad (14.8%), Kuwait (36.3%), the Philippines (33.6%), and China (34.6% in Shandong and 38.3% in Shanghai).

Wide variations in availability were noted within WHO regions. In western Pacific countries, public sector availability of generics ranged from 22.2% in the Philippines to 79.2% in Mongolia. Similarly, private sector availability of generics in Africa ranged widely, from 14.8% in Chad to 79.1% in Ethiopia.

Public sector availability of generic medicines was similar across World Bank income groups (figure 1), ranging from 27.0% in upper-middle income countries to 44.3% in lower-middle income countries. However, a greater degree of variability was seen in low-income countries (9.7% in Yemen to 79.2% in Mongolia) than in higher income groups. Private sector availability was similar for low-income countries (60.7%), lower-middle income countries (64.3%), and upper-middle income countries (65.8%). Originator brands were less available than generics in low-income countries (22.3%) and lower-middle income countries (43.7%), but only slightly less available in upper-middle income countries (61.8%). Within all income groups, country-level private sector availability varied widely; for lowest-priced generics it ranged from 14.8% (Chad) to 82.1% (Sudan, Khartoum) in low-income countries, and from 33.6% (Philippines) to 97.5% (Syria) in lower-middle income countries. Private sector availability of originator brands ranged from 0.3% (Mongolia) to 59.1% (Pakistan) in low-income countries, and from 8.2% (China, Shandong) to 80.8% (Morocco) in lower-middle income countries.

For the basket of 15 medicines studied, the average median price ratio in the 39 surveys with public procurement data was 1.11. Public sector procurements in the Americas, eastern Mediterranean, and southeast Asia achieved generic medicine prices that were close to or lower than international reference prices, whereas Africa, Europe, and western Pacific procurements averaged 34%–44% more than international reference prices (table 4). Results varied for the individual medicines examined, with salbutamol usually procured at prices lower than its international reference price in all regions except the Americas, while ciprofloxacin cost substantially more than its international

reference price in all regions. Several countries were also procuring originator brand ciprofloxacin at many times the international reference price – e.g. Morocco, the Philippines, and Nigeria were paying 66.7, 33.6, and 28.4 times the international reference price, respectively.

Public sector procurement prices for lowest-priced generics also varied widely within World Bank income group (figure 2). Median price ratios of lowest-priced generics in low-income countries ranged from 0.09 in Sudan (Khartoum) to 5.37 in Nigeria, whereas in lower-middle income countries, prices ranged from 0.33 in Jordan to 2.94 in the Philippines.

In many countries, medicines are free in the public sector, but availability is often poor. Where public sector patients pay for medicines, even lowest-priced generics can cost many times the international reference price; regional median price ratios for the basket of 15 medicines varied from 3.18 in the Americas to 11.95 in western Pacific countries (table 5). However, public sector patient prices were still generally lower than prices in the private sector in most regions. In Europe and western Pacific, prices of lowest-priced generics in the two sectors were similar, whereas originator brands in the private sector were more highly priced.

Similar to procurement prices, patient prices for ciprofloxacin 500 mg capsules or tablets were consistently high, with private sector median price ratios for lowest priced generics ranging from 19 to 53 across WHO regions. Prices of salbutamol 0.1 mg/dose inhaler were substantially lower in all WHO regions; median price ratios for lowest-priced generics ranged from 3 to 7 in the private sector.

The percentage difference in price between originator brands and lowest-priced generics (brand premium) in the private sector was over 300% in lower-middle income countries and low-income countries, whereas in upper-middle income countries it was substantially lower (152%), and in India it was only 6% (figure 3).

The affordability of treating one acute infection and three chronic illnesses was assessed in the public and private sectors (table 6). Many medicines were not consistently available in the public sector. Therefore even when the public sector provides medicines for free or at a low cost, patients might still need to purchase medicines from the private sector where they are frequently unaffordable. For example, a month's course of lowest-priced generic ranitidine (150 mg capsules or tablets, two a day for 30 days) to treat an ulcer cost more than 3 days' wages in Africa, eastern Mediterranean, and Europe.

Data for price components were only available for a few countries (table 7). In countries such as El Salvador, India, and Mali, multiple duties and taxes were applied. Although the amounts charged are small, they have a substantial cumulative effect if

applied early in the supply chain. In countries where value added tax was applied, it varied from 4% (India) to 15% (Mongolia). Wholesale mark-ups ranged from 2% in Pakistan to a combined mark-up by importers, distributors, and wholesalers of 380% in El Salvador. Retail mark-ups ranged from 10% in Mongolia to 552% in El Salvador. Different mark-ups were often applied to originator brands and generics, with higher mark-ups generally applied to generics. Although add-on costs in the medicine supply chain can be substantial, in some cases the manufacturer's selling price is the largest contributor to the final price. In Pakistan, for example, the manufacturer's selling price for locally-produced generic amoxicillin represented 78% of the final medicine price in the private sector.

In several countries (China, Ethiopia, Malaysia, Mali, Mongolia, and Uganda), wholesale or retail mark-ups were also applied in the public sector, suggesting the use of medicine sales as a revenue-generating mechanism.

Discussion

The WHO/HAI survey methodology allows for the measurement of medicine prices and availability in a standardised way, with multiple steps to ensure data quality. The common list of core medicines with specified dosage forms and strengths allows for more reliable international comparisons, whereas supplementary medicines identified at the country level ensure local relevance.

The survey's target medicine list and outlet sample approach have been validated in a medicine prices survey done in Peru in 2005, which showed that more remote outlets were similar to those selected using the standardised methodology, and availability of therapeutic alternatives were generally similar to those of the WHO/HAI core medicines. The results of this single-country validation exercise suggest that the target medicine list and sample selection are methodologically sound. Further, originator brand prices from the WHO/HAI validation survey in Peru had a high (99%) correlation with pharmacy invoice prices from Intercontinental Medical Statistics Health.

Although international comparisons should compare prices of identical products across countries, the same product can still have a different role in the pharmaceutical market in different countries (23). For this reason, results were reported for both individual medicines and for 15 medicines found in at least 80% of surveys. The list of core medicines has since been revised to 14 commonly found products, with additional lists to account for regional variations (24).

Despite its strengths, the WHO/HAI methodology has several limitations. First, differences in quality across products, and differences in patent status between countries, are not accounted for (25). Second, availability and price are determined for the specific list of survey medicines, and do not account for alternate dosage forms of these products or therapeutic alternatives. Third, the reliability of median price ratios as a metric for comparison depends on the number of supplier prices used to determine the median international reference price for each medicine. When few supplier prices are available or when the buyer price is used as a proxy, median price ratio results can be skewed by a particularly high or low international reference price.

Availability data only refer to the day of data collection at each facility and might not indicate average availability of medicines over time. However, since surveys are done in several facilities over a period of time, the data provide a reasonable estimate of the overall situation and are indicative of the real-life situation faced by patients on a daily basis. Additionally, in countries where survey medicines are not included on the national essential medicines list (government-approved selective list used for procurement or reimbursement), public sector facilities would not be expected to stock some of the survey medicines. We were unable to assess the current data this way due to lack of information on which medicines were on the national essential medicines lists at the time of the survey.

The daily wage of the lowest-paid government worker is used to estimate treatment affordability. However, in many countries a substantial proportion of the population earns less than this amount. Further, the need for other non-discretionary expenditures (e.g. food or housing), seasonal fluctuations in income, the number of dependants who live on this wage, and the full costs of treatment, are not accounted for. Nevertheless, this wage is a universally available metric to assess the affordability of medicines. Others, such as the national minimum wage, have proven less reliable in other WHO surveys. Comparisons to the median daily wage or per head gross domestic product are possible where these are available, but are not as informative or easily interpreted. When the daily wage of the lowest-paid government worker was compared with the gross national income per head of population for ten countries in sub-Saharan Africa where pricing surveys had been done, a correlation (R^2=0.2677) between the two measures was obtained. Further work is underway to identify alternate measures of affordability that could be included in the WHO/HAI methodology.

Average public procurement prices for generics range from below international reference prices in some regions to moderately (34–44%) higher in others, which indicates that most countries procure medicines at competitive prices, but that procurement ef-

ficiency can be improved in some countries, especially in low-income countries and lower-middle income countries.

Public sector availability of medicines was consistently low, which could be due to variations in the products included in national essential medicines lists or poor compliance with their recommendations. In this sector, even when medicines are available for free or at low cost, access is limited by low availability. Low availability in the public sector can be due to a combination of factors, such as inadequate funding, lack of incentives for maintaining stocks, inability to forecast accurately, inefficient distribution systems, or leakage of medicines for private resale. Although availability in the private sector was consistently higher, in many countries it was also low, and high private sector prices could further hinder access. However, enforcing low prices could have a perverse effect on availability by providing a disincentive for stocking these products.

Wide variability in the availability of originator brands and generics was observed across countries in all income groups. Generics were more widely available than brands in the private sector in low-income countries and lower-middle income countries, whereas in upper-middle income countries the availability of brands and generics was similar. Since originator brands are generally more expensive, patients might be paying more to purchase these products when cheaper alternatives exist. In India, the low brand premium of 6% results in part from the large number of generic manufacturers in the country and the pricing regulations in force.

In some countries, similar patient prices are seen in public and private sector facilities. For example, median price ratios for lowest-priced generics in the public and private sectors of Khartoum State are 11.1 and 12.1, respectively. Given generally low public procurement costs, this suggests that some public facilities are using medicine sales to subsidise other parts of the health-care system. Similar observations have been made for the non-governmental organisation sectors in Senegal, Kenya, and Uganda, where revenue from medicine sales is being used to cover general operating expenses. Since public facilities are a primary treatment option for the poor, such practices are inherently inequitable and alternate methods of equitable health-system financing should be used, such as insurance coverage for essential medicines. Alternative financing mechanisms are especially important for the very poor for whom any price would be unaffordable.

Although treatments for conditions such as acute respiratory infection and diabetes using lowest-priced generics were fairly affordable in most regions, costs escalate when originator brands are used. Although treatments seem affordable, substantial proportions of developing country populations are earning less than the lowest-paid government worker. Furthermore, this affordability measure only includes medicines and does not account for other treatment costs (eg, diagnostics). As such, the true degree

of unaffordability is likely to be underestimated. For chronic disease medicines, affordability is assessed based on monthly treatment costs; given that these conditions need long-term treatment they can be much less affordable than a one-time expenditure to treat an acute illness.

Similar to results reported elsewhere (15), chronic disease medicines were unaffordable for large proportions of the population. Increased emphasis should be placed on reducing the cost of these medicines in light of the high burden of non-communicable diseases (26). The affordability of chronic disease treatments is further constrained by the frequent need for more costly combination therapies, and by the ongoing nature of treatment. Although patients might be able to afford treatment for acute illness as a one-time expenditure, they may not be able to afford continuous treatment for chronic diseases.

Many countries still apply value added tax and other taxes and tariffs to medicines. Considering that these are essentially a tax on the sick, there is a strong rationale for exempting medicines from taxes (27). Although the taxes and tariffs might be small, they can still have a large cumulative effect when applied early in the supply chain.

Price component studies have only been done in a few countries, which indicates the difficulty in collecting such information in opaque environments that allow for substantial, unjustified mark-ups. In countries where data were available, wide variations in importer, wholesale, and retail mark-ups were observed. Further research is needed to establish appropriate mark-up levels that promote medicine availability and affordability while ensuring the economic viability of the supply chain. Mark-ups were generally higher for generics than for originator brands, but if generics are low-priced, they could still result in a lower return. Higher mark-ups for generics might therefore be justified if they provide an incentive to stock low-priced products. Substantive mark-ups were also seen in the public sector of several countries, suggesting that public sectors are generating revenue from medicine sales to subsidise other parts of the health care system. While taxes or mark-ups added substantially to the selling price in some cases, in others the manufacturer's selling price was the major component of the final price. Additional data from various countries are needed to draw conclusions on the determinants of final medicine prices, recognising the need to maintain a viable supply chain to ensure access.

A range of policy options are available to address issues of high prices and low availability of medicines. The most appropriate actions to follow depend on a country's individual survey results and their underlying determinants, as well as local factors including existing pharmaceutical policies and market situations.

Low public sector availability can be addressed through improved procurement efficiency (eg, national pooled purchasing, procurement by generic name) and adequate, equitable, and sustainable financing. In practice this could mean schemes to make chronic disease medicines available in the private sector at subsidised prices, or through the promotion of differential pricing schemes that offer reduced prices in poorer countries. Manufacturers of antiretrovirals (28), antimalarials (29), and insulin (30) all offer differentially-priced products.

Resource-constrained public sectors might need to target widespread access to a reduced number of essential generic medicines, rather than attempting to supply a larger number of both originator brand and generic medicines. As recommended elsewhere (15,31), improved public sector support is needed for chronic disease medicines.

Medicine prices can be reduced by eliminating duties and taxes on medicines (27), a policy measure which has been implemented in many countries. Monitoring is needed to ensure that savings are passed on to patients. Regulating mark-ups is another strategy to avoid excessive add-on costs in the supply chain. However, maximum percentage mark-ups provide incentives to sell higher-priced products to obtain a higher return. Regressive mark-up schemes avoid this problem by allowing higher mark-ups for lower-priced products. In Syria, for example, private pharmacy mark-ups range from 30% when the pharmacy procurement price is 40 Syrian Pounds (SYP) or less, to 8% when the procurement price is 501 SYP or higher (32). Despite the positive effects of these policies on mark-ups, reducing the manufacturer's selling price will generally have a greater effect on the final cost.

Increased use of generic medicines could improve affordability in most countries where generic products are priced substantially lower than originator brands. Several options are available to promote use of generics, including preferential registration procedures, ensuring the quality of generic products, encouraging price competition, and increasing the confidence of physicians, pharmacists, and patients in the quality of generics. A multipronged approach will generally be needed in countries attempting to increase generic uptake.

Data from the WHO/HAI Project on Medicine Prices and Availability confirm that substantial opportunities exist to increase availability, lower prices, and improve affordability of medicines in all regions and at all levels of country development. Using such data, countries should develop and implement national policies to improve the availability and affordability of essential medicines. The evaluation of such policies, including measuring progress against predetermined benchmarks and timelines, is crucial. Medicine prices, availability, affordability, and price components should be surveyed at least every 2 years using the WHO/HAI methodology, and should be routinely monitored

and reported on a more frequent basis. Currently, evidence is limited on the effect of various policy options to make medicines more affordable; regular monitoring will be needed to assess whether policies are effective.

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Tables and figures

Table 1: Surveys included in the secondary analysis

Country (survey date)	WHO region	World Bank Income Group (2007/08)
Armenia (11/2001)[*,†,‡]	European	lower-middle
Brazil, Rio de Janeiro State (10/2001)[*,†,§]	Americas	upper-middle
Cameroon (05/2002)[*,‡]	Africa	lower-middle
Chad (05/2004)	Africa	low
China, Shandong Province (10/2004)	Western Pacific	lower-middle
China, Shanghai Province (09/2004)	Western Pacific	lower-middle
El Salvador (11/2006)	Americas	lower-middle
Ethiopia (09/2004)	Africa	low
Fiji (09/2004)[†]	Western Pacific	lower-middle
Ghana (10/2004)	Africa	low
India, Chennai State (01/2004)	South-East Asia	low
India, Haryana State (10/2004)	South-East Asia	low
India, Karnataka State (11/2004)	South-East Asia	low
India, Maharashtra State, 12 districts (10/2004)	South-East Asia	low
India, Maharashtra State, 4 regions (01/2005)	South-East Asia	low
India, Rajasthan State (06/2003)	South-East Asia	low
India, West Bengal State (12/2004)	South-East Asia	low
Indonesia (08/2004)	South-East Asia	lower-middle
Jordan (05/2004)	Eastern Mediterranean	lower-middle
Kazakhstan (11/2004)	European	upper-middle
Kenya (11/2004)	Africa	low
Kuwait (06/2004)	Eastern Mediterranean	high
Kyrgyzstan (02/2005)[†]	European	low
Lebanon (02/2004)	Eastern Mediterranean	upper-middle
Malaysia (10/2004)	Western Pacific	upper-middle

Table 1: Surveys included in the secondary analysis *(continued)*

Country (survey date	WHO region	World Bank Income Group (2007/08)
Mali (03/2004)	Africa	low
Mongolia (11/2004)	Western Pacific	low
Morocco (04/2004)	Eastern Mediterranean	lower-middle
Nigeria (09/2006)	Africa	low
Pakistan (07/2004)	Eastern Mediterranean	low
Peru (09/2005)	Americas	lower-middle
Philippines (02/2005)	Western Pacific	lower-middle
South Africa, Kwazulu Natal State (09/2001)[*,†,§]	Africa	upper-middle
Sri Lanka (09/2001)[*,†,‡,§]	South-East Asia	lower-middle
Sudan, Gadarif State (02/2006)	Eastern Mediterranean	low
Sudan, Kordofan State (02/2006)	Eastern Mediterranean	low
Sudan, Khartoum State (06/2005)	Eastern Mediterranean	low
Syrian Arab Republic (12/2003)[†]	Eastern Mediterranean	lower-middle
Tajikistan (02/2005)[‡]	European	low
Tunisia (03/2004)	Eastern Mediterranean	lower-middle
Uganda (04/2004)	Africa	low
United Arab Emirates (12/2006)	Eastern Mediterranean	high
United Republic of Tanzania (09/2004)	Africa	low
Uzbekistan (12/2004)[†]	European	low
Yemen (07/2006)	Eastern Mediterranean	low

[*]Pilot studies. Except for South Africa, Kwazulu Natal State, availability data were excluded since they were not assessed using the current WHO/HAI methodology. [†]Did not survey public sector medicine outlets. [‡]Did not survey public sector procurement prices. [§]Private sector data on lowest-priced generic medicines excluded since they were not surveyed using the current WHO/HAI methodology.

Table 2. Basket of 15 medicines found in at least 80% of surveys

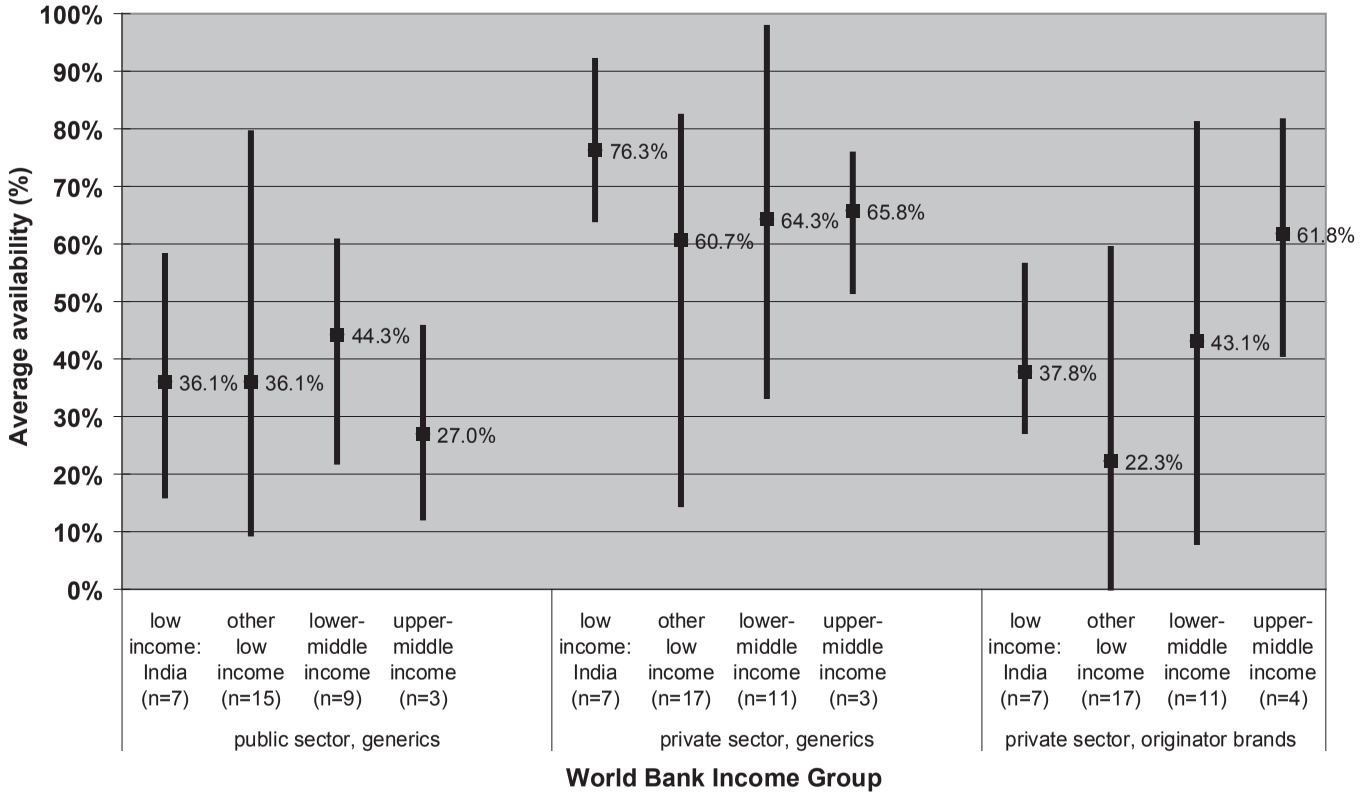
Medicine	Medicine category	% of surveys with medicine
Salbutamol 0.1 mg/dose inhaler	Antiasthmatic	100%
Captopril 25 mg capsule/tablet	Antihypertensive	96%
Ciprofloxacin 500 mg capsule/tablet	Antibacterial	96%
Amitriptyline 25 mg capsule/tablet	Antidepressant	93%
Omeprazole 20 mg capsule/tablet	Antacid	93%
Ranitidine 150 mg capsule/tablet	Antacid	93%
Aciclovir 200 mg capsule/tablet	Antiviral	91%
Glibenclamide 5 mg capsule/tablet	Antidiabetic	91%
Amoxicillin 250 mg capsule/tablet	Antibacterial	89%
Ceftriaxone 1 g/vial injection	Antibacterial	89%
Co-trimoxazole 8+40 mg/ml suspension	Antibacterial	89%
Fluoxetine 20 mg capsule/tablet	Antidepressant	89%
Hydrochlorothiazide 25 mg capsule/tablet	Antihypertensive	89%
Atenolol 50 mg capsule/tablet	Antihypertensive	87%
Beclometasone 0.05 mg/dose inhaler	Antiasthmatic	84%

Table 3. Average of country-level mean percentage availability of any generic product, by WHO region

	Mean availability (range) - public sector (%)							Mean availability (range) - private sector (%)						
	AFR n=8*	AMR n=2†	EMR n=11‡	EUR n=2§	SEAR n=8–	WPR n=5**	All surveys n=36	AFR n=8	AMR n=2	EMR n=12	EUR n=4	SEAR n=8	WPR n=6	All surveys n=40
Basket of 15 medicines	29.4 (20.3, 41.2)	54.4 (52.7 56.0)	39.6 (9.7, 60.4)	40.5 (23.1, 57.9)	38.3 (16.3, 57.9)	43.0 (22.2, 79.2)	38.4 (9.7, 79.2)	54.6 (14.8, 79.1)	68.6 (66.6, 70.6)	68.9 (36.3, 97.5)	66.9 (61.4, 70.7)	75.1 (64.3, 91.8)	50.1 (33.6 77.6)	64.2 (14.8, 97.5)
Amoxicillin 250 mg capsule/tablet	80.9 (66.7, 92.9)	42.3 (0.0, 84.6)	62.0 (0.0, 100)	45.0 (0.0, 90.0)	76.2 (45.8, 100)	74.0 (30.8, 100)	68.7 (0.0, 100)	65.7 (0.0, 100)	46.2 (30.8, 61.5)	69.4 (0.0, 100)	79.6 (70.0, 93.3)	93.7 (82.8, 100)	87.9 (72.5, 100)	76.0 (0.0, 100)
Ciprofloxacin 500 mg capsule/tablet	50.4 (4.2, 82.1)	94.2 (92.3, 96.2)	49.3 (0.0, 100)	42.5 (0.0, 85.0)	62.8 (0.0, 100)	24.5 (0.0, 75.0)	52.0 (0.0, 100)	79.3 (27.3, 96.0)	97.6 (96.2, 99.0)	92.3 (66.7, 100)	82.7 (43.3, 97.5)	92.8 (68.6, 100)	57.3 (0.0, 97.2)	82.4 (0.0, 100)
Glibenclamide 5mg capsule/ tablet	37.3 (4.8, 79.4)	79.9 (63.4, 96.2)	69.1 (5.0, 100)	95.0 (90.0, 100)	53.4 (3.8, 100)	40.6 (0.0, 100)	56.6 (0.0, 100)	60.6 (0.0, 100)	90.8 (87.5, 94.2)	88.2 (44.0, 100)	89.4 (80.0, 100)	62.5 (20.0, 100)	45.0 (0., 94.4)	71.3 (0.0, 100)
Salbutamol 0.1 mg/dose inhaler	14.0 (0.0, 55.9)	88.4 (86.5, 90.4)	35.5 (0.0, 95.0)	42.5 (0.0, 85.0)	5.1 (0.0, 30.0)	48.3 (0.0, 100)	29.1 (0.0, 100)	47.0 (0.0, 95.0)	55.2 (50.0, 60.4)	63.8 (0.0, 100)	74.2 (35.0, 96.7)	79.0 (0.0, 100)	52.0 (7.8, 97.2)	60.8 (0.0, 100)

WHO Region: AFR=Africa. AMR=Americas. EMR=eastern Mediterranean. EUR=European. SEAR= southeast Asia. WPR=western Pacific. South Africa did not survey the public sector; no availability data for Cameroon (pilot). † no availability data for Brazil, Rio de Janeiro State (pilot). ‡ Syria did not survey the public sector. § Kryrgyzstan and Uzbekistan did not survey the public sector; no availability data for Armenia (pilot). ⁻ No availability data for Sri Lanka (pilot). ** Fiji did not survey the public sector.*

Figure 1. Average of country-level mean % availability of medicines, by World Bank Income Group



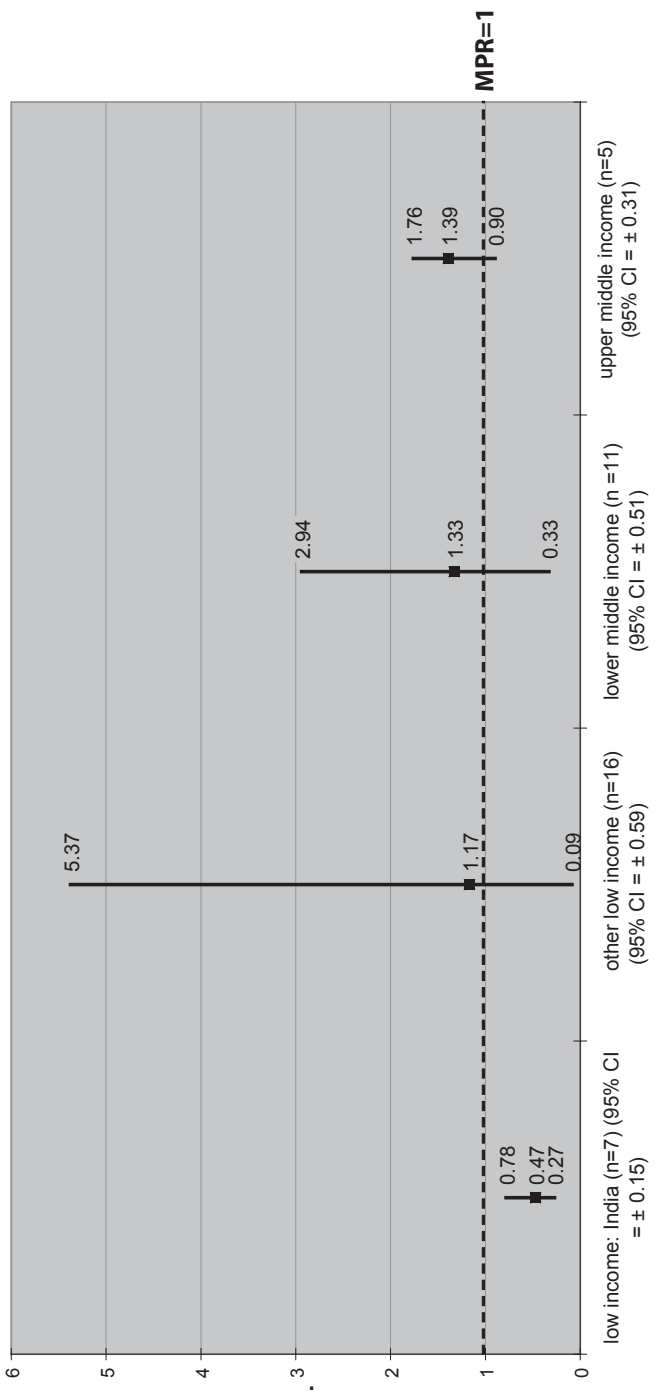
Data are mean (maximum/minimum).

Table 4. Median price ratios* of public sector procurement prices for lowest-priced generics, overall and by WHO region

	AFR	AMR	EMR	EUR	SEAR	WPR	All surveys
Median across basket of 15 medicines	1.34 (n=9) (0.55, 5.37)	1.15 (n=3) (0.70, 1.71)	1.01 (n=12) (0.09†, 2.81)	1.40 (n=3) (1.11, 1.76)	0.63 (n=8) (0.27, 1.72)	1.44 (n=6) (0.59, 2.94)	1.11 (n=41) (0.09, 5.37)
Amoxicillin 250 mg capsule/tablet	1.18 (n=7) (0.64, 3.06)	1.70 (n=1) (1.70, 1.70)	1.14 (n=6) (0.58, 2.31)	2.46 (n=3) (1.94, 2.91)	1.28 (n=8) (0.68, 2.14)	1.23 (n=4) (0.70, 1.99)	1.36 (n=29) (0.58, 3.06)
Ciprofloxacin 500mg capsule/tablet	2.07 (n=6) (0.46, 7.10)	1.52 (n=3) (0.74, 2.92)	4.32 (n=10) (0.09, 25.35)	1.55 (n=3) (0.76, 2.90)	1.90 (n=7) (0.57, 6.28)	2.55 (n=1) (2.55, 2.55)	2.69 (n=30) (0.09, 25.35)
Glibenclamide 5mg capsule/tablet	3.42 (n=7) (0.60, 17.37)	1.03 (n=2) (0.70, 1.36)	1.95 (n=11) (0.41, 4.96)	3.10 (n=2) (2.50, 3.71)	1.52 (n=7) (0.27, 4.52)	1.68 (n=4) (0.30, 5.24)	2.15 (n=33) (0.27, 17.37)
Salbutamol 200-dose inhaler 0.1mg/dose	0.61 (n=5) (0.43, 1.04)	1.57 (n=3) (0.62, 3.01)	0.85 (n=8) (0.46, 1.54)	0.74 (n=2) (0.61, 0.87)	0.59 (n=1) (0.59, 0.59)	0.95 (n=4) (0.77, 1.10)	0.89 (n=23) (0.43, 3.01)

*Data are mean (number of surveys) (range). WHO Region: AFR=Africa. AMR=Americas. EMR=eastern Mediterranean. EUR=European. SEAR= southeast Asia. WPR=western Pacific. *Ratio of the median procurement price to the MSH international reference price. † Based on a basket of 3 widely-available antibiotics (amoxicillin 250mg, ciprofloxacin 500mg and co-trimoxazole 8+40 mg/ml suspension).*

Figure 2. MPR for lowest priced generics in public procurement, by World Bank Income Group



Data are mean (maximum/minimum).

Table 5. Median price ratios* of originator brands and lowest-priced generics in the private sector, and of lowest-priced generics in the public sector, by WHO region

	AFR			AMR			EMR			EUR			SEAR			WPR		
	Private OB	Private LPG	Public LPG	Private OB	Private LPG	Public LPG	Private OB	Private LPG	Public LPG	Private OB	Private LPG	Public LPG	Private OB	Private LPG	Public LPG	Private OB	Private LPG	Public LPG
Median across basket of 15 medicines	62.92 (n=9)	21.23 (n=9)	6.79 (n=8)	52.66 (n=3)	25.21 (n=2)	3.18 (n=1)	24.54 (n=12)	13.75 (n=12)	6.88 (n=5)	24.96 (n=5)	8.69 (n=5)	8.19 (n=2)	21.28 (n=9)	9.61 (n=8)	6.84 (n=1)	34.21 (n=5)	11.25 (n=6)	11.95 (n=4)
Amoxicillin 250 mg capsule/tablet	59.01 (n=6)	7.69 (n=6)	5.96 (n= 6)	53.22 (n=1)	29.63 (n=2)	4.55 (n=1)	35.47 (n=5)	14.11 (n=9)	5.67 (n=5)	21.97 (n=1)	13.78 (n=5)	10.49 (n=1)	31.17 (n=4)	22.12 (n=8)	7.46 (n=1)	26.23 (n=2)	11.08 (n=5)	9.32 (n=3)
Ciprofloxacin 500mg capsule/tablet	268.46 (n=4)	22.04 (n=7)	21.07 (n= 6)	242.09 (n=3)	53.10 (n=2)	2.06 (n=1)	154.89 (n=7)	50.47 (n=12)	13.79 (n =4)	257.73 (n=2)	22.12 (n=5)	6.79 (n=1)	57.46 (n=8)	19.22 (n=8)	19.31 (n=1)	195.96 (n=3)	32.94 (n=4)	81.71 (n=1)
Glibenclamide 5mg capsule/ tablet	161.97 (n=7)	33.87 (n=7)	17.65 (n=7)	211.86 (n=1)	67.56 (n=2)	3.18 (n=1)	59.85 (n=8)	25.06 (n=12)	17.97 (n=4)	12.77 (n=1)	12.98 (n=4)	10.54 (n=2)	48.10 (n=8)	19.06 (n=8)	17.65 (n=1)	99.57 (n=3)	34.59 (n=4)	56.97 (n=1)
Salbutamol 200-dose inhaler 0.1mg/ dose	14.26 (n=8)	7.19 (n=6)	3.58 (n= 2)	9.05 (n=2)	5.58 (n=2)	1.82 (n=1)	6.00 (n=11)	3.28 (n=10)	3.02 (n=3)	5.58 (n=4)	4.05 (n=5)	3.73 (n=1)	6.47 (n=9)	4.56 (n=7)	---	8.60 (n=5)	4.32 (n=6)	4.64 (n=2)

*WHO Region: AFR=Africa. AMR=Americas. EMR=eastern Mediterranean. EUR=European. SEAR= southeast Asia. WPR=western Pacific. OB=originator brand. LPG=lowest-priced generic.*Ratio of the median final (patient) price to the MSH international reference price*

Figure 3. Median price difference between originator brands and lowest priced generics for matched pairs of medicines, private sector, by World Bank Income Group

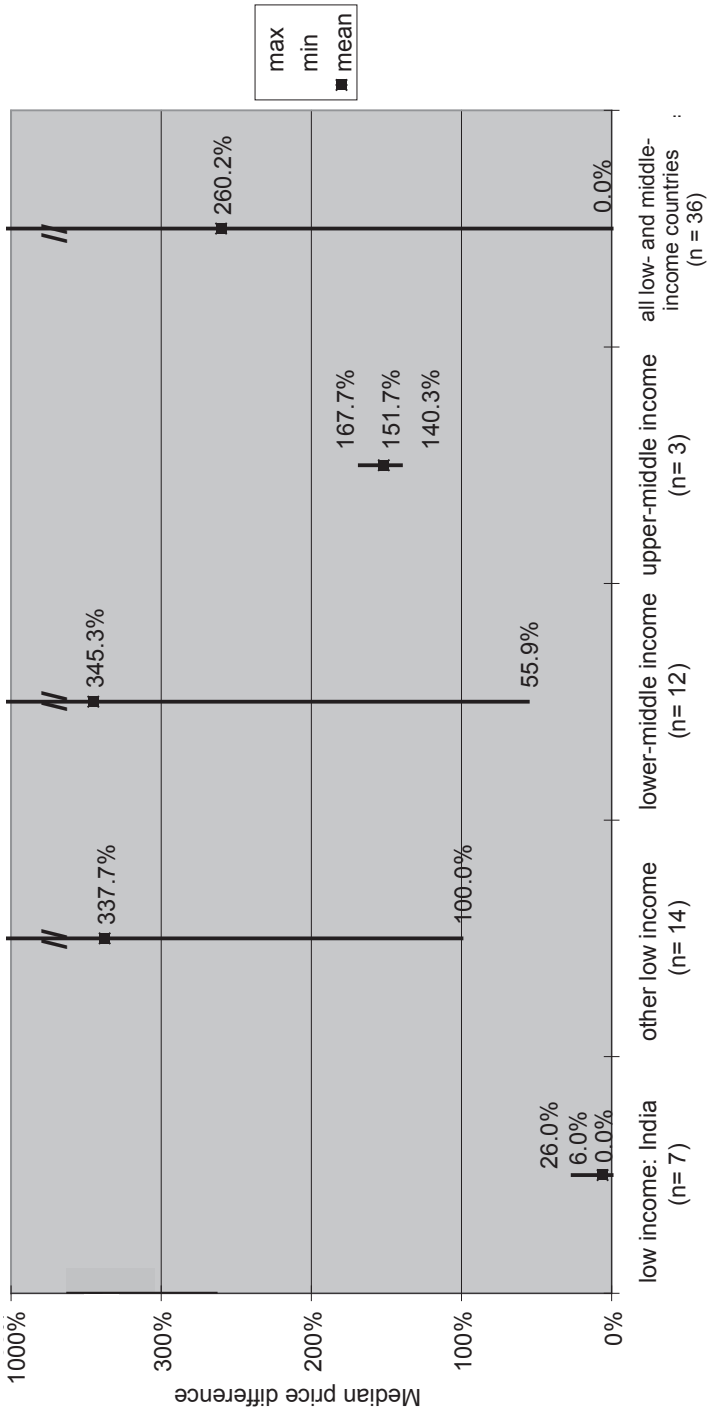


Table 6. Mean number of day's wages of the lowest-paid unskilled government worker needed to purchase a course of treatment, by WHO Region

		AFR	AMR	EMR	EUR	SEAR	WPR
Adult respiratory infection Amoxicillin 250mg capsule/ tablet, three per day for 7 days	Private sector OB	2.9 (n=6)	1.9 (n=1)	1.6 (n=5)	1.4 (n=1)	1.2 (n=4)	0.5 (n=2)
	Private sector LPG	0.5 (n=6)	1.0 (n=2)	0.6 (n=8)	2.9 (n=5)	0.6 (n=8)	0.4 (n=4)
	Public sector LPG	0.5 (n=6)	0.2 (n=1)	0.3 (n=4)	7.9 (n=1)	0.4 (n=1)	0.4 (n=3)
Diabetes Glibenclamide 5mg capsule/tablet, two per day for 30 days*	Private sector OB	8.4 (n=7)	4.5 (n=1)	2.1 (n=8)	0.5 (n=1)	1.3 (n=8)	1.6 (n=3)
	Private sector LPG	1.8 (n=7)	1.5 (n=2)	0.9 (n=12)	1.8 (n=4)	0.4 (n=8)	0.7 (n=4)
	Public sector LPG	1.1 (n=7)	0.1 (n=1)	0.5 (n=4)	2.5 (n=2)	0.6 (n=1)	0.7 (n=1)
Asthma Salbutamol 0.1 mg/dose inhaler, 200 doses	Private sector OB	4.4 (n=8)	2.0 (n=3)	1.6 (n=11)	3.6 (n=4)	1.2 (n=9)	1.4 (n=5)
	Private sector LPG	2.5 (n=6)	1.0 (n=2)	0.8 (n=10)	5.0 (n=5)	0.6 (n=7)	0.7 (n=6)
	Public sector LPG	1.6 (n=2)	0.6 (n=1)	0.7 (n=3)	15.0 (n=1)	---	1.1 (n=2)
Ulcer Ranitidine 150 mg capsule/ tablet, two per day for 30 days*	Private sector OB	35.4 (n=6)	9.0 (n=3)	8.5 (n=9)	21.1 (n=3)	2.7 (n=9)	5.5 (n=3)
	Private sector LPG	5.0 (n=6)	2.8 (n=2)	3.8 (n=11)	4.6 (n=5)	0.5 (n=8)	1.7 (n=6)
	Public sector LPG	6.3 (n=4)	0.6 (n=1)	1.3 (n=4)	6.3 (n=2)	2.2 (n=1)	1.2 (n=4)

*WHO Region: AFR=Africa. AMR=Americas. EMR=eastern Mediterranean. EUR=European. SEAR= southeast Asia. WPR=western Pacific. OB=originator brand. LPG=lowest-priced generic. *One month has been used as the course of treatment for chronic diseases.*

Table 7: Cumulative percentage mark-ups between manufacturer's selling price or Cost, Insurance and Freight price, and final patient price in the public and private sectors

Country	Total cumulative % mark-up, public sector	Total cumulative % mark-up, private sector
China (Shandong)*	24-35%	11-33%
El Salvador*		165-6894%
Ethiopia*	79-83%	76-148%
India†		29-694%
Malaysia‡	19-46%	65-149%
Mali*	77-84%	87-118%
Mongolia*	32%	68-98%
Morocco‡		53-93%
Uganda‡	30-66%	100-358%
United Republic of Tanzania*	17%	56%
Pakistan‡		28-35%

**Country surveys of price components using WHO/HAI standard methodology. †Kotwani A, Levison L. Price components and access to medicines in Delhi, India. http://www.dfidhealthrc.org/meta/documents/Price%20component%20Report_Delhi%20%20India_MeTA.pdf (accessed June 20, 2008).*
‡ Levison L. Investigating price components: medicine costs between procurement and point of delivery. Draft report on initial field studies. Unpublished (2008).

Appendix

Survey of medicine prices, availability, affordability, and price components in Peru

In 2002, HAI Latin America Coordination Office undertook a survey of medicine prices and availability in Peru using the WHO/HAI methodology. The prices of 38 medicines were measured in an expanded sample of 52 public health care facilities and 96 pharmacies in six regions, as well as for public procurement (1).

In the public sector, procurement prices of lowest-priced generics were 1.28 times MSH reference prices, which may reflect the difference between Peruvian prices, which are include insurance and freight, and MSH prices, which are usually Ex-works. However, a wide range of price ratios were observed across individual medicines, with 25% of medicines purchased at 3.6 times the IRP or more. Patient prices of lowest-priced generics in the public sector were 1.4 time MSH reference prices, with a median availability of only 62%. However, six survey medicines were not on the Essential Medicines List in Peru, and a further 8 were not commonly used at community health facilities; these 14 medicine were therefore not expected to be available in the majority of the public sector sample. For other medicines public sector availability ranged from 11% to 100%.

In the private sector, median prices of originator brands and lowest-priced generics were 27.8 and 5.6 times the MSH prices, respectively. Restricting the analysis to medicines found as both product types, originator brands were found to cost about 5 times more than their lowest-price generic equivalent. In this sector median % availability was 15% for originator brands and 61% for generics.

When medicines are not available in public health facilities patients may be forced to purchase medicines from the private sector. Restricting the analysis to medicines found in both sectors, lowest-priced generic products were found to be 3.8 times more expensive in the private sector than in the public sector. For some patients, this price differential may mean the difference between purchasing a medicine or going without. For example, in a public facility the lowest-paid government worker would need to spend 0.1 days' wages to purchase treatment for an uncomplicated urinary tract infection. In a private pharmacy, the cost escalates to 0.5 days' wages to purchase the lowest-priced generic product, and 11 days' wages to buy the originator brand.

Estimated price component data based primarily on interviews found a cumulative mark-up of 238% for captopril 25 mg in the private sector, which includes importer, wholesale and retail mark-ups of 30, 25% and 50%, respectively. In the public sector,

the cumulative mark-up for ciprofloxacin 500mg was 108%, including a public facility mark-up of 25%.

Several policy options could be explored for improving medicine prices and availability in Peru. In public procurement, high MPRs for individual medicines suggests that there may be opportunities to improve procurement efficiency and in turn increase availability at public facilities. In the private sector, though generic prices were high compared to MSH prices, they were still much lower than brand prices. Thus, options for promoting generic use, and reducing their prices (e.g. by regulation of mark-ups) should be explored. It should be noted that in 2001 the Peruvian government exempted a range of cancer medicines and ARVs from their import tax (21%) and general sales tax (19%), however it has been shown that this savings is not being passed on to patients (2). This underscores the importance of adequate policy enforcement, combined with routine monitoring to ensure that policy actions are having the desired effects.

References

1. HAI Latin America Coordination Office. Medicine prices, availability, affordability and price components in Peru (report on the Internet). 2007 July (cited 2008 June 11). Available from: http://www.haiweb.org/medicineprices/surveys/200509PE/sdocs/survey_report.pdf

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Chapter 3

Differences in the availability of medicines for chronic and acute conditions in the public and private sectors of developing countries

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Summary

Objective

To investigate potential differences in the availability of medicines for chronic and acute conditions in low- and middle-income countries.

Methods

Data on the availability of 30 commonly-surveyed medicines – 15 for acute and 15 for chronic conditions – were obtained from facility-based surveys conducted in 40 developing countries. Results were aggregated by World Bank country income group and World Health Organization region.

Findings

The availability of medicines for both acute and chronic conditions was suboptimal across countries, particularly in the public sector. Generic medicines for chronic conditions were significantly less available than generic medicines for acute conditions in both the public sector (36.0% availability versus 53.5%; $P = 0.001$) and the private sector (54.7% versus 66.2%; $P = 0.007$). Antiasthmatics, antiepileptics and antidepressants, followed by antihypertensives, were the drivers of the observed differences. An inverse association was found between country income level and the availability gap between groups of medicines, particularly in the public sector. In low- and lower-middle income countries, drugs for acute conditions were 33.9% and 12.9% more available, respectively, in the public sector than medicines for chronic conditions. Differences in availability were smaller in the private sector than in the public sector in all country income groups.

Conclusion

Current disease patterns do not explain the significant gaps observed in the availability of medicines for chronic and acute conditions. Measures are needed to better respond to the epidemiological transition towards chronic conditions in developing countries alongside current efforts to scale up treatment for communicable diseases.

Introduction

Chronic, noncommunicable diseases such as cardiovascular diseases, diabetes and asthma impose a large and growing health burden on developing countries (1). Chronic diseases are responsible for at least 50% of the deaths that occur in all World Health Organization (WHO) regions except Africa, where they still account for 25% of all deaths. While the proportion of deaths from chronic diseases is largest in high-income countries, in low- and middle-income countries chronic diseases continue to cause 39% and 72% of all deaths, respectively (2). Cardiovascular diseases alone account for 30% of all deaths in the world (2), 80% of which occur in low- and middle-income countries (1). It has been estimated that an additional reduction of 2% annually in deaths from chronic conditions would avert 28 million deaths in low- and middle-income countries between 2005 and 2015 (3). Chronic conditions also cause substantial morbidity in terms of disability-adjusted life years (DALYs), a measure of the potential life lost due to premature mortality and of the productive life lost due to disability. Chronic conditions account for one third of DALYs in low-income countries and for nearly two thirds in middle-income countries (2). In Africa, where chronic disease morbidity is lowest, these conditions still account for 21% of DALYs.

Developing countries undergoing an epidemiological transition from infectious and parasitic diseases to chronic diseases require health systems modifications to address the long-term nature of chronic conditions, in addition to prevention efforts. The WHO Action Plan for the Global Strategy for the Prevention and Control of Noncommunicable Diseases recommends addressing management in the context of overall health system strengthening (4). Continuous access to essential medicines, with an emphasis on rational selection, affordable prices and sustainable financing, should be a key component of the policy framework (1). Appropriate pharmacological treatment has been shown to significantly reduce morbidity and mortality from chronic conditions (5–9), yet the necessary medicines are not equitably distributed or used as widely as required (3).

Several studies have found that low drug availability limits access to medicines in low- and middle-income countries (10–18). Cameron et al. investigated the availability of 15 generic medicines used for a range of conditions in 36 developing countries and found it to be 38% and 64% in the public and private sectors, respectively (11). Studies focused on medicines used to treat chronic conditions have shown similar results (19–25). However, no studies to date have investigated whether medicines for chronic conditions are less available than medicines in other therapeutic categories. We hypothesized that in countries with weak health systems that have historically focused on infectious diseases, medicines for chronic conditions requiring ongoing management are less available than

medicines used to treat acute episodes of illness. This study investigates potential differences in the availability of medicines for chronic and acute conditions in low- and middle-income countries.

Methods

Data source

Data were obtained from drug price and availability surveys conducted using a standard, validated methodology developed by WHO and Health Action International (HAI)(26–28). In the survey, the availability of 50 medicines was investigated through visits to public and private sector facilities. Data were collected on standard medicines that enable international comparisons and on medicines selected by each country for their importance nationally (e.g. drugs for high-burden diseases). Availability was determined for: (i) the originator brand first authorized worldwide for marketing (normally as a patented product) on the basis of the documentation of its efficacy, safety and quality, according to requirements at the time of authorization; and (ii) generic equivalents intended to be interchangeable with the originator brand product. Availability is reported as the percentage of facilities where a product was found on the day of data collection. The difference or gap in availability was calculated by subtracting the availability of medicines for chronic conditions from the availability of medicines for acute conditions.

Survey inclusion

All surveys conducted following the WHO/HAI method and included in the HAI database (29) on 24 September 2009 were considered for inclusion, with the exception of nine pilot surveys that measured availability using different methods. In countries where repeat surveys were conducted, the most recent data set was used. In countries where multiple surveys were conducted at the state/provincial level, results were averaged without weighting. In total 50 surveys conducted in 40 countries between 2003 and 2008 were included in the analysis, yielding a sample of 2779 medicine outlets (Table 1).

Medicine selection

Any medicine covered in at least one survey was considered for inclusion and was classified as being for either acute or chronic treatment according to its primary indication for use. In accordance with methods published previously (11), the 15 medicines most frequently covered in WHO/HAI surveys for acute and chronic conditions were included

in the analysis to maximize the comparability of data across countries. Such medicines are effective based on the evidence, are used to treat high-burden conditions and are widely used internationally (26,27).

Data analysis

The per cent availability of each medicine was extracted for both originator brand and generic products in both the public and private sectors. When alternate strengths of the same medicine were included in a survey, the availability of each of the two strengths was combined on a facility-by-facility basis to determine the overall availability of the medicine. Alternate strengths were only combined when used for the same indication; adult and paediatric dosage forms were kept separate.

Availability was analysed for: (i) the originator brand, (ii) the generic equivalent and (iii) any product (brand or generic). For the last category, the availability of originator brands and generics was combined on a facility-by-facility basis to determine the overall availability of each medicine.

The mean availability of each basket of medicines (for acute and chronic conditions) was calculated and, as data were normally distributed, the unpaired *t*-test was used to test the difference in mean availability between baskets. As availability was measured in the same facilities in each country, confounding factors such as facility type and location were eliminated. To investigate whether the availability of medicines for chronic conditions differed by indication, the mean availability of each therapeutic class represented in this medicines basket was calculated and compared with the mean availability of the 15 medicines in the acute conditions basket.

To examine potential differences in medicine availability by country income status, data were analysed by World Bank country income groups effective from 1 July 2009: low-income countries, lower-middle-income countries, upper-middle-income countries and high-income countries (30). Results were also aggregated by WHO Region: African (AFR), Americas (AMR), European (EUR), Eastern Mediterranean (EMR), South-East Asia (SEAR) and Western Pacific (WPR). Due to the small number of countries in some categories, results are descriptive only. To investigate any relationship between per cent availability of acute and chronic medicine baskets and level of income disparity, availability was analysed as a function of country Gini index, which measures the extent to which income distribution among individuals and households within an economy deviates from being perfectly equal (31).

Results

Table 2 shows the 30 medicines included in the analysis. In the basket of medicines used to treat acute conditions, the frequency with which individual medicines were included in WHO/HAI surveys ranged from 24% to 100%; in the basket of medicines for chronic conditions, it ranged from 72% to 100%. This is not an indication of medicine availability at individual facilities, but rather, of greater consistency in the selection of chronic disease medicines for inclusion in individual surveys. With the exception of the combination sulfadoxine plus pyrimethamine, medicines for the treatment of human immunodeficiency virus (HIV) infection and acquired immunodeficiency syndrome (AIDS), tuberculosis and malaria are notably absent. These treatments are usually provided through vertical programmes that address specific health problems and consequently are often excluded from WHO/HAI surveys.

In the public sector, the mean availability of generic medicines was low for both baskets: 53.5% for medicines for acute conditions and 36.0% for medicines for chronic conditions, with medicines for acute conditions significantly more available ($P = 0.001$) (Table 3). Originator brands of medicines in both the acute and chronic condition baskets were rarely available in the public sector. When product types were combined to yield the availability of any given product (originator brand or generic) at each facility, the difference in availability between the two baskets (14.3%) remained statistically significant ($P = 0.009$).

In the private sector, the mean availability of generics in each basket was higher than in the public sector (66.2% for generics for acute conditions and 54.7% for generics for chronic conditions), but it was still low. The availability of generic products differed significantly between the two baskets (11.5%; $P = 0.007$), but the availability of originator brands was the same (39.1%). The difference in the availability of any product type (originator or generic) was 5.6% ($P = 0.070$).

When the availability of medicines for chronic conditions was disaggregated by therapeutic classes, in both the public and the private sector antiulcerants and antidiabetics were the drugs most widely available for the chronic indications studied, with availability comparable to that of the basket of medicines for acute indications (Fig. 1). In fact, in the private sector the average availability of antiulcerants was higher than that of the 15 medicines for acute conditions. Antihypertensives and cardiovascular medicines had the next highest availability among the drugs for chronic indications, but their availability was 8.5% and 21.4% lower than that of medicines for acute conditions in the private and the public sectors, respectively. Antiasthmatics, antiepileptics and antidepressants had similarly low availability (28–30% and 40–45% in the public and private sectors, respectively) and showed the largest difference in availability with respect to the acute

conditions basket. The availability of individual medicines in the countries studied can be obtained from the corresponding author upon request.

Mean differences in the per cent availability of the baskets of medicines for acute and chronic conditions in each country are shown by World Bank income group (Fig. 2) and WHO region (Fig. 3). Fig. 2 shows an inverse relationship between income level and the gap in availability between medicines for acute and chronic conditions, particularly in the public sector. In low- and lower-middle-income countries, the mean differences in availability were 33.9% and 12.9%, respectively, while in upper-middle-income countries the availability was nearly equal and in high-income countries medicines for chronic conditions had higher availability. In the private sector the availability gap was smaller than in the public sector in all country income groups. No relationship was found in the public or private sector between the gap in the availability of medicines for acute or chronic conditions and level of income disparity (R^2 = 0.0283 and 0.0118, respectively) (data available from the corresponding author upon request).

The African region showed a substantially larger average difference (nearly 40%) than other regions in the availability of medicines for acute and chronic conditions in the public sector (Fig. 3). In the South-East Asia Region, the Region of the Americas and the Eastern Mediterranean Region, medicines for acute conditions were 4% to 14% more available in the public sector, on average, than those for chronic conditions, while in the European Region and the Western Pacific Region medicines for chronic conditions were somewhat more available than those for acute conditions in the public sector. In the private sector, the African region again showed the largest difference in availability between medicines for acute and for chronic conditions (16.7%), but this difference was less pronounced than in the public sector. In the Region of the Americas, the European Region and the South-East Asia Region, medicines for acute conditions were more available than those for chronic conditions in the private sector, while in the Eastern Mediterranean Region two medicine baskets had comparable availability and in the Western Pacific Region medicines for chronic conditions were more available than those for acute conditions.

Discussion

The WHO has set a benchmark of 80% for medicine availability, (33) against which the values found in this study were sub-optimal for both the acute and chronic condition medicine baskets, particularly in the public sector. Low public sector availability can result from factors such as inadequate funding, lack of incentives for maintaining stocks, inability to forecast needs accurately, inefficient purchasing/distribution systems or leak-

age of medicines for private resale (11). The low availability of medicines in the public sector is a general problem, and this study shows that medicines for chronic conditions are even less available than medicines for acute conditions, particularly in low- and lower-middle-income countries. This may be the result of government policies that do not provide for widespread access to medicines for chronic conditions through the public sector, or it could stem from technical and resource-related factors hindering the adaptation of health systems to the changing epidemiological profile of their populations.

The difference in availability between the two medicine categories was consistently smaller in the private sector than in the public sector (11.5% versus 17.5%). This suggests that the current demand for medicines for chronic conditions exceeds what the public sector is providing and that low demand resulting from low diagnostic rates or other factors does not account for the low availability observed in the public sector. However, the availability of generics in the private sector was still low and probably not enough to compensate for the lack of availability in the public sector. Further, in the private sector, medicines for chronic conditions usually cost substantially more than in the public sector and are often unaffordable (11,19–25,34). Chronic disease patients, who need lifelong treatment, may find these medicines even less affordable than other patients. In developing countries, catastrophic health spending (e.g. spending on drugs and health care in excess of 40% of the income remaining after meeting subsistence needs) is common (35). Health policies should therefore be designed to protect people from these expenditures by increasing financial risk protection through health insurance schemes that cover essential medicines for outpatients, including drugs for chronic conditions. The cost of medicines to both patients and health systems can also be reduced by promoting quality-assured, low-cost generic medicines through preferential registration procedures, financial incentives for prescribing and dispensing generics, generic substitution and measures to heighten trust among physicians, pharmacists and patients in the quality of generics (11).

In both the public and private sectors, antiasthmatics, antiepileptics and antidepressants, and antihypertensives to a lesser extent, were the drivers of the gaps in the availability of drugs in the acute and chronic condition baskets (Fig. 1). However, as previously reported (19), in some therapeutic classes (e.g. antidiabetics and antihypertensives) substantial variation was observed in the availability of individual medicines. Results may also have been influenced by the treatment options included in each class. For example, the availability of antidiabetics may have been influenced by the exclusion of insulin, whose availability was low in a previous study (23) The reliability of our findings is supported by the fact that the therapeutic classes with the highest to lowest availability followed the same pattern in both the public and private sectors.

As the income level of a country decreases, the difference in availability between medicines for acute and chronic conditions increases, particularly in the public sector (Fig. 2). Priority should therefore be given to improving the availability of medicines for chronic conditions in low- and lower-middle-income countries, where the availability gaps are largest. According to a similar analysis by WHO region, the availability of the two treatment types differs most widely in countries in the African Region (Fig. 3). Since 25% of all deaths in Africa are caused by chronic conditions, current disease patterns do not explain the observed gap. Disease patterns vary by individual country, but the medicines in this study are used to treat very common chronic conditions and should be available in sufficient quantities in any health system.

This analysis improves upon a previous analysis of medicine availability based on data from WHO/HAI surveys (11) in that alternate strengths of the same medicine were combined to account for country-level differences in medicine use. However, availability data only apply to the day of data collection and may not reflect average availability over time. Nevertheless, the data were collected in at least 20 facilities per country using a validated sampling frame (28) and therefore provide a reasonable estimate of the overall situation. Further, the analysis is more concerned with the relative availability of medicines used for acute and chronic conditions than with their absolute availability. Another limitation is that the availability of individual medicines in the public sector may be influenced by whether or not they are on the national essential medicines list (a government-approved selective list used for procurement or reimbursement) and by the level(s) of care for which they are expected to be available.

The choice of medicines for the secondary analysis, which was restricted to the medicines included in WHO/HAI surveys, may also have limited the results. These surveys comprise both common medicine formulations that enable international comparisons and medicines of national importance, which are selected in accordance with disease burden, medicine usage patterns and recommendations in standard treatment guidelines. The selection process for survey medicines is described in detail elsewhere (26,27). However, country variations in medicine use may limit the comparability of results.

Prior to 2008, when all but two of the surveys were conducted, the WHO/HAI recommended a global list of 30 medicines for inclusion in all surveys, plus 20 medicines selected nationally (26). Among the medicines most frequently surveyed and as such included in the analysis, all 15 of the drugs used to treat chronic conditions were on the global list, versus only 9 (60%) of the drugs used to treat acute conditions. More local adaptations were therefore made for the latter than for the former, perhaps because treatment alternatives for chronic conditions were fewer and the use of these drugs consequently more consistent across countries. In developing the second edition of the

WHO/HAI survey manual, Intercontinental Marketing Services Health (IMS Health) consumption data were used to analyse the medicines surveyed and those recommended for chronic conditions were found to be widely used worldwide (27). However, a further limitation is that the lack of a clear distinction between acute and chronic indications for some medicines that are used intermittently over long time periods (e.g. antimalarials) and for medicines used to treat acute episodes of chronic disease (e.g. diazepam). In addition, while all of the medicines studied are off patent, the date of patent expiry may have affected the availability of multisource generic products on the market. Certain products, such as omeprazole, losartan, ciprofloxacin and fluconazole, have been off patent for less than 10 years and the persistence of the originator brand product following patent expiry may have reduced the availability of generics of these products.

Despite these limitations, this study raises important concerns about access to treatment for the millions of people with chronic conditions who live in developing countries. Governments should prioritize the supply of medicines for chronic conditions through their public health systems to ensure that people have access to the treatment they need. Low availability in the public sector can be through improved procurement efficiency and supply chain management as well as adequate, equitable and sustainable financing. In practice this could mean implementing schemes to make medicines for chronic conditions available through the private sector at no cost or at subsidized prices, as is done in Jamaica and in Trinidad and Tobago (36,37). International financing can also strongly affect public sector availability. In Kenya, for example, the availability of the antimalarial combination composed of artemether-lumefantrine increased from 4% to 91% the year following a grant from the Global Fund to Fight AIDS, Tuberculosis and Malaria (16). While this study addresses the supply-side barriers to access to treatment for chronic conditions, efforts to address demand-side issues are also required. Supply that remains on the shelf is of little use; conversely, stimulating demand makes no sense if there is no supply. The extent to which a low demand for medicines for chronic conditions affects their availability is outside the scope of this analysis and warrants further investigation. However, our analysis suggests that current demand outweighs supply in the public sector and that no efforts should be made to further increase demand unless an adequate and ongoing supply of medicines can be ensured.

Successes in scaling-up treatment for HIV infection can offer lessons in connection with other chronic conditions. For example, HIV/AIDS treatment programmes in sub-Saharan Africa have shown relatively high patient adherence (77%) to complex antiretroviral regimens (38). Ensuring sustained medicine availability is clearly an essential precondition to achieving high adherence rates. Success in the field of HIV/AIDS stems largely from global and national efforts in the areas of mobilization and advocacy, financing and engagement of civil society (39). Alongside current efforts in connection with com-

municable diseases, international agencies, governments and other stakeholders should work together to raise the profile of chronic diseases on health and development agendas and to advocate for a balanced approach that addresses both prevention and treatment.

To date, the control of chronic diseases in developing countries has received little international attention (3,40). The UN Summit on Non-communicable Diseases to be held in September 2011 is a positive step towards recognizing the importance of chronic diseases on the global health agenda. Our study shows that reorienting and strengthening health systems to enable a more effective and equitable response to chronic diseases should be a key priority, as recommended in the WHO Action Plan for the Global Strategy for the Prevention and Control of Chronic Diseases. Target 8.E of the Millennium Development Goals deals with access to affordable essential medicines in developing countries (10,12,16). To achieve this target, special efforts will be required to ensure universal and sustained availability of medicines for chronic conditions.

Conclusion

Although the disease burden from chronic conditions in developing countries is large, wide gaps exist in the availability of medicines for chronic conditions. This study shows that such medicines are less available than those for acute conditions, which have traditionally been the focus of health systems in these countries. To ensure equitable access to treatment for different types of diseases, greater national and international attention should be given to chronic disease control, including access to medicines.

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Tables and figures

Table 1: Surveys included in secondary analysis of data in study comparing the availability of medicines for chronic and acute conditions in 40 developing countries

Country (survey date)	Number of facilities surveyed[a]	WHO region	World Bank income group[b]
Cameroon (07/2005)	40	Africa	lower-middle
Chad (05/2004)	35	Africa	low
China, Shandong Province (10/2004)	40	Western Pacific	lower-middle
China, Shanghai (09/2004)	50	Western Pacific	lower-middle
Colombia (10/2008)	59	Americas	upper-middle
Congo (07/2007)	50	Africa	lower-middle
El Salvador (11/2006)	104	Americas	lower-middle
Ethiopia (09/2004)	59	Africa	low
Fiji (09/2004)[c]	36	Western Pacific	upper-middle
Ghana (10/2004)	84	Africa	low
India, Chennai State (10/2004)	60	South-East Asia	lower-middle
India, Haryana State (10/2004)	60	South-East Asia	lower-middle
India, Karnataka State (11/2004)	64	South-East Asia	lower-middle
India, Maharashtra State, 12 districts (10/2004)	120	South-East Asia	lower-middle
India, Maharashtra State, 4 regions (01/2005)	68	South-East Asia	lower-middle
India, Rajasthan State (04/2003)	40	South-East Asia	lower-middle
India, West Bengal State (12/2004)	61	South-East Asia	lower-middle
Indonesia (08/2004)	73	South-East Asia	lower-middle
Iran (12/2007)	60	Eastern Mediterranean	lower-middle
Jordan (05/2004)	38	Eastern Mediterranean	lower-middle
Kazakhstan (11/2004)	21	European	upper-middle
Kenya (11/2004)	113	Africa	low
Kuwait (06/2004)	50	Eastern Mediterranean	high
Kyrgyzstan (02/2005)[c]	30	European	low
Lebanon (02/2004)	60	Eastern Mediterranean	upper-middle

Malaysia (10/2004)	52	Western Pacific	upper-middle
Mali (03/2004)	41	Africa	low
Mongolia (11/2004)	29	Western Pacific	low
Morocco (04/2004)	40	Eastern Mediterranean	lower-middle
Nigeria (09/2004)	87	Africa	lower-middle
Oman (10/2007)	62	Eastern Mediterranean	high
Pakistan (07/2004)	78	Eastern Mediterranean	lower-middle
Peru (09/2005)	148	Americas	upper-middle
Philippines (02/2005)	77	Western Pacific	lower-middle
São Tomé and Principe (05/2008)	41	Africa	lower-middle
South Africa, Gauteng Province (11/2004)[c]	30	Africa	upper-middle
Sudan, Gadarif State (02/2006)	40	Eastern Mediterranean	lower-middle
Sudan, Khartoum State (06/2005)	40	Eastern Mediterranean	lower-middle
Sudan, North Kordofan State (02/2006)	29	Eastern Mediterranean	lower-middle
Sudan, Northern State (02/2006)	36	Eastern Mediterranean	lower-middle
Syrian Arab Republic (12/2003)[c]	57	Eastern Mediterranean	lower-middle
Tajikistan (02/2005)	40	European	low
Thailand (10/2006)	41	South-East Asia	lower-middle
Tunisia (03/2004)	62	Eastern Mediterranean	lower-middle
Uganda (04/2004)	40	Africa	low
Ukraine (09/2007)	33	European	lower-middle
United Arab Emirates (12/2006)	41	Eastern Mediterranean	high
United Republic of Tanzania (09/2004)	80	Africa	low
Uzbekistan (12/2004)[c]	40	European	low
Yemen (07/2006)	40	Eastern Mediterranean	low
Total facilities surveyed	2779		

WB, The World Bank. WHO, World Health Organization.

[a] *Public and private.*

[b] *On 1 July 2009.*

[c] *Did not survey public sector medicine outlets.*

Table 2. Medicines included in secondary analysis of data in study comparing the availability of medicines for chronic and acute conditions in 40 developing countries

Medicines for acute conditions		
Generic name	**Therapeutic group[a]**	**No. of surveys (%)**
Amoxicillin 250 or 500 mg capsule/tablet	Antibacterial	50 (100)
Ciprofloxacin 250 or 500 mg capsule/tablet	Antibacterial	50 (100)
Co-trimoxazole 8+40 mg/ml suspension	Antibacterial	48 (96)
Ceftriaxone 1 g/vial injection	Antibacterial	47 (94)
Diclofenac 25 or 50 mg capsule/tablet	Antiinflammatory/antirheumatic	47 (94)
Aciclovir 200 mg capsule/tablet	Antiviral	44 (88)
Diazepam 5 or 10 mg capsule/tablet	Psycholeptic	44 (88)
Fluconazole 50, 150 or 200 mg capsule/tablet	Antimycotic	38 (76)
Metronidazole 200, 250, 400 or 500 mg capsule/tablet	Antibacterial	29 (58)
Sulfadoxine+pyrimethamine 500+25 mg capsule/tablet	Antiprotozoal (antimalarial)	27 (54)
Ibuprofen 200 or 400 mg capsule/tablet	Antiinflammatory/antirheumatic	24 (48)
Mebendazole 100 mg capsule/tablet	Anthelmintic	19 (38)
Erythromycin 250 or 500 mg capsule/tablet	Antibacterial	16 (32)
Albendazole 200 or 400 mg capsule/tablet	Anthelmintic	15 (30)
Cephalexin 250 or 500 mg capsule/tablet	Antibacterial	12 (24)

Medicines for chronic conditions

Generic name	Therapeutic group[a]	No. of surveys (%)
Glibenclamide 5 mg capsule/tablet	Drugs used in diabetes	50 (100)
Salbutamol 0.1 mg inhaler	Drugs for obstructive airway diseases	50 (100)
Captopril 25 mg capsule/tablet	Agents acting on the renin-angiotensin system	49 (98)
Atenolol 50 or 100 mg capsule/tablet	Beta blocking agent	48 (96)
Carbamazepine 200 mg capsule/tablet	Antiepileptic	48 (96)
Omeprazole 20 mg capsule/tablet	Drugs for acid related disorders	47 (94)
Metformin 500 or 850 mg capsule/tablet	Drugs used in diabetes	47 (94)
Ranitidine 150 mg capsule/tablet	Drugs for acid related disorders	47 (94)
Amitriptyline 25 mg capsule/tablet	Psychoanaleptic (antidepressant)	45 (90)
Nifedipine Retard 20 or 30 mg tablet	calcium channel blocker	45 (90)
Fluoxetine 20 mg capsule/tablet	Psychoanaleptic (antidepressant)	44 (88)
Hydrochlorothiazide 25 or 50 mg capsule/tablet	Diuretic	43 (86)
Beclometasone 0.25 or 0.5 mg inhaler	Drugs for obstructive airway diseases	42 (84)
Phenytoin 100 mg capsule/tablet	Antiepileptic	42 (84)
Losartan 25 or 50 mg capsule/tablet	Agents acting on the renin-angiotensin system	36 (72)

[a] *Anatomical Therapeutic Chemical (ATC) classification system, 2nd level.*
Source: Reference [32].

Table 3: Mean availability of medicines used for acute and chronic conditions in 40 developing countries

Sector and product type[a]	Mean availability[b], medicines for acute conditions (95% CI)	Mean availability[b], medicines for chronic conditions (95% CI)	Difference in mean availability[c] (95 %CI)	*P*
Public sector, generics (n=35)	53.5 (46.23, 60.8)	36.0 (27.4, 44.6)	17.5 (6.5, 28.6)	0.001
Public sector, originator brands (n=34)	5.5	9.6	-4.1	[d]
Public sector, any product type (n=35)	55.9 (48.9, 63.0)	41.6 (32.1, 51.2)	14.3 (2.6, 25.9)	0.009
Private sector, generics (n=40)	66.2 (60.4, 72.1)	54.7 (47.6, 61.9)	11.5 (2.4, 20.6)	0.007
Private sector, originator brands (n=39)	39.1 (31.0, 47.3)	39.1 (31.1, 47.1)	0.0 (-11.2, 11.2)	0.500
Private sector, any product type (n=40)	74.8 (70.2, 79.4)	69.2 (63.3, 75.2)	5.6 (-1.9, 13.0)	0.070

CI, confidence interval.

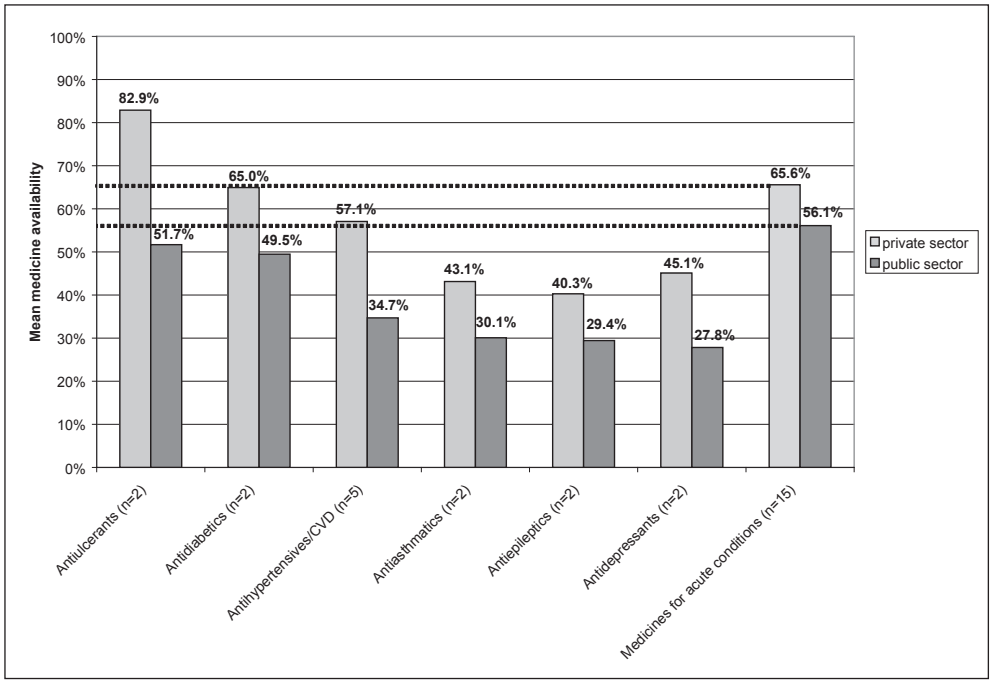
[a] The number of countries included in the analysis varies because of differences in the products and sectors surveyed.

[b] Availability is expressed as the percentage of facilities where a product was found on the day of data collection.

[c] The values represent the mean availability of medicines for acute conditions minus the mean availability of medicines for chronic conditions.

[d] The availability of originator brands in the public sector was 0% in several countries. This skewed the data and prevented the calculation of statistical significance.

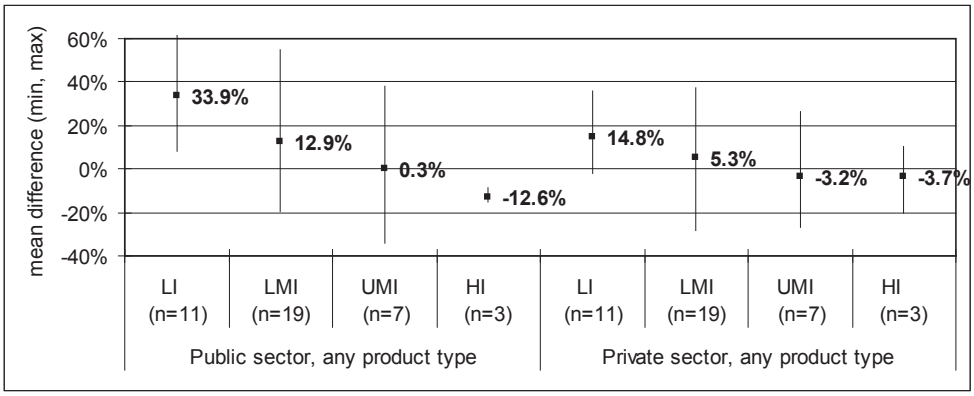
Figure 1. Comparison of mean availability of individual medicines for chronic conditions, by therapeutic class, and of 15 medicines for acute conditions, in 40 developing countries



CVD, cardiovascular disease.

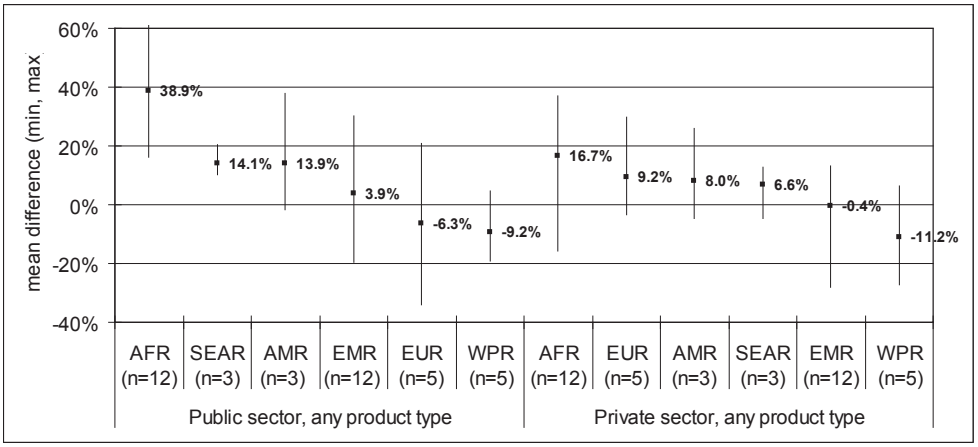
[a] *Availability is expressed as the percentage of facilities where a product was found on the day of data collection.*

Figure 2. Mean difference in the availability[a] of medicines for acute and chronic conditions in 40 developing countries, by World Bank income group[b]



[a] Availability is expressed as the percentage of facilities where a product was found on the day of data collection.
[b] World Bank income groups: HI, high-income; UMI, upper-middle-income; LMI, lower-middle-income; LI, low-income.

Figure 3. Mean difference in the availability[a] of medicines for acute and chronic conditions in 40 developing countries, by World Health Organization region[b]



[a] Availability is expressed as the percentage of facilities where a product was found on the day of data collection.
[b] World Health Organization regions: AFR, Africa; AMR, Americas; EMR, Eastern Mediterranean; EUR, European; SEAR, South-East Asia; WPR, Western Pacific.

Appendix

Appendix 1: Country-level availability of individual medicines

a. Medicines used for acute conditions, lowest-priced generics, public sector

Country	Aciclovir 200 mg cap/tab	Albendazole 200 and 400 mg cap/tab	Amoxicillin 250 and 500 mg cap/tab	Ceftriaxone 1 g/vial injection	Cephalexin 250 and 500 mg cap/tab	Ciprofloxacin 250 and 500 mg cap/tab	Co-trimoxazole 8+40 mg/ml suspension	Diazepam 5 and 10 mg cap/tab	Diclofenac 25 and 50 mg cap/tab	Erythromycin 250 and 500 mg cap/tab	Fluconazole 50, 150 and 200 mg cap/tab	Ibuprofen 200 and 400 mg cap/tab	Mebendazole 100 mg cap/tab	Metronidazole 200, 250, 400 and 500 mg cap/tab	Sulfadoxine+ pyrimethamine 500+25 mg cap/tab
Cameroon	72.2%		88.9%	27.8%		50.0%	66.7%	77.8%	11.1%		11.1%	72.2%	77.8%	88.9%	77.8%
Chad			83.3%			4.2%	45.8%	58.3%					87.5%	91.7%	58.3%
China	35.0%	0.0%	88.4%	65.9%		15.0%	0.0%	10.0%	2.5%	10.0%	16.7%				
Colombia		86.7%	100.0%	73.3%	86.7%	96.7%	83.3%		93.3%		90.0%	100.0%		100.0%	
Congo	3.8%		57.7%	15.4%		38.5%	42.3%		19.2%			46.2%	80.8%	57.7%	73.1%
El Salvador	75.0%		0.0%	30.8%		92.3%	63.5%	0.0%	0.0%		0.0%	96.2%	86.5%	90.4%	
Ethiopia	14.7%		97.1%	44.1%		64.7%	94.1%	88.2%	55.9%		2.9%		97.1%	97.1%	70.6%
Ghana	0.0%	25.0%	92.9%	21.4%		82.1%	85.7%	85.7%	85.7%		10.7%	85.7%	21.4%	89.3%	46.4%
India	15.7%	73.0%	78.5%	25.4%	30.8%	60.3%	42.1%	60.6%	69.6%	100.0%	1.4%	63.9%		25.4%	2.9%
Indonesia	73.3%		93.3%	60.0%		80.0%	53.3%	80.0%	60.0%	40.0%	6.7%				33.3%
Iran		53.3%	100.0%	100.0%		100.0%	96.7%	100.0%	100.0%		90.0%	96.7%	93.3%	96.7%	
Jordan	27.8%		77.8%	11.1%		77.8%	83.3%	55.6%	0.0%		16.7%				
Kazakhstan	0.0%		0.0%	0.0%		0.0%			0.0%		0.0%		0.0%	100.0%	
Kenya	5.7%	20.8%	90.6%	17.0%		9.4%	86.8%	83.0%	3.8%		9.4%	52.8%		90.6%	98.1%
Kuwait	28.0%		100.0%	8.0%	100.0%	12.0%	100.0%	0.0%	88.0%		0.0%	16.0%			
Lebanon	0.0%		20.0%	0.0%	20.0%	0.0%	75.0%	0.0%	0.0%			30.0%		45.0%	
Malaysia	75.0%		85.0%	0.0%		0.0%	25.0%	55.0%	5.0%	35.0%	0.0%	95.0%			35.0%
Mali			100.0%	19.0%		61.9%	76.2%		100.0%	90.5%		85.7%	95.2%	85.7%	61.9%
Mongolia	100.0%		100.0%		100.0%	75.0%	0.0%	75.0%	100.0%	100.0%	0.0%	50.0%	100.0%	100.0%	
Morocco	20.0%		100.0%	50.0%		75.0%	100.0%	0.0%	0.0%		0.0%				
Nigeria	7.1%		92.2%	33.3%		69.0%	78.6%	54.8%							73.8%
Oman		20.0%	100.0%	33.3%		66.7%	43.3%	86.7%	100.0%			100.0%		96.7%	
Pakistan	3.3%		66.7%	16.7%		50.0%	30.0%	60.0%	33.3%		3.3%				3.3%
Peru	69.2%		100.0%	84.6%		96.2%	98.1%	84.6%	7.7%	84.6%	59.6%	100.0%		96.2%	0.0%
Philippines	15.4%		30.8%	46.2%		23.1%	34.6%		7.7%		0.0%			65.4%	0.0%
São Tomé and Principe	18.8%	65.6%	56.3%	15.6%	3.1%	75.0%	68.8%	56.3%	84.4%	40.6%		87.5%	93.8%	81.3%	0.0%
Sudan	1.3%		83.5%	36.3%		72.4%	91.1%	73.5%	69.4%	88.6%	6.3%	62.4%	84.7%		100.0%
Tajikistan	40.0%		90.0%			85.0%	40.0%	5.0%	85.0%	95.0%	5.0%	95.0%	70.0%	100.0%	
Tanzania	15.6%	50.0%	84.4%	25.0%	3.1%	46.9%	81.3%	53.1%	59.4%	59.4%	0.0%			93.8%	84.4%
Thailand	90.0%		100.0%	95.0%		25.0%	75.0%	100.0%	100.0%		100.0%				
Tunisia	0.0%		95.2%	33.3%		95.2%	66.7%	47.4%	9.5%		0.0%				
Uganda	70.0%	20.0%	75.0%	10.0%	0.0%	65.0%	15.0%	70.0%	0.0%	85.0%	0.0%			70.0%	100.0%
Ukraine	83.3%		100.0%	100.0%		100.0%	50.0%	50.0%	100.0%		100.0%				
United Arab Emirates	22.2%		100.0%	38.9%		22.2%	94.4%	100.0%	72.2%		33.3%				
Yemen	0.0%		20.0%	25.0%		15.0%	20.0%	15.0%	10.0%		5.0%		0.0%	15.0%	10.0%
Mean	32.7%	41.4%	78.5%	36.3%	43.0%	69.0%	62.0%	56.2%	46.4%	69.1%	20.3%	85.7%	70.6%	80.8%	48.9%
Standard error	6.0%	8.9%	5.0%	5.1%	15.9%	5.6%	5.0%	6.0%	7.2%	8.8%	6.3%	6.2%	9.5%	5.2%	8.5%

b. Medicines used for acute conditions, lowest-priced generics, private sector

Country	Aciclovir 200 mg cap/tab	Albendazole 200 and 400 mg cap/tab	Amoxicillin 250 and 500 mg cap/tab	Ceftriaxone 1 g/vial injection	Cephalexin 250 and 500 mg cap/tab	Ciprofloxacin 250 and 500 mg cap/tab	Co-trimoxazole 8+40 mg/ml suspension	Diazepam 5 and 10 mg cap/tab	Diclofenac 25 and 50 mg cap/tab	Erythromycin 250 and 500 mg cap/tab	Fluconazole 50, 150 and 200 mg cap/tab	Ibuprofen 200 and 400 mg cap/tab	Mebendazole 100 mg cap/tab	Metronidazole 200, 250, 400 and 500 mg cap/tab	Sulfadoxine+ pyrimethamine 500+25 mg cap/tab
Cameroon	70.0%		90.0%	60.0%		95.0%	75.0%	5.0%	55.0%		40.0%	50.0%	50.0%	65.0%	90.0%
Chad			18.2%			27.3%	9.1%	0.0%					27.3%	36.4%	63.6%
China	42.5%	0.0%	85.0%	45.0%		17.5%	0.0%	5.0%	12.5%	15.0%	30.0%				
Colombia		96.6%	86.2%	69.0%	96.6%	96.6%	72.4%		93.1%		93.1%	100.0%		93.1%	
Congo	20.8%		87.5%	25.0%		70.8%	70.8%		62.5%			45.8%	62.5%	41.7%	87.5%
El Salvador	94.2%		30.8%	80.8%		96.2%	67.3%	9.6%	46.2%		53.8%	100.0%	96.2%	90.4%	
Ethiopia	88.0%		100.0%	100.0%		96.0%	100.0%	56.0%	100.0%		0.0%		100.0%	100.0%	88.0%
Fiji	80.6%		94.4%	0.0%		97.2%	69.4%	88.9%	47.2%		0.0%				0.0%
Ghana	35.7%	58.9%	94.6%	33.9%		82.1%	85.7%	80.4%	85.7%		55.4%	76.8%	37.5%	92.9%	58.9%
India	73.2%	82.3%	95.3%	78.7%	88.5%	92.8%	89.0%	72.9%	69.6%	97.5%	66.4%	69.3%		83.8%	68.8%
Indonesia	91.4%		100.0%	51.7%		93.1%	77.6%	81.0%	74.1%	65.5%	10.3%				43.1%
Iran		50.0%	100.0%	100.0%		96.7%	100.0%	100.0%	96.7%		93.3%	96.7%	90.0%	96.7%	
Jordan	80.0%		70.0%	95.0%		95.0%	95.0%	60.0%	75.0%		85.0%				
Kazakhstan	100.0%		70.0%	80.0%		95.0%			85.0%		80.0%		0.0%	60.0%	
Kenya	58.6%	84.5%	93.1%	63.8%		87.9%	84.5%	82.8%	36.2%		51.7%	93.1%		84.5%	93.1%
Kuwait	0.0%		0.0%	64.0%	0.0%	80.0%	40.0%	0.0%	80.0%		0.0%	100.0%			
Kyrgyzstan	53.3%		93.3%	10.0%		43.3%	60.0%	53.3%	93.3%		43.3%		6.7%	100.0%	
Lebanon	55.0%		100.0%	47.5%	50.0%	100.0%	77.5%	0.0%	100.0%			97.5%		100.0%	
Malaysia	56.3%		87.5%	0.0%		40.6%	3.1%	0.0%	71.9%	50.0%	46.9%	43.8%			3.1%
Mali			95.0%	30.0%		85.0%	80.0%		90.0%	80.0%		70.0%	85.0%	100.0%	85.0%
Mongolia	68.0%		100.0%		12.0%	80.0%	32.0%	20.0%	72.0%	96.0%	24.0%	84.0%	92.0%	100.0%	
Morocco	60.0%		100.0%	55.0%		100.0%	95.0%	0.0%	100.0%		100.0%				
Nigeria	27.3%		90.9%	38.6%		93.2%	79.5%	29.5%							97.7%
Oman		40.6%	96.9%	50.0%		100.0%	81.3%	0.0%	100.0%			90.6%		68.8%	
Pakistan	10.4%		83.3%	54.2%		66.7%	81.3%	31.3%	31.3%		4.2%				41.7%
Peru	93.8%		100.0%	90.6%		99.0%	89.6%	78.1%	18.8%	90.6%	88.5%	96.9%		88.5%	0.0%
Philippines	5.9%		72.5%	47.1%		68.6%	33.3%		15.7%		2.0%			72.5%	0.0%
São Tomé and Principe	22.2%	33.3%	55.6%	11.1%	0.0%	55.6%	33.3%	11.1%	55.6%	22.2%		66.7%	44.4%	55.6%	0.0%
South Africa, Gauteng	83.3%		83.3%	3.3%		96.7%	73.3%	80.0%	73.3%		83.3%	93.3%			0.0%
Sudan	20.0%		98.8%	62.0%		90.8%	94.6%	74.1%	97.5%	89.8%	29.5%	76.6%	86.9%		95.0%
Syria	98.2%		94.7%	98.2%		100.0%	98.2%	100.0%	100.0%		96.5%			98.2%	
Tajikistan	50.0%		85.0%			95.0%	85.0%	10.0%	95.0%	95.0%	35.0%	100.0%	85.0%	100.0%	
Tanzania	50.0%	91.7%	85.4%	43.8%	43.8%	72.9%	83.3%	66.7%	95.8%	81.3%	6.3%			91.7%	97.9%
Thailand	100.0%		90.5%	33.3%		95.2%	42.9%	14.3%	100.0%		57.1%				
Tunisia	0.0%		100.0%	12.2%		100.0%	97.6%	14.6%	95.1%		0.0%				
Uganda	85.0%	100.0%	100.0%	65.0%	50.0%	90.0%	80.0%	80.0%	0.0%	100.0%	65.0%			95.0%	100.0%
Ukraine	96.3%		96.3%	100.0%		100.0%	88.9%	3.7%	100.0%		88.9%				
United Arab Emirates	87.0%		95.7%	39.1%		91.3%	91.3%	17.4%	95.7%		78.3%				
Uzbekistan	75.0%		70.0%	70.0%		97.5%	17.5%	0.0%	97.5%	95.0%	40.0%		57.5%	92.5%	
Yemen	70.0%		75.0%	100.0%		100.0%	100.0%	80.0%	95.0%		80.0%		100.0%	95.0%	55.0%
Mean	60.1%	63.8%	84.1%	54.3%	42.6%	84.5%	70.1%	40.2%	74.0%	75.2%	49.3%	81.6%	63.8%	84.1%	55.6%
Standard error	5.3%	10.4%	3.6%	5.0%	13.2%	3.3%	4.6%	6.1%	4.7%	8.0%	5.9%	4.4%	8.3%	3.8%	8.6%

c. Medicines used for chronic conditions, lowest-priced generics, public sector

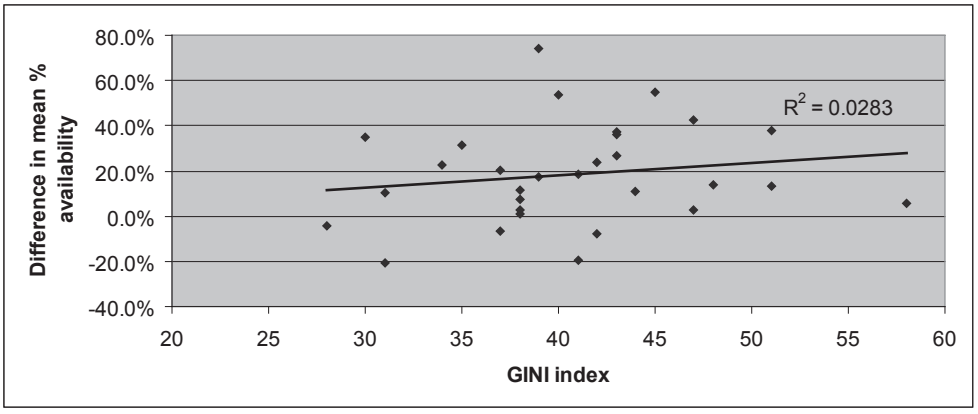
	Antidiabetics		Antiasthmatics		Antihypertensive/CVD					Antiepileptics		Antiulcerants		Antidepressants	
Country	Glibenclamide 5mg cap/tab	Metformin 500 and 850 mg cap/tab	Salbutamol 0.1 mg/dose inhaler	Beclometasone 0.25 and 0.5 mg/dose inhaler	Captopril 25 mg cap/tab	Atenolol 50 mg and 100 mg cap/tab	Nifedipine Retard 20 and 30 mg tab	Hydrochloro-thiazide 25 and 50 mg cap/tab	Losartan 25 and 50 mg cap/tab	Carbamazepine 200 mgcap/tab	Phenytoin 100 mg cap/tab	Omeprazole 20 mg cap/tab	Ranitidine 150 mg cap/tab	Amitriptyline 25 mg cap/tab	Fluoxetine 20 mg cap/tab
Cameroon	44.4%	5.6%	5.6%	0.0%	0.0%		0.0%	0.0%		0.0%	5.6%		0.0%		0.0%
Chad	16.7%	0.0%	12.5%	0.0%	0.0%	0.0%		41.7%		0.0%				0.0%	
China	2.5%	23.4%	30.9%	0.0%	50.0%	0.0%	45.0%	88.4%	0.0%	0.0%	67.5%	75.0%	62.5%	10.9%	23.4%
Colombia	93.3%	80.0%	93.3%	80.0%	96.7%	3.3%	90.0%	100.0%	93.3%	100.0%	70.0%	96.7%	96.7%	96.7%	93.3%
Congo	0.0%	0.0%	0.0%	0.0%	3.8%	0.0%	7.7%			0.0%		0.0%	0.0%	0.0%	
El Salvador	96.2%	0.0%	90.4%	0.0%	51.9%	0.0%	0.0%	78.8%	28.8%	53.8%	78.8%	30.8%	98.1%	55.8%	26.9%
Ethiopia	79.4%	11.8%	55.9%	0.0%	41.2%	5.9%	26.5%	73.5%		20.6%	20.6%	41.2%	23.5%	38.2%	0.0%
Ghana	39.3%	32.1%	10.7%	0.0%	3.6%	28.6%	92.9%	17.9%	0.0%	14.3%	14.3%	25.0%	14.3%	14.3%	0.0%
India	50.6%	36.3%	5.8%	4.2%	0.0%	57.7%	2.7%	1.2%	2.2%	39.0%	30.3%	56.8%	70.7%	24.4%	8.7%
Indonesia	73.3%	46.7%	0.0%	0.0%	93.3%	33.3%	0.0%	86.7%	40.0%	60.0%	33.3%	73.3%	80.0%	60.0%	13.3%
Iran	100.0%	100.0%	100.0%	76.7%	96.7%	100.0%	0.0%	100.0%	100.0%	93.3%	100.0%	100.0%	100.0%	96.7%	93.3%
Jordan	77.8%	0.0%	5.6%	27.8%	61.1%	16.7%	27.8%	5.6%	0.0%	66.7%	0.0%	27.8%	50.0%	11.1%	22.2%
Kazakhstan	100.0%	0.0%	0.0%	0.0%	0.0%	0.0%	100.0%	100.0%	0.0%	0.0%	0.0%	100.0%	100.0%	0.0%	0.0%
Kenya	75.5%	62.3%	7.5%	1.9%	5.7%	7.5%	79.2%	5.7%	1.9%	88.7%	34.0%	9.4%	37.7%	79.2%	3.8%
Kuwait	72.0%	36.0%	0.0%	92.0%	96.0%	92.0%	0.0%	16.0%		0.0%	0.0%	20.0%	96.0%	0.0%	12.0%
Lebanon	10.0%	0.0%	10.0%	45.0%	15.0%	10.0%	5.0%	0.0%	0.0%	10.0%	0.0%	0.0%	5.0%	5.0%	0.0%
Malaysia	100.0%	90.0%	80.0%	0.0%	0.0%	5.0%	0.0%	0.0%	0.0%	5.0%	0.0%	95.0%	100.0%	70.0%	0.0%
Mali	4.8%		0.0%		9.5%		0.0%								
Mongolia	75.0%	50.0%	100.0%	0.0%	100.0%	100.0%		75.0%		100.0%		100.0%	100.0%	100.0%	
Morocco	100.0%	5.0%	95.0%	65.0%	0.0%	0.0%	0.0%	0.0%	0.0%	25.0%	0.0%	60.0%	0.0%	20.0%	0.0%
Nigeria	45.2%	18.6%	0.0%	0.0%	21.4%	21.4%	61.9%	7.1%		11.9%	4.8%	35.7%	38.1%	26.2%	0.0%
Oman	100.0%	100.0%	96.7%	96.7%	100.0%	100.0%	16.7%			0.0%		50.0%	100.0%	0.0%	70.0%
Pakistan	40.0%	73.3%	3.3%	0.0%	56.7%	66.7%	0.0%	0.0%	0.0%	0.0%	0.0%	13.3%	3.3%	26.7%	6.7%
Peru	63.5%	0.0%	86.5%	0.0%	86.5%	15.4%	0.0%	13.5%	0.0%	80.8%	42.3%	63.5%	65.4%	9.6%	3.8%
Philippines	23.1%	30.8%	0.0%	0.0%	46.2%	15.4%	0.0%	0.0%		0.0%		11.5%	34.6%		7.7%
São Tomé and Principe	50.0%	18.8%	37.5%		78.1%	28.1%	87.5%	75.0%		28.1%	6.3%	25.0%		9.4%	
Sudan	83.5%	14.6%	58.1%		21.1%	57.6%	54.3%	9.3%	3.8%	44.3%	14.8%	56.2%	42.7%	12.9%	0.0%
Tajikistan	90.0%	0.0%	85.0%	0.0%	15.0%	95.0%		65.0%		0.0%	0.0%	80.0%	70.0%	5.0%	
Tanzania	12.5%	15.6%	25.0%	3.1%	18.8%	18.8%	28.1%	0.0%	3.1%	34.4%	65.6%	15.6%	9.4%	34.4%	3.1%
Thailand	95.0%	100.0%	10.0%	10.0%	35.0%	80.0%	30.0%	65.0%	0.0%	80.0%	40.0%	100.0%	100.0%	100.0%	85.0%
Tunisia	100.0%	100.0%	90.5%	81.0%	95.2%	61.9%	90.5%		0.0%	100.0%	0.0%	57.1%	0.0%	90.5%	14.3%
Uganda	100.0%	94.4%	27.8%	11.1%	66.7%	94.4%	72.2%	77.8%	0.0%	5.6%	0.0%	61.1%	100.0%	11.1%	27.8%
Ukraine	25.0%	25.0%	0.0%		20.0%	10.0%	25.0%		0.0%	40.0%	60.0%	0.0%	5.0%	15.0%	5.0%
United Arab Emirates	100.0%	100.0%	100.0%	66.7%	83.3%	100.0%	66.7%	100.0%	100.0%			100.0%	100.0%	83.3%	66.7%
Yemen	5.0%	0.0%	0.0%	0.0%	30.0%	0.0%	0.0%	0.0%	0.0%	5.0%	0.0%	5.0%	20.0%	5.0%	0.0%
Mean	**61.2%**	**37.4%**	**37.8%**	**21.3%**	**42.8%**	**37.1%**	**31.6%**	**40.1%**	**16.2%**	**33.5%**	**24.6%**	**49.5%**	**53.8%**	**34.7%**	**20.2%**
Standard error	**6.0%**	**6.5%**	**6.8%**	**6.1%**	**6.3%**	**6.7%**	**6.3%**	**7.4%**	**7.0%**	**6.3%**	**5.7%**	**6.2%**	**7.1%**	**6.3%**	**5.6%**

d. Medicines used for chronic conditions, lowest-priced generics, private sector

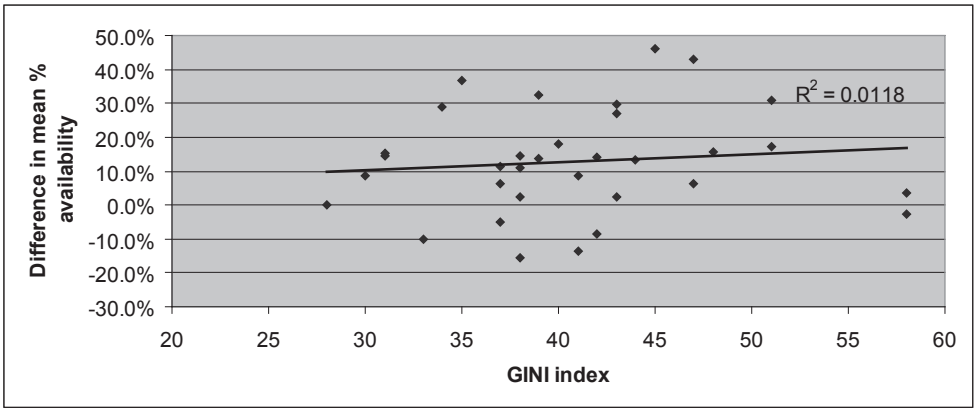
	Antidiabetics		Antiasthmatics		Antihypertensive/CVD					Antiepileptics		Antiulcerants		Antidepressants	
Country	**Glibenclamide 5mg cap/tab**	**Metformin 500 and 850 mg cap/tab**	**Salbutamol 0.1 mg/dose inhaler**	**Beclometasone 0.25 and 0.5 mg/dose inhaler**	**Captopril 25 mg cap/tab**	**Atenolol 50 mg and 100 mg cap/tab**	**Nifedipine Retard 20 and 30 mg tab**	**Hydrochloro-thiazide 25 and 50 mg cap/tab**	**Losartan 25 and 50 mg cap/tab**	**Carbamazepine 200 mgcap/tab**	**Phenytoin 100 mg cap/tab**	**Omeprazole 20 mg cap/tab**	**Ranitidine 150 mg cap/tab**	**Amitriptyline 25 mg cap/tab**	**Fluoxetine 20 mg cap/tab**
Cameroon	35.0%	0.0%	30.0%	10.0%	5.0%		0.0%	65.0%		0.0%	0.0%		25.0%		5.0%
Chad	0.0%	0.0%	0.0%	0.0%	18.2%	9.1%		0.0%		0.0%				45.5%	
China	2.5%	2.5%	25.0%	2.5%	77.5%	7.5%	75.0%	80.0%	0.0%	0.0%	42.5%	75.0%	97.5%	10.0%	10.0%
Colombia	96.6%	96.6%	93.1%	89.7%	100.0%	3.4%	82.8%	100.0%	93.1%	96.6%	82.8%	100.0%	93.1%	89.7%	75.9%
Congo	20.8%	4.2%	25.0%	4.2%	33.3%	4.2%	20.8%			0.0%		29.2%	16.7%	0.0%	
El Salvador	94.2%	42.3%	50.0%	40.4%	69.2%	53.8%	19.2%	75.0%	92.3%	69.2%	36.5%	88.5%	94.2%	75.0%	50.0%
Ethiopia	100.0%	80.0%	84.0%	4.0%	88.0%	60.0%	100.0%	100.0%		72.0%	64.0%	100.0%	96.0%	92.0%	20.0%
Fiji	94.4%	100.0%	97.2%	22.2%	88.9%	97.2%	80.6%	66.7%	52.8%	80.6%	27.8%	97.2%	100.0%	86.1%	61.1%
Ghana	71.4%	64.3%	33.9%	1.8%	25.0%	66.1%	78.6%	39.3%	7.1%	28.6%	39.3%	58.9%	44.6%	46.4%	1.8%
India	57.6%	89.2%	90.3%	38.4%	26.0%	96.5%	79.4%	27.8%	70.7%	59.5%	84.9%	97.4%	96.8%	52.1%	71.4%
Indonesia	96.6%	50.0%	0.0%	0.0%	98.3%	62.1%	0.0%	89.7%	62.1%	70.7%	60.3%	87.9%	84.5%	74.1%	29.3%
Iran	100.0%	93.3%	90.0%	96.7%	96.7%	96.7%	0.0%	100.0%	96.7%	100.0%	90.0%	100.0%	100.0%	96.7%	100.0%
Jordan	95.0%	80.0%	75.0%	35.0%	90.0%	95.0%	60.0%	40.0%	65.0%	60.0%	0.0%	95.0%	85.0%	80.0%	65.0%
Kazakhstan	95.0%	15.0%	35.0%	25.0%	90.0%	95.0%	80.0%	90.0%	10.0%	70.0%	20.0%	90.0%	80.0%	40.0%	15.0%
Kenya	70.7%	65.5%	67.2%	15.5%	62.1%	60.3%	82.8%	15.5%	44.8%	81.0%	67.2%	79.3%	91.4%	72.4%	32.8%
Kuwait	44.0%	28.0%	12.0%	4.0%	16.0%	56.0%	0.0%	0.0%		0.0%	0.0%	100.0%	88.0%	0.0%	4.0%
Kyrgyzstan	80.0%		96.7%	0.0%	90.0%	100.0%	80.0%	96.7%		70.0%	10.0%	86.7%	90.0%	53.3%	3.3%
Lebanon	97.5%	82.5%	97.5%	97.5%	100.0%	100.0%	97.5%	85.0%	35.0%	27.5%	5.0%	95.0%	92.5%	0.0%	97.5%
Malaysia	87.5%	87.5%	96.9%	18.8%	15.6%	93.8%	68.8%	46.9%	0.0%	28.1%	12.5%	87.5%	93.8%	43.8%	0.0%
Mali	45.0%		40.0%		60.0%		45.0%								
Mongolia	44.0%	20.0%	60.0%	4.0%	100.0%	80.0%		52.0%		80.0%		80.0%	88.0%	36.0%	
Morocco	100.0%	45.0%	100.0%	50.0%	70.0%	95.0%	75.0%	95.0%	0.0%	0.0%	0.0%	100.0%	100.0%	95.0%	90.0%
Nigeria	75.0%	36.4%	0.0%	0.0%	38.6%	40.9%	84.1%	18.2%		15.9%	25.0%	70.5%	63.6%	31.8%	0.0%
Oman	93.8%	75.0%	93.8%	31.3%	3.1%	90.6%	3.1%			3.1%		93.8%	96.9%	0.0%	21.9%
Pakistan	50.0%	43.8%	12.5%	0.0%	50.0%	58.3%	6.3%	0.0%	12.5%	33.3%	10.4%	70.8%	35.4%	2.1%	58.3%
Peru	87.5%	8.3%	60.4%	7.3%	100.0%	39.6%	0.0%	27.1%	9.4%	86.5%	33.3%	94.8%	85.4%	18.8%	43.8%
Philippines	39.2%	45.1%	7.8%	0.0%	49.0%	31.4%	5.9%	0.0%		3.9%		15.7%	64.7%		2.0%
São Tomé and Principe	11.1%	0.0%	0.0%		44.4%	22.2%	11.1%	33.3%		0.0%	0.0%	55.6%		0.0%	
South Africa, Gauteng	90.0%	66.7%	96.7%	63.3%	70.0%	86.7%	63.3%	100.0%	0.0%	80.0%	20.0%	50.0%	80.0%	86.7%	90.0%
Sudan	92.1%	56.0%	80.0%		65.6%	82.9%	81.6%	48.1%	23.6%	85.4%	59.5%	79.8%	78.1%	58.5%	23.2%
Syria	98.2%	98.2%	93.0%	96.5%	98.2%	96.5%			96.5%	98.2%	98.2%	96.5%	98.2%	100.0%	98.2%
Tajikistan	100.0%	5.0%	95.0%	0.0%	20.0%	85.0%		85.0%		5.0%	0.0%	80.0%	85.0%	5.0%	
Tanzania	37.5%	45.8%	56.3%	2.1%	50.0%	41.7%	47.9%	0.0%	25.0%	37.5%	8.3%	56.3%	45.8%	41.7%	6.3%
Thailand	100.0%	85.7%	0.0%	0.0%	0.0%	95.2%	52.4%	71.4%	0.0%	28.6%	28.6%	100.0%	95.2%	81.0%	47.6%
Tunisia	97.6%	95.1%	0.0%	95.1%	100.0%	100.0%	95.1%		0.0%	95.1%	0.0%	100.0%	97.6%	2.4%	48.4%
Uganda	85.0%	85.0%	95.0%		75.0%	60.0%	85.0%		50.0%	80.0%	75.0%	95.0%	80.0%	75.0%	40.0%
Ukraine	100.0%	74.1%	100.0%	29.6%	96.3%	92.6%	85.2%	92.6%	63.0%			96.3%	100.0%	81.5%	81.5%
United Arab Emirates	95.7%	82.6%	43.5%	0.0%	17.4%	95.7%	69.6%	100.0%	0.0%	17.4%	0.0%	95.7%	91.3%	0.0%	0.0%
Uzbekistan	82.5%		70.0%	55.0%	92.5%	87.5%	65.0%	57.5%		55.0%		97.5%	90.0%	72.5%	12.5%
Yemen	100.0%	90.0%	100.0%	35.0%	100.0%	95.0%	90.0%	0.0%	25.0%	100.0%	0.0%	95.0%	100.0%	70.0%	80.0%
Mean	**74.1%**	**55.1%**	**57.6%**	**27.1%**	**62.2%**	**69.3%**	**54.8%**	**55.8%**	**35.9%**	**47.9%**	**25.0%**	**83.5%**	**82.3%**	**49.1%**	**40.8%**
Standard error	**4.8%**	**5.6%**	**5.9%**	**5.5%**	**5.3%**	**5.0%**	**5.9%**	**6.3%**	**6.8%**	**5.9%**	**5.6%**	**3.4%**	**3.6%**	**5.7%**	**5.9%**

Appendix 2. Difference in mean % availability of medicines for acute and chronic conditions as a function of a country's level of income disparity (GINI Index, most recent data available)

a. public sector



b. private sector



Chapter 4

Medicine prices and availability for individual disease areas

Chapter 4.1

Availability, price and affordability of cardiovascular medicines: A comparison across 36 countries using WHO/HAI data

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Summary

Background

The global burden of cardiovascular disease (CVD) continues to rise. Successful treatment of CVD requires adequate pharmaceutical management. The aim was to examine the availability, pricing and affordability of cardiovascular medicines in developing countries using the standardized data collected according to the World Health Organization/Health Action International methodology.

Methods

The following medicines were included: atenolol, captopril, hydrochlorothiazide, losartan and nifedipine. Data from 36 countries were analyzed. Outcome measures were percentage availability, price ratios to international reference prices and number of day's wages needed by the lowest-paid unskilled government worker to purchase one month of chronic treatment. Patient prices were adjusted for inflation and purchasing power, procurement prices only for inflation. Data were analyzed for both generic and originator brand products and the public and private sector and summarized by World Bank Income Groups.

Results

For all measures, there was great variability across surveys. The overall availability of cardiovascular medicines was poor (mean 26.3% in public sector, 57.3% private sector). Procurement prices were very competitive in some countries, whereas others consistently paid high prices. Patient prices were generally substantially higher than international references prices; some countries, however, performed well. Chronic treatment with anti-hypertensive medication cost more than one day's wages in many cases. In particular when monotherapy is insufficient, treatment became unaffordable.

Conclusions

The results of this study emphasize the need of focusing attention and financing on making chronic disease medicines accessible, in particular in the public sector. Several policy options are suggested to reach this goal.

Background

The global burden of cardiovascular diseases (CVD) is on the rise and at present 30% of all deaths worldwide are due to cardiovascular conditions (1). The great majority (80%) of these deaths now occur in developing countries (2). Recent projections on the global burden of disease predict that mortality rates of cardiovascular diseases will continue to increase and CVD will rank as leading cause of death in all parts of the world by 2030 (3). The epidemiological transition describes how changes in lifestyle and healthcare system lead to an increasing percentage of deaths due to chronic cardiovascular conditions (4). In order to successfully treat these conditions and reach to the next stage of the epidemiological transition in which deaths are prevented and the onset of disease is delayed, adequate treatment and prevention programs need to be implemented. Within this treatment strategy, ongoing pharmaceutical management with combination therapy using multiple medicines is of great importance. Recurrences of CVD can be diminished by 75% when adequate combination therapy is used (5).

The WHO-PREMISE study investigating the secondary prevention of CVD in ten low- and middle income countries found that pharmaceutical use was often insufficient. Among the patients with coronary heart disease, 18.8% did not receive aspirin, 51.9% did not receive a beta-blocker, 60.2% did not receive an angiotensin-converting enzyme (ACE) inhibitor and 79.2% did not receive a statin (6). Whether this lack of pharmaceutical treatment was due to non-compliance or limited access to medicines was not investigated in this study, however these results call for further research.

In the past, a number of studies on medicine availability and prices have been undertaken, some of which focused specifically on cardiovascular medicines. A Mexican study found that hydrochlorothiazide was the only treatment option that did not become less affordable between 1990 and 1996; 1.1% of the minimum wage was needed to pay for chronic treatment. Other CVD medicines increased up to threefold in price and treatment cost as much as 47% of the minimum wage (7). A study performed in Ghana found that 93% of patients did not comply with their antihypertensive treatment regimen, 96% of which reported high medicine prices as the reason for not complying (8). Other studies investigating medicine pricing in general, including cardiovascular medicines, found that medicines were generally poorly available and highly priced (9-12).

Many of the investigations, however, did not use a standardized methodology, which makes it difficult to compare results across studies. In order to facilitate more standardized research into medicine prices, Health Action International (HAI) and the World Health Organization (WHO) have developed a standardized survey methodology to investigate medicine prices, availability, affordability and price components in the supply chain. Previous analyses of WHO/HAI data for medicines used to treat chronic con-

ditions such as hypertension, asthma and diabetes showed that medicines were poorly available, in particular in public sector facilities. Prices of medicines varied greatly across countries and the public sector was usually less expensive than the private sector, as were generics compared to originator brand products. Many treatment options were not affordable, especially when treatment with multiple medicines was necessary (13,14). Another analysis of the data for a basket of medicines across 36 countries, which corrected for inflation and purchasing power, showed very similar results (15).

The aim of this study is to perform a secondary analysis of the availability, price and affordability of chronic-care cardiovascular medicines in developing countries using the WHO/HAI data, and correcting for inflation and purchasing power. The medicines studied are atenolol, captopril, hydrochlorothiazide, losartan and nifedipine, all of which can be used to treat hypertension.

Methods

WHO/HAI data collection

The WHO/HAI methodology aims to generate reliable information concerning the availability, price and affordabilityof medicines and is briefly summarized here. All surveys analysed in this research used the methodology described in the first edition of the manual (16).

In each survey, data on availability and patient prices are collected in a sample of outlets in the public and private sector. Public sector procurement prices are also collected, usually at a central level such as the Ministry of Health or the Central Medical Store. In each survey, one major urban centre and three randomly-chosen administrative regions within one day's travel of the urban area are selected as survey areas. In each survey area, the main public hospital and at least four other public medicine outlets are selected to obtain data on public sector patient prices. The private sector sample is chosen by selecting the private outlet closest to each sampled public sector outlet. Thus, a minimum of 20 outlets per survey per sector are sampled. In 2008, a second edition with slightly different methodology was published (17).

Surveys are performed according to a standardized protocol with results double-entered into a uniform workbook for data analysis. In each survey, data are collected on 30 (global) core medicines and up to 20 supplementary medicines of local or regional importance. For each medicine a fixed dosage form and strength is used. Surveys are usu-

ally performed on a national level, but large countries such as India and China have been surveyed on a sub-national basis.

Outcome measures

Availability is expressed as the percentage of facilities where the medicine is found on the day of data collection. Only formulations of the same strength and dosage form are included.

Price is expressed as a price per unit (e.g. tablet, dose) and converted to a median price ration (MPR) by dividing the median local price by an international reference price (IRP). The IRP is obtained from the Management Sciences for Health International Drug Price Indicator Guide which reports median prices of high quality multisource medicines offered to developing and middle-income countries by different suppliers (18). Each survey uses the IRP for the year prior to the survey and the IRP is converted to local currency using the exchange rate on the first day of data collection. Price ratios are not calculated when the medicine was present in less than four outlets. In addition, treatment affordability is estimated by calculating the number of day's wages the lowest-paid unskilled government worker needs to purchase one month's supply of medicines according to a standard treatment regimen.

Secondary data analysis

The following anti-hypertensive medicines have been included: captopril 25 mg, atenolol 50 mg, hydrochlorothiazide 25 mg, nifedipine retard 20 mg and losartan 50 mg, all in either tablet or capsule form. Out of 19 antihypertensive medicines in the database, these medicines were chosen because they are the most-surveyed representatives of five major pharmaceutical classes. Price information was not analysed for losartan because there was no reliable IRP available; losartan is not widely produced as a generic formulation because it is still under patent in many countries (19). At the time of the study, 45 surveys from 36 countries were available for analysis (table 1). The most recent data were extracted from the WHO/HAI database which is available online (20).

In order to compare prices across different countries and regions, several data adjustments have been made. All prices have been converted back to the year 2004, as the majority of surveys were conducted in this year. Prices were standardized to IRPs for 2003 and to a common US dollar exchange rate as published by the International Monetary Fund (21). For Uzbekistan the exchange rate published by the United Nations Economic Commission for Europe was used; due to the multiple exchange rates for Syria the exchange rate used in the surveys was left unchanged.

To correct for either inflation or deflation that may have occurred between the survey year and the base year (2004), prices were adjusted using the consumer price index (CPI) (21). The consumer price index is a standardised measure of inflation which is calculated by comparing the price of a standardised basket of goods in the current year to a baseline year. Adjusting prices to represent the survey year 2004 (thus using 2003 IRPs and correcting prices using the CPI) allowed for evaluation of public procurement prices across surveys and comparison of procurement prices with public sector patient prices within surveys.

In order to compare patient prices across countries and/or regions, prices were also adjusted for purchasing power parity (PPP) (21). PPP quantifies how much of a basket of goods a specific quantity of US dollars will buy in a specific country. Procurement prices were not corrected for PPP because the pharmaceutical procurement market is international and competitive and the price a country pays generally does not depend on the purchasing power of its inhabitants.

Brand premiums were calculated by dividing the adjusted MPR for an originator product by the adjusted MPR for its lowest-priced generic equivalent.

Data have been analysed by 2007 World Bank Income Groups (Table 1) (22). Results are reported as averages for each income group.

Finally, in El-Salvador, India, Kuwait, Malaysia, Morocco, Pakistan, Tunisia, Uganda and the United Arab Emirates medicines were provided free-of-charge in the public sector and as such no pricing data was analyzed for the public sector in these countries.

Results

Availability

Availability of cardiovascular medicines varied considerably across the surveyed countries, even within income groups. Availabilities ranging from 0 to 100% within one income group were no exception (tables 2 and 3).

Overall, atenolol 50 mg had the highest availability for the lowest-priced generic (LPG) in both the public and private sectors (38.9% and 73.3% respectively) and losartan the lowest. The entire basket of cardiovascular medicines had an average availability of 26.3% for the LPG in the public sector and 57.3% in the private sector (LPG). For all medicines, the private sector had better availability than the public sector, both for LPGs and originator brand products (OB). In nearly all surveys, LPGs had a higher

availability than originator brand products. The only exception to this was losartan, which is still under patent; ten out of thirty surveys had better availability of the OB. Across income groups, in both the public and private sector, higher income regions tended to have better availability than lower income regions. In the private sector, higher income areas with a low availability of LPGs had a high availability of OBs.

Public sector procurement prices

A comparison of public sector procurement prices showed that they varied greatly both across medicines and countries/regions. For example, the CPI-adjusted MPR for captopril was 0.21 in Peru and the United Arab Emirates and 12.75 in Morocco. This means that prices ranged from 0.21 to 12.75 times the international reference price. The average procurement MPR for both generic and originator products are summarized in Figure 1. It is important to realize that MPR is a measure relative to the international reference price, not an absolute measure. This may explain the high MPR for hydrochlorothiazide. There was no data available concerning the procurement of originator brand hydrochlorothiazide.

No particular relationship could be found across World Bank Income Groups. Nigeria and Mongolia had the highest procurement prices for several medicines. Some countries were capable of obtaining consistently low procurement prices, in particular Ethiopia, Fiji and Jordan.

Data matched by medicine, which allow for comparison of procurement prices and public sector patient prices within one survey, were only available for a very limited number of surveys and medicines (data not shown). It could be seen that in Ethiopia and Tanzania patient prices were at least 50% more expensive than the procurement price for three out of four medicines. On the other hand, patient prices were lower than procurement prices for several medicines in Nigeria.

Patient prices

Figure 2 summarizes the average median price ratios for the LPG and the OB in the public and private sector. Data classified by income group is presented in tables 4 and 5.

Across the cardiovascular medicines, captopril (LPG) had the lowest MPR in both the public and private sector. The highest MPR was found for hydrochlorothiazide. When comparing the public and private sector, it can be seen that for LPGs, the private sector was on average more expensive for all medicines. Importantly, countries that provide medicines for free in the public sector were not included to calculate the average MPR. For originator brand products, a direct comparison between the public and private

sector could not be made due to the very limited availability of OB products in the public sector.

Lower income countries (LI and LMI) tended to have higher adjusted prices than the upper income countries (UMI and HI), both in the public and private sector. Again, some countries had consistently high or low prices across multiple medicines. High prices were found in El- Salvador and the Philippines, while low prices were often found in Fiji and Yemen.

Brand premiums

Brand premiums were calculated when possible; there was insufficient data available to calculate brand premiums in the public sector due to the low availability of OB products. Results are presented in figure 3. It was found that on average, brand premiums were lower in higher income countries as compared to lower income areas.Countries with high brand premiums for multiple medicines were Fiji and Peru, while low brand premiums could often be found in El-Salvador, Kuwait and the UAE.

Affordability

Data for affordability were limited, in particular in the public sector; for losartan and nifedipine data were only available from two and three surveys, respectively. Therefore, the results may not always be representative of the entire sample.

In the public sector (n = 28, from 18 countries/regions), it cost on average 2.0 (LPG) and 8.3 (OB) day's wages to purchase one month of treatment with one of the cardiovascular medicines. On average affordability was better in the private sector (1.8 and 5.3 day's wages for the LPG and OB). When countries were matched, however, the private sector was usually less affordable than the public sector. Atenolol was most affordable, with an average of 1.1 day's wages for the LPG. When matched across surveys, the LPG was in all cases more affordable than the OB product, both in the public and private sector. Overall, cardiovascular medicines were least affordable in the low income regions. Upper-middle income countries scored particularly well, especially when compared to high income regions.

Discussion

Findings

Overall availability of the five cardiovascular medicines was low, with an average availability of 57.3% in the private sector and 26.3% in the public sector. However, availabilities of over 80% were observed in some countries (public and/or private sector). Availability of the lowest-priced generics was higher than originator brand products in most surveys and private sector availability was higher than public sector availability in all surveys. However, even in the private sector availability was not universal and prices were nearly always higher. In general, higher income countries had higher medicine availability than lower income countries, both in the public and private sector. Differences in the presence of CVD medicines on National Essential Medicines Lists, where they exist, may explain the (poor) availability of medicines in some countries. For example, in some countries enalapril was chosen as an essential ACE-inhibitor rather than captopril which was surveyed (23).

Average public sector procurement prices were relatively high; in the past, a MPR equal to or below 1.0 has been described as a reasonable procurement price (13). Some countries achieved procurement prices well below the international reference price for a number of medicines, whereas others consistently paid higher prices (24). As would be expected, generics were procured at lower prices than originator products. When comparing public sector procurement and patient prices, it was seen that in some cases patients were charged less than the procurement price. This could reflect that countries are aware of the high prices for essential chronic disease medicines and are using a cross-subsidizing system to lower these prices. In other cases however, patient prices in the public sector were much higher than procurement prices, which could be due to high mark-ups and taxes along the supply chain.

As with availability, patient prices varied greatly among surveys. In countries in which patients paid for medicines in the public sector, the average cost of LPGs was less than in the private sector for all medicines. However, a lack of availability in the public sector may force patients to purchase their medicines in the more highly priced private sector or forgo treatment altogether. For example, captopril had an adjusted MPR of 0.67 in the public sector in Jordan but only 61% availability. In the private sector, captopril had a much higher availability (90%), but the patient would need to pay 19.02 times the IRP.

As would be expected, generics were priced lower than originator brand products in nearly all surveys for all medicines. Our calculations of brand premiums show that to purchase an originator brand medicine costs 4.2 times as much as buying the lowest-

priced generic. Interestingly, brand premiums were on average lower in upper-middle and high income countries. One would hope this smaller price differential was due to lower prices for the originator brand, but unfortunately this was due to higher prices being charged for generic products. This can occur when price regulations set the price for the generics discounted from the price charged for originator brand products, as occurs in Kuwait (13).

Overall, patient prices for cardiovascular medicines were high compared to international reference prices. For LPGs, the average adjusted MPR for the entire group of medicines was 15.5 in the public sector and 30.2 in the private sector.

The affordability data showed that on average one month of chronic treatment with one medicine for hypertension cost 1.8 day's wages. In all cases, originator brand products and the private sector were less affordable. Skipping one or two meals was often not enough to purchase treatment and often more than one day's wages were needed to purchase one month of treatment; therefore cardiovascular medicines may be labeled as unaffordable in a significant proportion of countries. Furthermore, an important part of the patient population requires combination therapy with multiple anti-hypertensives to reach treatment goals, amounting to an unaffordable treatment package. Finally, in one-income families, chronic treatment becomes particularly unaffordable if more than one family member has a medical condition that requires treatment.

Strengths and weaknesses

The strength of this research lies in the standardized WHO/HAI methodology which has been validated through pilot and validation studies and adapted accordingly (17).

However, some difficulties do exist. Outcome measures, in particular availability, may be affected by the exclusion of alternate dosage forms and strengths or therapeutic alternatives. Also, availability data do not reflect average availability over time since availability data is only collected on one specific day. Furthermore, median price ratios may be skewed when international reference prices are based on limited data (18). For this reason, price data for losartan were not analysed. It is important to realize that the MPR is a relative measure of price and does not provide information on the absolute price of a medicine; thus the absolute price of hydrochlorothiazide may be lower than that of nifedipine even though the latter has a lower MPR.

In some cases, data in one or more income group may have been skewed due to the small number of surveys in that category or dominance of one country within one income group. The latter occurred a number of times with surveys from India, which due to the unique nature of the Indian pharmaceutical market and the large number of Indian surveys, may have influenced outcomes in the low income group.

Calculating affordability based on the wage of the government worker may lead to an over-optimistic result since a significant proportion of the population earns less than this amount (14). Alternative measures for affordability are currently under investigation (25). A further problem for the affordability analysis was that only a limited number of surveys calculated affordability of these medicines.

Implications

Based on the outcomes of this analysis, several implications for policy making can be emphasized. The poor availability in the public sector limits patient access to medical treatment by forcing them to resort to the more highly priced private sector, which has better, although not optimal, availability. The public sector is often seen as a last resort, but as our data show, the private sector fails to meet the needs of those least able to afford highly priced products. Improving public sector availability can be achieved by implementing more efficient procurement in the countries that pay high procurement prices, improving distribution systems and providing adequate and sustainable financing. Furthermore, focusing (limited) resources on a selected group of generic essential chronic disease medicines instead of aiming to supply a broad range of generic and originator brand medicines may lead to better availability of priority treatments (15).

In some countries, lowering procurement prices could help bring patient prices down (26). Strategies to improve procurement efficiency include competitive procurement with price transparency, national pooled purchasing and purchasing by generic name (17). Differential pricing based on the wealth of countries could also lower prices. This differential pricing already occurs for originator brand products to some degree, but not as much for generic products (27). Promoting differential pricing could benefit lower income countries, not only affecting medicine prices, but also improving the availability of medicines. Options and strategies for differential pricing are currently being explored and promoted (28,29).

Addressing excessive mark-ups between procurement and patient prices could help bring prices down. For example in Syria, the maximum percentage mark-up allowed is determined based on the cost of the medicine; more expensive medicines are allotted a relatively lower mark-up to prevent preferential selling of highly priced products (15,30). Furthermore, exempting medicines from tariffs and taxes, such as the value-added tax, will lower prices and prevent taxing of the sick (14,26). It must then be ensured that savings obtained are passed on to patients. Furthermore, it has been found that in some countries, particularly in Sudan and China, revenue from medicine sales in the public sector is used to finance other parts of the public health care system (15,31,32). Because the public sector is primarily used by the poor, this practice is inequitable and alternative sources of financing should be sought (15).

Furthermore, continuous support for the use of generic products can contribute to keeping the costs of medicines down, both in the public and private sector. Several strategies have been proposed, including ensuring product quality, encouraging or requiring generic substitution, preferential registration procedures and education of health care professionals and consumers (14).

Although generic medicines were usually priced lower and were more available than originator products in the private sector, some were still relatively overpriced as can be seen by the small brand premiums in high income countries (13). In some cases, this could be prevented by implementing policies that do not regulate generic prices based on the price charged for brand products.

No matter how inexpensive medicines are in the private sector, the poorest sections of population in developing countries will still not be able to afford them. Further, chronic disease treatment requires lifelong therapy in order to prevent potentially life-threatening complications. Such demand is predictable and creates a responsibility on the health care system to ensure continued availability. Health insurance which covers out-patient chronic disease medicines is therefore of key importance. In this line of reasoning, investing in expensive facilities such as stroke or cardiac care units should only occur when reliable access to hypertensive medicines has been achieved.

Conclusions

This analysis reveals that many problems remain with the availability, prices and affordability of cardiovascular medicines. To improve the situation, medicine policies should be adapted to promote the use of generic medicines, promote sustainable and reliable methods of procurement and financing and prevent excessive mark-ups in the supply chain. Also, continuing research into medicine pricing is necessary, as medicine prices continue to evolve and policy changes continue to have effects. Implementing medicine price monitoring programmes and performing price component analyses should be conducted to gain more insight into medicine prices and allow for adaptation of policies to specific countries.

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Tables and figures

Table 1 - Countries surveyed classified by World Bank income group

Income group	Countries surveyed
Low income (LI)	Chad, Ethiopia, Ghana, India (Chennai, Haryana, Karnataka, Maharashtra 12 districts, Maharashtra 4 regions, Rajasthan, West-Bengal), Kenya, Kyrgyzstan, Mali, Mongolia, Nigeria, Pakistan, Sudan (Gadarif, Khartoum, Kordofan), Tajikistan, Tanzania, Uganda, Uzbekistan, Yemen.
Lower-middle income (LMI)	Armenia, Cameroon, China (Shandong, Shanghai), El-Salvador, Fiji, Indonesia, Jordan, Morocco, Peru, Philippines, Sri Lanka, Syria, Tunisia.
Upper-middle income (UMI)	Brazil (Rio de Janeiro), Kazakhstan, Lebanon, Malaysia, South Africa (Kwazulu Natal State)
High income (HI)	Kuwait, United Arab Emirates

Abbreviations: LI – Low income; LMI – Lower middle income; UMI – Upper middle income; HI – High income.

Table 2 – Public sector percentage availability by World Bank income group (weighted averages)

	Atenolol		Captopril		HCT		Losartan		Nifedipine		All	
	LPG	OB	LPG	OB	LPG	OB	LPG	OB	LPG	OB	LPG	OB
	% (n)	% (n)	% (n)	% (n)	% (n)	% (n)	% (n)	% (n)	% (n)	% (n)	% (n)	% (n)
LI	40.7 (20)	0.8 (20)	18.6 (21)	1.4 (21)	15.0 (21)	0.4 (16)	2.2 (16)	0.0 (13)	24.5 (19)	0.2 (19)	20.8	0.6
LMI	17.8 (8)	3.8 (8)	59.4 (9)	8.7 (9)	51.3 (9)	0.0 (9)	8.6 (8)	12.1 (8)	20.4 (8)	21.5 (8)	32.6	9.0
UMI	5.0 (3)	3.3 (3)	5.0 (3)	66.7 (3)	33.3 (2)	0.0 (2)	0.0 (3)	30.0 (3)	35.0 (3)	0.0 (3)	14.4	21.4
HI	93.0 (2)	10.5 (2)	81.3 (2)	5.6 (2)	46.9 (2)	0.0 (1)	0.0 (1)	72.2 (1)	50.0 (2)	100.0 (2)	60.3	38.1
All	**38.9 (33)**	**2.3 (33)**	**31.5 (35)**	**9.1 (35)**	**27.7 (34)**	**0.2 (28)**	**3.7 (28)**	**10.4 (25)**	**26.0 (32)**	**11.7 (32)**	**26.3**	**6.8**

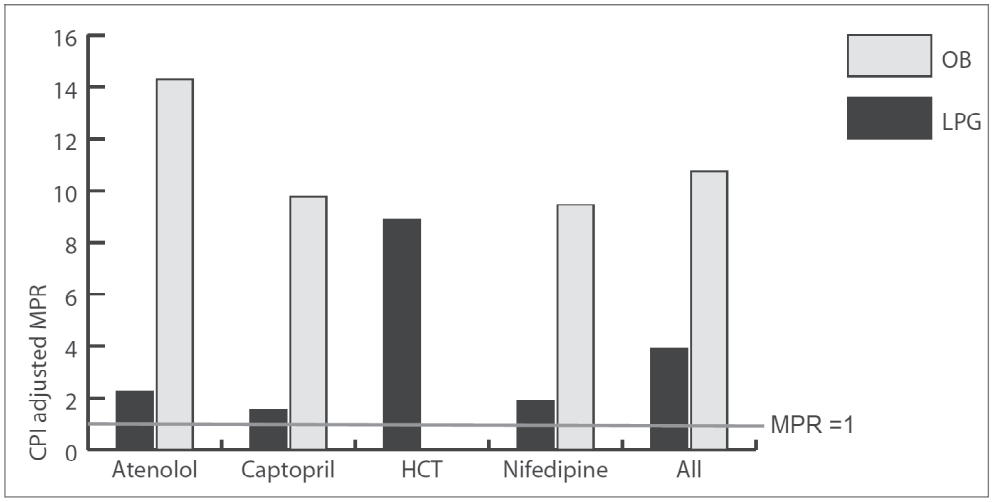
Abbreviations: HCT – hydrochlorothiazide; LPG – lowest priced generic; OB – originator brand; LI – Low income; LMI – Lower middle income; UMI – Upper middle income; HI – High income.

Table 3. Private sector percentage availability by World Bank income group (weighted averages)

	Atenolol		Captopril		HCT		Losartan		Nifedipine		All	
	LPG	OB	LPG	OB	LPG	OB	LPG	OB	LPG	OB	LPG	OB
	% (n)	% (n)	% (n)	% (n)	% (n)	% (n)	% (n)	% (n)	% (n)	% (n)	% (n)	% (n)
LI	79.7 (22)	32.5 (22)	25.9 (23)	24.0 (23)	35.5 (22)	1.7 (18)	46.0 (16)	5.7 (13)	74.8 (21)	13.0 (21)	52.3	17.0
LMI	59.1 (10)	38.9 (10)	83.5 (11)	39.4 (11)	64.3 (10)	8.9 (10)	37.8 (10)	42.9 (10)	45.6 (9)	38.6 (9)	58.8	33.9
UMI	72.3 (4)	66.8 (4)	68.5 (4)	84.4 (4)	55.5 (3)	21.7 (3)	15.0 (3)	66.7 (3)	82.1 (3)	36.9 (3)	60.1	57.7
HI	76.0 (2)	98.0 (2)	16.7 (2)	94.0 (2)	50.0 (2)	0.0 (1)	0.0 (1)	100 (1)	34.8 (2)	98.0 (2)	39.4	85.0
All	**73.3 (38)**	**42.8 (38)**	**59.4 (40)**	**36.5 (40)**	**45.9 (37)**	**6.7 (32)**	**38.6 (30)**	**29.8 (27)**	**65.6 (35)**	**26.5 (35)**	**57.3**	**29.2**

Abbreviations: HCT – hydrochlorothiazide; LPG – lowest priced generic; OB – originator brand; LI – Low income; LMI – Lower middle income; UMI – Upper middle income; HI – High income.

Figure 1: Procurement MPRs (CPI adjusted) for the LPG and the OB



The line represents a price ratio equal to 1.0 (procurement at the same price as the international reference price). Abbreviations: HCT – hydrochlorothiazide; LPG – lowest-priced generic; OB – originator brand; MPR – Median Price Ratio.

Table 4. Public sector patient MPR (CPI and PPP adjusted), by World Bank income group (weighted averages)

	Atenolol		Captopril		HCT		Nifedipine		All	
	LPG (n)	OB (n)	LPG (n)	OB (n)	LPG (n)	OB (n)	LPG (n)	OB (n)	LPG (n)	OB (n)
LI	15.7 (7)		7.2 (7)	15.8 (1)	40.5 (4)		9.8 (6)		15.9	15.8
LMI	40.2 (3)	122.3 (1)	6.9 (6)	71.2 (2)	12.0 (4)		9.5 (2)	20.4 (1)	15.3	71.3
UMI				7.0 (1)	15.2 (1)		9.5 (1)		12.4	7.0
HI										
All	**23.0 (10)**	**122.3 (1)**	**7.0 (13)**	**41.3 (4)**	**25.0 (9)**		**9.7 (9)**	**20.4 (1)**	**15.5**	**51.3**

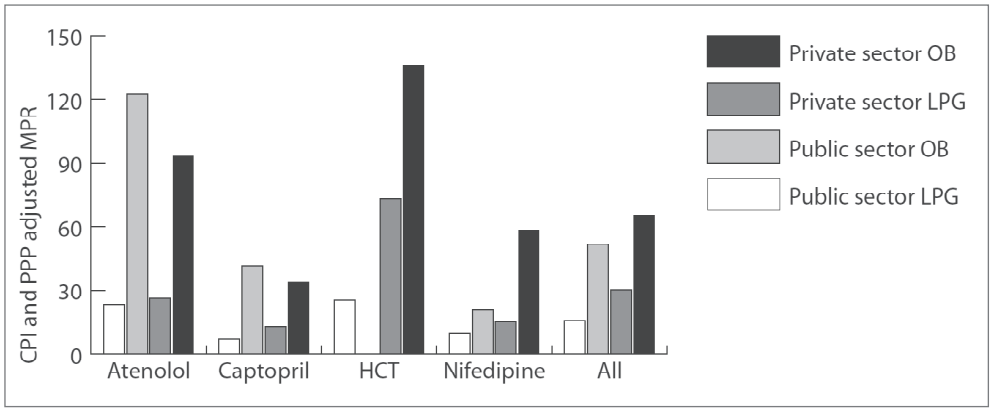
Blank cases are due to missing data. Abbreviations: LPG – lowest priced generic; OB – originator brand; HCT – hydrochlorothiazide; LI – low income; LMI – lower-middle income; UMI – upper middle income; HI – high income.

Table 5. Private sector patient MPR (CPI and PPP adjusted), by World Bank income group (weighted averages)

	Atenolol		Captopril		HCT		Nifedipine		All	
	LPG (n)	OB (n)	LPG (n)	OB (n)	LPG (n)	OB (n)	LPG (n)	OB (n)	LPG (n)	OB (n)
LI	21.0 (22)	107.3 (13)	12.4 (21)	3.9 (9)	85.2 (16)	73.0 (1)	11.8 (20)	51.6 (7)	35.6	74.9
LMI	41.5 (9)	87.6 (7)	14.7 (12)	39.8 (10)	66.6 (10)		27.8 (6)	81.8 (6)	45.7	70.0
UMI	13.2 (3)	83.4 (3)	8.9 (3)	31.6 (4)	36.0 (3)	156.8 (3)	11.1 (3)	46.0 (2)	22.4	81.6
HI	26.8 (2)	37.2 (2)	10.7 (2)	12.1 (2)	55.2 (1)		13.9 (1)	23.6 (2)	38.5	31.3
All	**25.8 (36)**	**93.2 (25)**	**12.7 (38)**	**34.1 (25)**	**73.0 (30)**	**135.8 (4)**	**15.0 (30)**	**58.3 (17)**	**30.2**	**65.4**

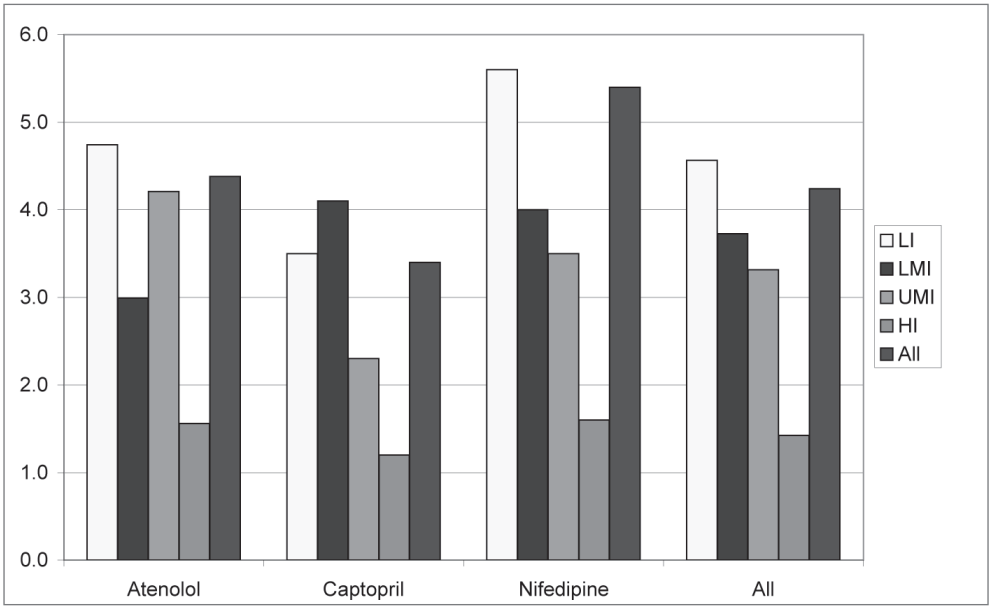
Blank cases are due to missing data. Abbreviations: LPG – lowest priced generic; OB – originator brand; HCT – hydrochlorothiazide; LI – low income; LMI – lower-middle income; UMI – upper middle income; HI – high income.

Figure 2: Average CPI and PPP adjusted MPRs for atenolol, captopril, hydrochlorothiazide and nifedipine



Abbreviations: HCT – hydrochlorothiazide; LPG – lowest priced generic; OB – originator brand; MPR – Median Price Ratio.

Figure 3: Brand premiums in the private sector, by medicine and World Bank income group



Abbreviations: LI – low income; LMI – lower-middle income; UMI – upper-middle income; HI – high income, HCT – hydrochlorothiazide, Capt – captopril.

Chapter 4.2

Mapping the availability, price, and affordability of antiepileptic drugs in 46 countries

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Summary

Purpose

In low- and middle-income countries (LMICs), a large proportion of people with epilepsy do not receive treatment. An analysis of the availability, price, and affordability of antiepileptic drugs (AEDs) was conducted to evaluate whether these factors contribute to the treatment gap.

Methods

Data for five AEDs (phenytoin, carbamazepine, valproic acid, phenobarbital, and diazepam) were obtained from facility-based surveys conducted in 46 countries using the World Health Organization/Health Action International (WHO/HAI) methodology. Outcome measures were percentage availability, ratios of local prices to international reference prices, and number of days' wages needed by the lowest-paid unskilled government worker to purchase treatment. Prices were adjusted for inflation/deflation and purchasing power parity.

Key findings

The average availability of generic AEDs in the public sector was <50% for all medicines except diazepam injection. Private sector availability of generic oral AEDs ranged from 42.2% for phenytoin to 69.6% for phenobarbital. Public sector patient prices for generic carbamazepine and phenytoin were 4.95 and 17.50 times higher than international reference prices, respectively, whereas private sector patient prices were 11.27 and 24.77 times higher, respectively. For both medicines, originator brand prices were about 30 times higher. The highest prices were observed in the lowest income countries. The lowest-paid government worker would need wages from 1–2.6 days' to purchase a month's supply of phenytoin, whereas carbamazepine would cost 2.7–16.2 days' wages. Despite its widespread use in LMICs, WHO/HAI survey data for phenobarbital was only available from a small number of countries.

Significance

In LMICs, availability and affordability of AEDs are poor and may be acting as a barrier to accessing treatment for epilepsy. Ensuring a consistent supply of AEDs at an affordable price should be a priority.

Introduction

Epilepsy is a common neurologic disorder accounting for 0.5% of the world's disease burden (1). A recent meta-analysis provided a global estimate of 70 million for cases of life-time epilepsy (2). More than 80% of people with epilepsy live in resource-poor countries where the incidence of epilepsy is two to three times higher than in high-income countries (3). People with epilepsy in resource-poor countries are about five times more likely to die prematurely than their peers in the general population; the risk is especially high among young people (4). When left untreated, epilepsy can result in multiple health problems such as fractures and burns. Epilepsy is also associated with social consequences, including human rights violations and discrimination resulting from the stigma of epilepsy (3).

It is estimated that up to 70–80% of people with epilepsy could lead normal lives if properly diagnosed and treated (5). However, despite the availability of cost-effective antiepileptic drugs (AEDs), the majority of affected individuals in resource-poor settings do not receive treatment. A recent systematic review estimated that the epilepsy "treatment gap," or the proportion of people with active epilepsy who were not receiving treatment, was >75% in low-income countries and >50% in most middleincome countries, compared to <10% in many high-income countries (6). It has been suggested that this treatment gap results from a combination of factors, including lack of prioritization on health agendas; insufficient health care financing; health systems issues, such as inadequate skilled manpower and poor drug supply; long travel times to reach health care facilities; and cultural beliefs, including the stigma associated with epilepsy (7-9).

The availability and affordability of medicines are two key factors that affect patients' access to treatment. A study of the availability and prices of AEDs carried out in southern Vietnam showed that only 57% of the public and private pharmacies surveyed had AEDs available. Monthly treatment costs ranged from US$ 3.30 for carbamazepine 200 mg to US$ 22.50 for valproic acid 200 mg (10). A second study conducted in Zambia found that nearly one-half of the government, private, and nongovernmental organization (NGO) pharmacies surveyed did not carry AEDs. Pediatric syrups were universally not available. Adult out-of-pocket monthly costs ranged from US$ 7.51for carbamazepine to US$ 29.88 for valproic acid (11).

Although the preceding two studies provide some insight into the magnitude of the availability and cost issues around AEDs, both have been conducted on a subnational level, limiting the generalizability of the results. Further, differences in the methodologies make it difficult to compare results across studies. The purpose of this article is, therefore, to conduct an analysis of the availability, price, and affordability of AEDs across a range of primarily low- and middle-income countries.

Methods

Primary data source

Data on the availability, price, and affordability of AEDs were obtained from facility-based surveys conducted using a standard method (12, 13). In the surveys, the availability and prices of approximately 50 medicines were collected during visits to a sample of medicine outlets in the public sector (primary health care facilities and hospital outpatient services) and private sector (pharmacies and licensed drug stores). Government procurement prices were also collected. The surveys included standard medicines collected in all surveys to enable international comparisons as well as supplementary medicines selected locally for their clinical relevance (12). For each medicine, a fixed dosage form and strength were used, and data were collected for both the originator brand first authorized worldwide for marketing (normally as a patented product), and the lowest priced generic equivalent found at each facility. In WHO/HAI surveys, generic medicines are defined as pharmaceutical products intended to be interchangeable with the originator brand product, manufactured without a license from the originator manufacturer, and marketed after the expiry of patent or other exclusivity rights (12). The survey was conducted by trained data collectors, following which data were double-entered into a preprogrammed Excel workbook (Microsoft Corp., Redmond,WA, U.S.A.) that allowed for standardized analysis. Availability was reported as the percentage of outlets in which individual medicines were found on the day of data collection. Prices were expressed as median price ratios (MPRs), calculated as ratios of median local unit prices to Management Sciences for Health (MSH) international reference prices (14). MSH prices represent recent procurement prices offered by suppliers to developing countries. Median prices were also used to estimate treatment affordability, calculated as the number of day's wages required for the lowest-paid government worker to purchase a course of treatment.

Secondary data analysis

Composite data on medicine availability and price (e.g., median price ratios, percentage availability) were extracted from the HAI global database of survey results for individual medicines summarized across medicine outlets (15). Affordability data were obtained from individual survey workbooks.

Survey inclusion criteria

All surveys that included data on the AEDs at the time of data extraction in February 2011 were included in the analysis. Where surveys were repeated in a country, the most

recent dataset was used. In countries where multiple surveys were carried out in subnational regions (India, China, and Sudan), results were averaged.

Selection of antiepileptic drugs

The AEDs included in this study were phenytoin 50- and100-mg tablets; phenobarbital 15-, 30-, and 100-mg capsules/tablets and 200 mg/ml injection; carbamazepine 100- and 200-mg capsules/tablets; valproic acid 200-mg capsules/tablets; and diazepam 5 mg/ml injection. The selection of individual AEDs was based on the data available and the inclusion of these medications on the WHO Model List of Essential Medicines (16).

Availability of antiepileptic drugs

The mean availability of both the originator brand product and the lowest-priced generic equivalent were calculated for each AED in both private and public sectors. Because individual countries surveyed different strengths ofeach AED based on local usage patterns, results for different strengths were combined to determine average availability of each AED across the countries studied. Average availability stratified by World Bank country income level (17) was also analyzed for carbamazepine and phenytoin, although given the relatively small number of countries in each income group, results are descriptive only. Other AEDs in the study had insufficient country data to allow for disaggregation by income level.

Price of AEDs

Price data were adjusted to increase comparability across countries as recommended by the WHO/HAI methodology WHO & HAI, 2008 methodology and as reported elsewhere (13, 18). Different sources of exchange rates used in the surveys were standardized against International Monetary Fund rates, and the Consumer Price Index (CPI) (19) was used to adjust prices for inflation/deflation. Patient prices (i.e., retail prices) were also adjusted for purchasing power parity (PPP) (19), to account for differences in purchasing power of individual currencies.

The mean MPRs were calculated for each AED, for both originator brands and lowest-price generic equivalents in each of the public and private sectors. In the price analysis, different strengths were kept separate as price levels would be expected to vary according to medicine strength. MPRs were also analyzed according to World Bank income group for phenytoin and carbamazepine (17). Surveys that provided price data on both the originator brand and the lowest-price generic equivalent of a given AED were iden-

tified so that any price differential between brands and generics ("brand premium") could be analyzed.

Affordability of AEDs

Treatment affordability was estimated as the number of days' wages that the lowest-paid government worker would need to purchase a month's supply of AEDs. The daily wage of the lowest-paid government worker was identified in each country survey. Monthly treatment costs for AEDs were estimated based on the defined daily doses (DDDs) published by the WHO Collaborating Centre for Drug Statistics Methodology (20). A DDD is defined as the assumed average maintenance dose per day for a drug used for its main indication in adults.

Results

A total of 46 countries were included in the analysis, corresponding to 57 surveys conducted between 2003 and 2010 (Table 1). Of the five study medicines (carbamazepine, phenobarbital, phenytoin, valproic acid, and diazepam), survey data were most frequently available for carbamazepine and phenytoin, particularly 200 and 100 mg strengths, respectively. Results, therefore, focus primarily on these two medicines.

Availability of AEDs

The availability of AEDs in the public sector was <50% for all medicines except diazepam injection (Table 2). The average availability of generic carbamazepine and phenytoin was 45.3% and 37.7%, respectively. In the private sector, the availability of oral AEDs (42–70% for generics) was consistently higher than in the public sector, whereas private sector availability of injectables (12–43% for generics) was lower than in the public sector. Generic AEDs were generally more available than their corresponding originator brands in both the public and private sectors; however, in the private sector the availability of originator brand phenytoin (48.7%) was slightly higher than that of generic equivalents (42.2%).

Analysis of medicine availability by World Bank Income Group showed that in low-income countries, generic phenytoin and carbamazepine were each available in about one third of the public sector facilities surveyed (data not shown). In the private sectors of low-income countries, availability was slightly higher but was still <50%. For some products (e.g., generic phenytoin and originator brand carbamazepine in the public

sector and originator brand phenytoin in the private sector), availability increased with increasing country income level.

Price of AEDs

Public sector procurement prices for generic carbamazepine and phenytoin were on average 1.56 and 2.53 times the international reference prices, respectively, whereas the prices of originator brands were 6.19 and 5.19 times higher (see Appendix S1). Data also showed that diazepam injection (available for only three countries) was being procured competitively at prices 13% lower than international reference prices.

In countries where patients pay for medicines in the public sector, the PPP-adjusted patient prices of generic carbamazepine and phenytoin were 4.95 and 17.50 times higher than international reference prices, respectively (Table 3). Originator brand products cost even more, although data were limited. Some data were also available on the price of injectable AEDs in the public sector, with phenobarbital and diazepam costing approximately four and five times more than international reference prices, respectively. When the prices of originator brands and their lowest-priced generics were compared in countries reporting prices on both product types, it was found that originator brand carbamazepine and phenytoin cost 2.4 and 2.8 times more, respectively, than their lowest-priced generic equivalents (data not shown).

In the private sector, the PPP-adjusted patient prices of generic carbamazepine and phenytoin were 11.27 and 24.77 times higher than international reference prices, respectively (Table 3). For both medicines, originator brand prices were more than 30 times higher than international reference prices. Originator brand carbamazepine and phenytoin cost 3.1 and 2.1 times more, respectively, than their lowestpriced generic equivalents (data not shown).

Analysis of private sector patient prices by World Bank country income level found that PPP-adjusted patient prices of generic phenytoin were comparable in low- and lowermiddle income countries, and were about two times more than in upper-middle income countries (Fig. 1A). No trends could be identified between country income level and price level for originator brands, possibly owing to the small number of countries in each income level. For both originator brand and generic carbamazepine, an inverse relationship was found between MPR and country income level (Fig. 1B). That is, medicine prices decreased with increasing income level, particularly for originator brand products.

Affordability of AEDs

Epilepsy treatment with phenytoin was found to cost the lowest-paid government worker 1–2.5 days' wages depending on the sector and product purchased (Table 4). Lowest-price generic carbamazepine was found to cost the lowest-paid government worker 2.7 and 5.2 days' wages in the public and private sectors, respectively, whereas the originator brand required 10.3 and 16.2 days' wages, respectively. In countries for which data on both carbamazepine and phenytoin were available, carbamazepine was consistently less affordable than phenytoin. In the private sector, treatment with generic carbamazepine was double the cost of the equivalent treatment using generic phenytoin, whereas treatment with originator brand carbamazepine cost 3.8 times more than the equivalent treatment with originator brand phenytoin (data not shown).

Discussion

The results of this study show that the availability of AEDs in low- and middle-income countries is poor. The average availability of generic AEDs in the public sector was <50% for all medicines except diazepam injection, the relatively high availability (79%) of which may be due to its use for treatment of acute seizures. The low availability of AEDs in the public sector, where the poor seek care, suggest that access to AEDs may be inequitable in that the poor may be particularly disadvantaged in terms of their access to AEDs. In the private sector the availability of oral AEDs was higher than in the public sector, but was still inadequate. Because epilepsy management requires sustained treatment with AEDs to avoid seizures and other health and social sequelae, the low availability observed in both the public and private sectors is a public health issue.

In countries where patients pay for medicines in the public sector, even lowest-priced generics cost over four times more than international reference prices, with generic phenytoin costing about 18 times more. Although MSH prices represent supplier prices (usually excluding the additional costs of insurance and freight) and do not include local distribution costs, these factors alone are insufficient to justify such a large price differential. Even when medicines are provided for free or at a low cost in the public sector, poor availability may force many patients to purchase medicines in the private sector, where they are often unaffordable. The poor affordability of AEDs observed in this study is of concern given that epilepsy is a chronic disease requiring lifelong treatment that is not amenable to short-term financial coping strategies such as borrowing or selling assets. In addition, the affordability metric used in this study does not include other treatment costs such as physician consultation fees, which would render treatment even more unaffordable. Furthermore, for the large segments of developing country

populations earning substantially less than the lowest-paid government worker, treatment would be even less affordable than reported here.

Because public sector procurement prices were found to be higher than international supplier prices, it may be possible to improve purchasing efficiency, for example, through price negotiation with manufacturers or national pooled procurement. A previous study has shown that many low- and middle-income countries are able to achieve medicine procurement prices that are equal to or lower than MSH reference prices (13). Shifting a proportion of the originator brand products purchased to lower-priced, quality-assured generics is another strategy for improving availability of AEDs at public facilities. The issue of the interchangeability of brand-name and generic AEDs has risen in prominence recently; concerns about drug quality and patient safety interact with financial considerations and conflicts of interest both for and against generics (21). A meta-analysis of studies comparing brand-name AEDs to generic drugs found no clinical difference in randomized clinical trials, although observational studies indicated differences in health services utilization (22). In addition to availability and affordability, the quality of AEDs is another important consideration, especially given their narrow therapeutic index and the resulting risk of loss of efficacy and/or toxicity. One cross-sectional study from Mauritania found that of 146 samples of phenobarbital collected from 45 pharmaceutical stores, 14% were of substandard quality (23). AEDs require stringent regulatory control including the capacity to ensure quality to allow the most cost-effective medicines to be used while minimizing the risks of adverse events and breakthrough seizures (24). In an effort to ensure that price data are collected for medicines that are of assured quality, the WHO/HAI survey methodology only collects data on registered products circulating in regulated pharmaceutical channels. As such, variation in quality is not likely to be a significant factor in the results presented in this study.

The results of this study are subject to certain limitations, the most significant of which is the small number of countries with data on certain important AEDs such as phenobarbital. Phenobarbital the most widely used AED in the developing world (25), is included on the essential medicine list of nearly all low-income countries (96%) (26) and has been previously reported as the least expensive AED (5). As this analysis was based on existing WHO/HAI survey data, it was not possible to obtain additional information on the availability and price of phenobarbital, but given its importance as a first-line treatment option, this should be a priority for future research. Conversely, the large volume of data on carbamazepine and phenytoin compared to other AEDs can be explained by the fact that until 2008 these agents were recommended for inclusion in all WHO/HAI surveys. This study is also limited in that availability results from WHO/HAI surveys reflect the availability of individual products on the day of data collection and not averages over time. Given that the treatment of epilepsy depends upon the

continuous supply of AEDs, it would have been useful to have data on the consistency in supply over time, particularly in the public sector; however, these data were not collected as part of the WHO/HAI surveys used in this analysis. Availability results are also specific to the individual formulation and strength included in the survey; the availability of othercommon strengths of the same medicine is unknown. However, medicines included in the surveys are selected to reflect medicines commonly used worldwide as well as those selected nationally based on disease and consumption patterns, and should therefore provide a reasonable estimate of availability. An additional limitation was the scarcity of data related to injectable and pediatric formulations. In relation to the affordability metric, it should be noted that results vary as a function of medicine price but also national wage levels. Differences in the interpretation of the "lowest-paid government worker" may have led to some variation in results across countries. In addition, the defined daily doses used to calculate affordability are estimates only, as the doses for individual patients and patient groups (e.g., children) vary.

Despite these limitations, this study raises important concerns about the availability and affordability of AEDs in low- and middle-income countries, including possible overreliance on higher-cost originator brand products. Reducing the cost of effective medications and improving their supply are part of the top five grand challenges for mental, neurologic, and substance use disorders (including epilepsy), that should serve as a starting point for immediate research and prioritization of policies (27). Treatment with AEDs has been shown to be cost-effective, and their scale-up to an 80% coverage rate could reduce the global burden of epilepsy by 36% (28). Efforts to improve the availability and affordability as well as quality of AEDs are therefore warranted. To thisend, greater attention should be given to rational selection, regulatory issues, and measures to ensure adequate and sustainable financing of AEDs. Supply and distribution should be assessed to analyze barriers and facilitators and to identify possible gains in efficiency. Implementation of epilepsy guidelines, together with advocacy and education targeted at health care providers and patients, are needed to ensure that the most cost-effective treatments are used. A step-wise approach to treatment should be adopted, with the use of more costly treatments on an as-needed basis.

Epilepsy is one of the noncommunicable diseases (NCDs), which have historically received little attention on health and development agendas (29,30). For example, a recent study showed that in low- and middle-income countries, medicines used for NCDs were significantly less available than those for acute illness (31). The study also found that the availability of AEDs was lower than medicines used for other NCDs such as hypertension. There is substantial evidence to suggest that epilepsy is associated with high mortality and premature death with significant economic burden. Epilepsy should therefore be recognized as a neglected NCD that requires greater priority in low- and middle-income countries.

Conclusion

Previous studies have quantified the epilepsy treatment gap in low- and middle-income countries and have found this to be substantial. This study shows that the availability and affordability of AEDs is suboptimal and may act as a barrier to accessing treatment for epilepsy.

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Tables and figures

Table 1. Countries included in the analysis

Low income countries (12)
Burkina Faso, Chad, Democratic Republic of Congo, Ethiopia, Ghana, Kenya, Kyrgyzstan, Mali, Tajikistan, Tanzania, Uganda
Lower-middle income countries (22)
Bolivia, Cameroon, China*, Congo, Ecuador, El Salvador, India†, Indonesia, Jordan, Mongolia, Morocco, Nicaragua, Nigeria, Pakistan, Philippines, São Tomé and Principe, Syria, Sudan‡, Thailand, Tunisia, Ukraine, Uzbekistan, Yemen
Upper-middle income countries (9)
Brazil§, Colombia, Fiji, Iran, Kazakhstan, Lebanon, Malaysia, Peru, South Africa¶
High Income countries (3)
Kuwait, Oman, United Arab Emirates

* *Average of 3 provincial surveys conducted in Shaanxi, Shandong and Shanghai.*
† *Average of 7 state surveys conducted in Chennai, Haryana, Karnataka, Maharashtra (12 districts), Maharashtra (4 regions), Rajasthan and West Bengal.*
‡ *Average of 4 state surveys conducted in Ghadarif, Khartoum, Kordofan and North Kordofan.*
§ *Rio Grande do Sul State*
¶ *Gauteng province*

Table 2. Average of country-level percent availability (%)* of individual AEDs

		Mean availability (%) (n = number of countries)					
Sector	**Product type**	**Carbamazepine 100/200mg† cap/tab (n)**	**Phenytoin 50/100mg cap/tab (n)**	**Phenobarbital 15/30/100mg cap/tab (n)**	**Valproic acid 200mg cap/tab (n)**	**Diazepam 5mg/ml inj (n)**	**Phenobarbital 200mg/ml inj (n)**
Public	**Originator brand**	29.8 (20)	27.5 (12)	NA (0)	15.0 (1)	5.5 (2)	NA (0)
	(min, max)	0.0, 100	0.0, 80.0	NA	15.0, 15.0	3.3, 7.7	NA
	Generic	45.3 (28)	37.7 (22)	44.0 (3)	NA (0)	78.6 (5)	29.0 (1)
	(min, max)	4.5, 100	2.8, 100	14.3, 96.7	NA	57.7, 100	29.0, 29.0
Private	**Originator brand**	57.7 (39)	48.7 (21)	55.0 (1)	100 (1)	38.7 (5)	NA (0)
	(min, max)	3.3, 100	2.1, 85.0	55.0, 55.0	100, 100	1.9, 61.8	NA
	Generic	60.3 (36)	42.2 (28)	69.6 (2)	NA (0)	43.1 (5)	11.8 (1)
	(min, max)	3.1, 100	0.0, 98.2	62.5, 76.7	NA	20.8, 50.0	11.8, 11.8

cap/tab - capsule/tablet; inj - injection; n - number of countries; min,max - minimum, maximum.

**Country-level availability is expressed as the percentage of facilities where a product was found on the day of data collection.*

†Strengths of individual medicines have been aggregated across countries and not within individual countries.

Table 3. Average of country-level median price ratios*, patient prices (CPI and PPP adjusted), public and private sector

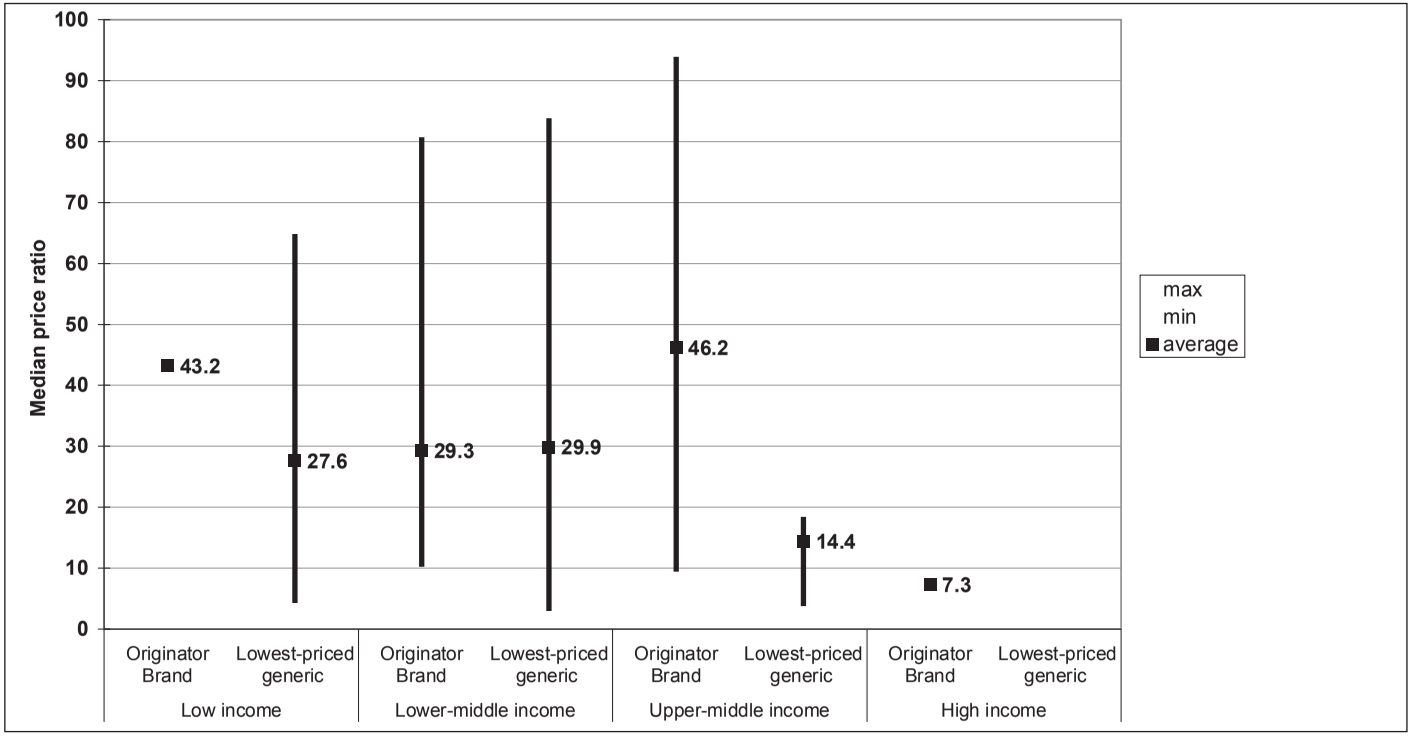
Sector	Product type	Carbamazepine 200mg cap/tab (n)	Phenytoin 100mg cap/ tab (n)	Phenobarbital 30mg cap/tab (n)	Phenobarbital 100mg cap/ tab (n)	Valproic acid 200mg cap/ tab (n)	Diazepam 5mg/ml inj (n)	Phenobarbital 200mg/ml inj (n)
Public	**Originator brand**	31.44 (4)	20.94 (2)	ND (0)	ND (0)	ND (0)	ND(0)	ND (0)
	(min, max)	16.42, 55.80	13.76, 28.11	NA	NA	NA	NA	NA
	LPG	4.95 (14)	17.50 (10)	ND (0)	ND (0)	ND (0)	5.28 (4)	4.17 (1)
	(min, max)	1.15, 11.64	2.89, 68.72	NA	NA	NA	3.44, 7.01	4.17, 4.17
Private	**Originator brand**	35.17 (35)	32.31 (18)	ND (0)	60.27 (1)	5.63 (1)	16.48 (3)	ND (0)
	(min, max)	4.07, 119.09	7.20, 93.87	NA	60.27, 60.27	5.63, 5.63	6.99, 27.30	NA
	LPG	11.27 (32)	24.77 (24)	34.54 (1)	ND (0)	ND (0)	6.59 (4)	4.85 (1)
	(min, max)	1.81, 40.80	2.95, 83.79	34.54, 34.54	NA	NA	5.16, 8.33	4.85, 4.85

CPI - Consumer Price Index; PPP - Purchasing Power Parity, cap/tab - capsule/tablet; inj - injection; n - number of countries; LPG - lowest-priced generic; ND - no; data; min,max - minimum, maximum

**Ratio of median local price to Management Sciences for Health international reference price*

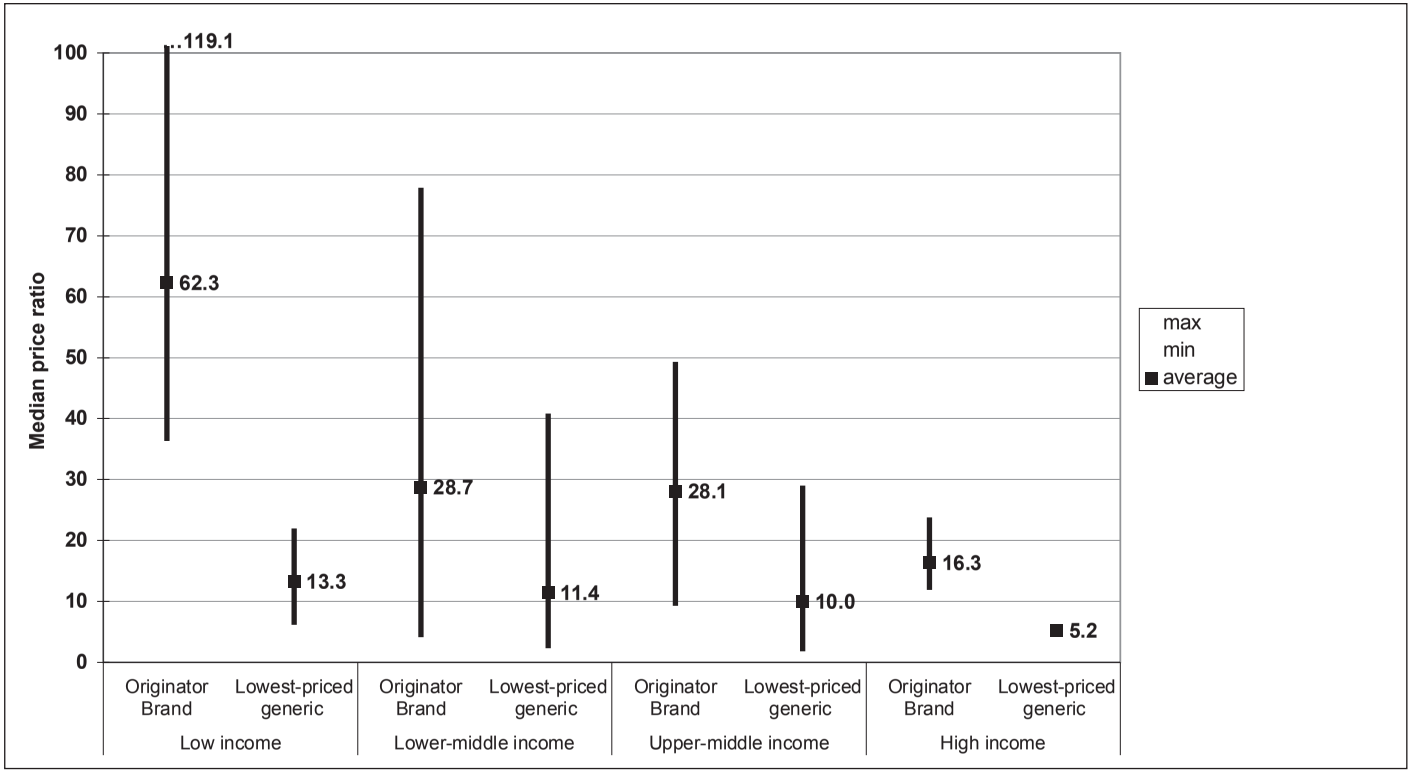
Figure 1. Average of country-level median price ratios*, patient prices (CPI and PPP adjusted), private sector, by World Bank Income Group†

a. Phenytoin 100mg cap/tab



CPI - Consumer Price Index; PPP - Purchasing Power Parity, cap/tab - capsule/tablet; OB - originator brand; LPG - lowest-price generic.
**Ratio of median local price to Management Sciences for Health international reference price*
†Number of countries in each income group: Low income: OB n= 1, LPG n=6; Lower middle income: OB n= 10, LPG n=11; Upper middle income: OB n= 5, LPG n=7; high income: OB n= 2, LPG n=0.

b. Carbamazepine 200mg cap/tab



**Ratio of median local price to Management Sciences for Health international reference price*

†Number of countries in each income group: Low income: OB n= 8, LPG n=7; Lower middle income: OB n= 17, LPG n=16; Upper middle income: OB n= 7, LPG n=8; high income: OB n= 3, LPG n=1.

Abbreviations: CPI - Consumer Price Index; PPP - Purchasing Power Parity, cap/tab - capsule/tablet; OB - originator brand; LPG - lowest-price generic.

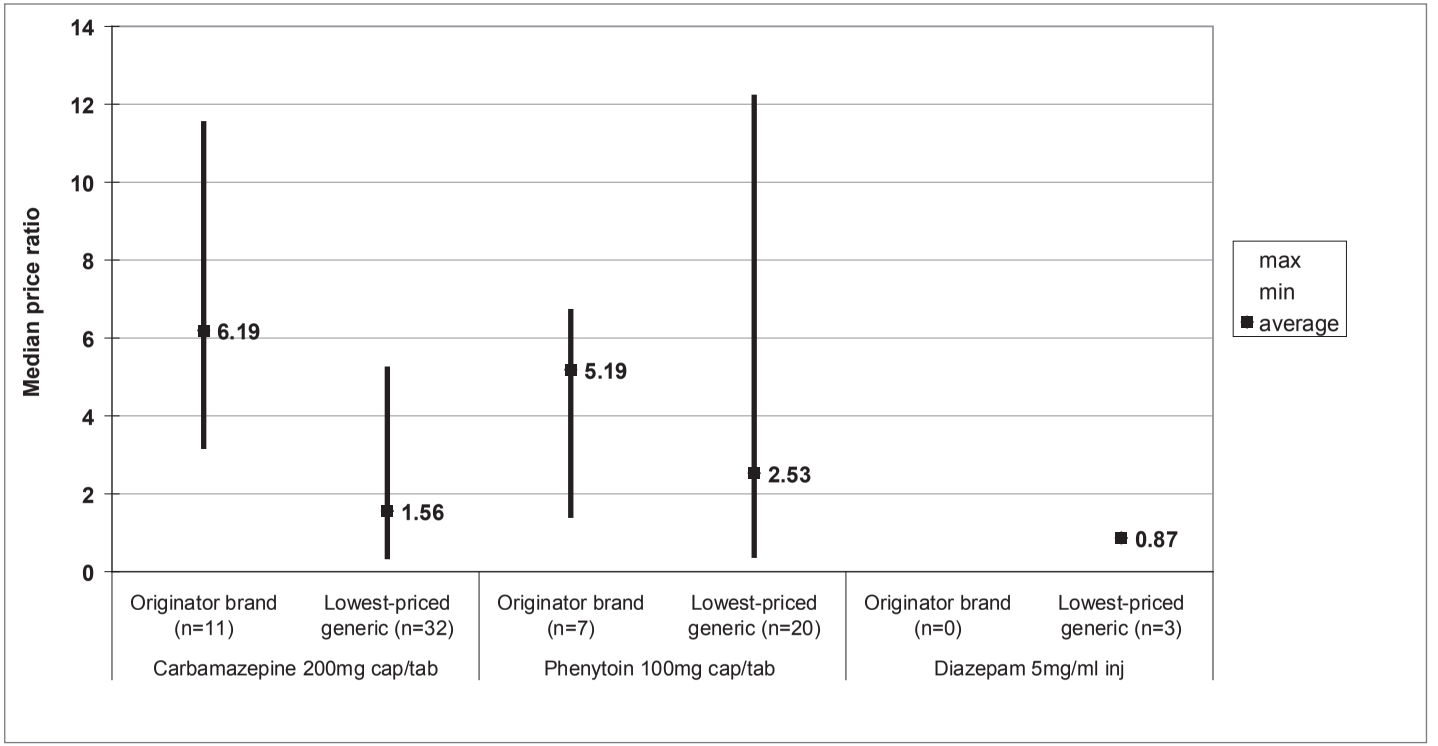
Table 4. Mean number of day's wages of the lowest-paid unskilled government worker needed to purchase a month of treatment (n = number of countries)

Sector	Product type	Carbamazepine 200mg cap/tab (n) DDD - 1000mg	Phenytoin 100mg cap/tab (n) DDD - 300mg	Phenobarbital 30mg cap/tab (n) DDD – 1000mg	Phenobarbital 100mg cap/tab (n) DDD – 1000mg	Valproic acid 200mg cap/tab (n) DDD – 1500mg
Public	**Originator brand**	10.34 (4)	1.05 (2)	ND (0)	ND (0)	ND (0)
	LPG	2.70 (14)	1.58 (10)	ND (0)	ND (0)	ND(0)
Private	**Originator brand**	16.17 (35)	2.59 (18)	ND (0)	3.00 (1)	7.76 (1)
	LPG	5.23 (32)	2.43 (24)	0.88 (1)	ND (0)	ND (0)

cap/tab - capsule/tablet; n - number of countries; LPG - lowest-price generic; ND - no data; DDD – defined daily dosage.

Appendix

A.1 Average of country-level median price ratios*, public sector procurement (CPI adjusted)



**Ratio of median local price to Management Sciences for Health international reference price*
Abbreviations: CPI - Consumer Price Index; cap/tab - capsule/tablet; inj - injection; n - number of countries.

A.2 Country-level results: availability, median price ratio and affordability of antiepileptic medicines

Notes regarding the data:

- Results for China represent the average of 3 provincial surveys conducted in Shaanxi, Shandong and Shanghai. Results for Sudan represent the average of 4 state surveys conducted in Ghadarif, Khartoum, Kordofan and North Kordofan. Results for India represent the average of 7 state surveys conducted in Chennai, Haryana, Karnataka, Maharashtra (12 districts), Maharashtra (4 regions), Rajasthan and West Bengal. Results for South Africa are for Gauteng province only, and results for Brazil are for Rio Grande do Sul state only.

- Availability refers to the percentage of outlets where a medicine was found on the day of data collection. Availability data was not collected for public sector procurement, as indicated by n/a - not applicable. Blank cells indicated that availability data was not collected in a given survey.

- Prices are expressed as median price ratios (MPRs), or the ratio of the median local price to the Management Sciences for Health international reference price, usually for the year preceding the survey. MSH prices are median prices of multisource medicines offered to developing and middle-income countries by different suppliers. The median price ratio is an expression of how much greater or less the median local medicine price is than the international reference price, e.g. an MPR of 2 would mean that the local medicine price is twice the international reference price. Blank cells indicate that price data was either not collected in a given survey, that insufficient price points were found to enable calculation of the MPR (minimum 4 required), or that medicines were provided free-of-charge.

- Procurement prices have been adjusted for inflation/deflation using the Consumer Price Index (CPI). Patient prices (i.e. retail prices) were adjusted inflation/deflation as well as for Purchasing Power Parity (PPP), to account for differences in purchasing power of individual currencies.

- Affordability refers to the number of day's wages required for the lowest-paid government worker to purchase a course of treatment, based on the median local medicine price. Affordability was only estimated for carbamazepine 200mg cap/tab, phenobarbital 200mg/ml injection, phenobarbital 30mg and 100mg cap/tab, phenytoin100mg cap/tab, and valproic acid 200mg cap/tab. Affordability data was not calculated for public sector procurement, as indicated by n/a - not applicable.

Bolivia, October 2008

a. public sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Phenytoin	100mg	cap/tab	Lowest price generic	21.7%	16.38	2.0
Carbamazepine	200mg	cap/tab	Lowest price generic	33.3%	5.66	3.3
Diazepam	5mg	cap/tab	Lowest price generic	29.0%	24.45	

b. private sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	3.3%		
Diazepam	5mg	cap/tab	Originator brand	6.7%		
Carbamazepine	200mg	cap/tab	Lowest price generic	93.3%	7.09	4.1
Diazepam	5mg	cap/tab	Lowest price generic	36.7%	81.49	
Phenytoin	100mg	cap/tab	Lowest price generic	60.0%	20.48	2.5

Brazil, Rio Grande do Sul State, November 2008

a. public sector procurement

Medicine	Strength	Form	Type	Availability	Adjusted MPR	Affordability
Phenytoin	100mg	cap/tab	Lowest price generic	n/a	3.25	n/a

b. public sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Lowest price generic	4.5%		
Phenytoin	100mg	cap/tab	Lowest price generic	18.2%		

c. private sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Phenytoin	100mg	cap/tab	Lowest price generic	60.0%	13.77	1.1
Carbamazepine	200mg	cap/tab	Originator brand	66.7%	20.04	7.5
Carbamazepine	200mg	cap/tab	Lowest price generic	86.7%	8.96	3.4
Diazepam	5mg	cap/tab	Lowest price generic	70.0%	37.10	
Diazepam	5mg	cap/tab	Originator brand	70.0%	60.13	

Burkina Faso, July 2009

a. public sector procurement

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Lowest price generic	n/a	1.20	n/a
Diazepam	5mg	cap/tab	Lowest price generic	n/a	0.92	n/a
Diazepam	5mg/ml	inj	Lowest price generic	n/a	0.91	n/a
Phenobarbitone	200mg/ml	inj	Lowest price generic	n/a	0.29	n/a

b. public sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Diazepam	5mg	cap/tab	Lowest price generic	93.5%	5.92	
Diazepam	5mg/ml	inj	Lowest price generic	93.5%	5.83	
Phenobarbitone	200mg/ml	inj	Lowest price generic	29.0%	4.17	2.2

c. private sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	47.1%	36.28	16.3
Diazepam	5mg	cap/tab	Originator brand	11.8%	106.02	
Diazepam	5mg/ml	inj	Originator brand	61.8%	27.30	
Diazepam	5mg	cap/tab	Lowest price generic	67.6%	9.85	
Diazepam	5mg/ml	inj	Lowest price generic	50.0%	7.25	
Phenobarbitone	200mg/ml	inj	Lowest price generic	11.8%	4.85	2.6

Cameroon, July 2005

a. public sector procurement

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Lowest price generic	n/a	0.55	n/a
Phenytoin	100mg	cap/tab	Lowest price generic	n/a	0.53	n/a
Diazepam	5mg	cap/tab	Lowest price generic	n/a	0.61	n/a

b. public sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Diazepam	5mg	cap/tab	Lowest price generic	80.0%	3.56	
Phenytoin	100mg	cap/tab	Lowest price generic	5.0%		

c. private sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	90.0%	21.74	18.5
Diazepam	5mg	cap/tab	Originator brand	50.0%	32.85	
Phenytoin	100mg	cap/tab	Originator brand	65.0%	24.37	4.4
Diazepam	5mg	cap/tab	Lowest price generic	5.0%		

Chad, May 2004

a. public sector procurement

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Diazepam	5mg	cap/tab	Lowest price generic	n/a	0.70	n/a

b. public sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Diazepam	5mg	cap/tab	Lowest price generic	58.3%	13.84	

c. private sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	63.6%	37.48	22.2
Diazepam	5mg	cap/tab	Originator brand	9.1%		

China, Shanghai (September 2006), Shandong Province (October 2004) and Shaanxi Province (September 2010)

a. public sector procurement

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	n/a	6.20	n/a

b. public sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Phenytoin	100mg	cap/tab	Lowest price generic	67.5%	2.89	0.2

c. private sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	42.5%	30.93	10.1
Phenytoin	100mg	cap/tab	Lowest price generic	42.5%	2.95	0.2

Colombia, October 2008

a. public sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	13.3%		
Diazepam	5mg/ml	inj	Originator brand	3.3%		
Phenytoin	100mg	cap/tab	Originator brand	13.3%		
Carbamazepine	200mg	cap/tab	Lowest price generic	100.0%		
Diazepam	5mg/ml	inj	Lowest price generic	66.6%		
Phenytoin	100mg	cap/tab	Lowest price generic	70.0%		

b. private sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	6.9%		
Diazepam	5mg/ml	inj	Originator brand	20.7%		
Phenytoin	100mg	cap/tab	Originator brand	17.2%		
Carbamazepine	200mg	cap/tab	Lowest price generic	96.6%		
Diazepam	5mg/ml	inj	Lowest price generic	48.3%		
Phenytoin	100mg	cap/tab	Lowest price generic	82.8%		

Congo, June 2007

a. public sector procurement

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Lowest price generic	n/a	0.60	n/a
Diazepam	5mg/ml	inj	Lowest price generic	n/a	0.82	n/a

b. public sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Diazepam	5mg/ml	inj	Originator brand	7.7%		
Diazepam	5mg/ml	inj	Lowest price generic	57.7%	3.44	

c. private sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	41.7%	9.49	11.1
Diazepam	5mg/ml	inj	Originator brand	54.2%	6.99	
Diazepam	5mg/ml	inj	Lowest price generic	20.8%	5.16	

Democratic Republic of Congo, July 2007

a. public sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	5.6%		
Carbamazepine	200mg	cap/tab	Lowest price generic	5.6%		
Diazepam	5mg/ml	inj	Lowest price generic	75.0%	7.01	
Phenytoin	100mg	cap/tab	Lowest price generic	2.8%		

b. private sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	53.8%	38.24	39.5
Diazepam	5mg/ml	inj	Originator brand	1.9%		
Carbamazepine	200mg	cap/tab	Lowest price generic	15.4%	12.76	13.2
Diazepam	5mg/ml	inj	Lowest price generic	46.2%	5.61	
Phenytoin	100mg	cap/tab	Lowest price generic	7.7%	64.78	14.3

Ecuador, June 2008

a. public sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	0.0%		
Diazepam	5mg	cap/tab	Originator brand	0.0%		
Phenytoin	100mg	cap/tab	Originator brand	13.3%		
Carbamazepine	200mg	cap/tab	Lowest price generic	30.0%		
Diazepam	5mg	cap/tab	Lowest price generic	10.0%		
Phenytoin	100mg	cap/tab	Lowest price generic	6.7%		

b. private sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	96.7%	13.99	4.1
Diazepam	5mg	cap/tab	Originator brand	6.7%		
Phenytoin	100mg	cap/tab	Originator brand	23.3%	20.12	1.3
Carbamazepine	200mg	cap/tab	Lowest price generic	86.7%	8.14	2.4
Diazepam	5mg	cap/tab	Lowest price generic	33.3%	27.61	
Phenytoin	100mg	cap/tab	Lowest price generic	0.0%		

El Salvador, November 2006

a. public sector procurement

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/ tab	Lowest price generic	n/a	3.80	n/a
Phenytoin	100mg	cap/ tab	Lowest price generic	n/a	11.77	n/a

b. public sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	40.4%		
Phenytoin	100mg	cap/tab	Originator brand	1.9%		
Carbamazepine	200mg	cap/tab	Lowest price generic	53.8%		
Phenytoin	100mg	cap/tab	Lowest price generic	78.8%		

c. private sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	55.8%	57.33	14.8
Phenytoin	100mg	cap/tab	Originator brand	26.9%	80.66	4.5
Carbamazepine	200mg	cap/tab	Lowest price generic	69.2%	40.80	10.5
Diazepam	5mg	cap/tab	Lowest price generic	9.6%	162.62	
Phenytoin	100mg	cap/tab	Lowest price generic	36.5%	83.79	4.6

Ethiopia, September 2004

a. public sector procurement

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Lowest price generic	n/a	0.59	n/a
Diazepam	5mg	cap/tab	Lowest price generic	n/a	0.37	n/a
Phenytoin	100mg	cap/tab	Lowest price generic	n/a	0.43	n/a

b. public sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Lowest price generic	20.6%	4.45	2.5
Diazepam	5mg	cap/tab	Lowest price generic	88.2%	11.59	
Phenytoin	100mg	cap/tab	Lowest price generic	20.6%	7.36	0.9

c. private sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	20.0%	109.85	61.7
Diazepam	5mg	cap/tab	Originator brand	4.0%		
Carbamazepine	200mg	cap/tab	Lowest price generic	72.0%	19.18	10.8
Diazepam	5mg	cap/tab	Lowest price generic	56.0%	41.64	
Phenytoin	100mg	cap/tab	Lowest price generic	64.0%	11.33	1.4

Fiji, September 2004

a. public sector procurement

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Lowest price generic	n/a	0.77	n/a
Diazepam	5mg	cap/tab	Lowest price generic	n/a	0.78	n/a
Phenytoin	100mg	cap/tab	Lowest price generic	n/a	0.56	n/a

b. private sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	91.7%	14.98	2.1
Diazepam	5mg	cap/tab	Originator brand	55.6%	34.31	
Phenytoin	100mg	cap/tab	Originator brand	63.9%	18.00	0.5
Carbamazepine	200mg	cap/tab	Lowest price generic	80.6%	5.35	0.8
Diazepam	5mg	cap/tab	Lowest price generic	88.9%	7.35	
Phenytoin	100mg	cap/tab	Lowest price generic	27.8%	16.73	0.5

Ghana, October 2004

a. public sector procurement

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Lowest price generic	n/a	1.12	n/a
Diazepam	5mg	cap/tab	Lowest price generic	n/a	0.64	n/a
Phenytoin	100mg	cap/tab	Lowest price generic	n/a	2.03	n/a

b. public sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	3.6%		
Carbamazepine	200mg	cap/tab	Lowest price generic	14.3%	5.62	2.9
Diazepam	5mg	cap/tab	Lowest price generic	85.7%	4.02	
Phenytoin	100mg	cap/tab	Lowest price generic	14.3%	29.10	3.2

c. private sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	8.9%	70.34	35.8
Carbamazepine	200mg	cap/tab	Lowest price generic	28.6%	22.01	11.2
Diazepam	5mg	cap/tab	Lowest price generic	80.4%	7.31	
Phenytoin	100mg	cap/tab	Lowest price generic	39.3%	53.78	5.9

India, Maharashtra 4 regions (January 2005), West Bengal (December 2004), Karnataka (November 2004), Haryana (October 2004), Maharashtra 12 districts (October 2004), Chennai (October 2004), Rajasthan (April 2003)

a. public sector procurement

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Phenytoin	100mg	cap/tab	Lowest price generic	n/a	0.84	n/a

b. public sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Lowest price generic	45.5%		
Phenytoin	100mg	cap/tab	Lowest price generic	35.4%		

c. private sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	87.5%	9.32	1.8
Diazepam	5mg	cap/tab	Originator brand	72.1%	48.66	
Carbamazepine	200mg	cap/tab	Lowest price generic	59.5%	9.21	1.8
Phenytoin	100mg	cap/tab	Lowest price generic	84.9%	19.90	0.8

Indonesia, August 2004

a. public sector procurement

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Lowest price generic	n/a	2.18	n/a
Diazepam	5mg	cap/tab	Lowest price generic	n/a	0.89	n/a
Phenytoin	100mg	cap/tab	Lowest price generic	n/a	2.17	n/a

b. public sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	6.7%		
Diazepam	5mg	cap/tab	Originator brand	6.7%		
Carbamazepine	200mg	cap/tab	Lowest price generic	60.0%	9.09	3.7
Diazepam	5mg	cap/tab	Lowest price generic	80.0%	13.72	
Phenytoin	100mg	cap/tab	Lowest price generic	33.3%	68.72	6.0

c. private sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	65.5%	60.59	24.5
Diazepam	5mg	cap/tab	Originator brand	48.3%	263.13	
Carbamazepine	200mg	cap/tab	Lowest price generic	70.7%	9.00	3.6
Diazepam	5mg	cap/tab	Lowest price generic	81.0%	17.46	
Phenytoin	100mg	cap/tab	Lowest price generic	60.3%	77.24	6.7

Iran, December 2007

a. public sector procurement

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	n/a	7.56	n/a
Carbamazepine	200mg	cap/tab	Lowest price generic	n/a	0.84	n/a
Diazepam	5mg	cap/tab	Lowest price generic	n/a	1.29	n/a
Phenytoin	100mg	cap/tab	Lowest price generic	n/a	1.76	n/a

b. public sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	10.0%		
Carbamazepine	200mg	cap/tab	Lowest price generic	93.3%	1.81	0.3
Diazepam	5mg	cap/tab	Lowest price generic	100.0%	2.82	
Phenobarbitone	15mg	cap/tab	Lowest price generic	96.7%		
Phenytoin	100mg	cap/tab	Lowest price generic	100.0%	3.81	0.1

c. private sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	10.0%		
Carbamazepine	200mg	cap/tab	Lowest price generic	100.0%	1.81	0.3
Diazepam	5mg	cap/tab	Lowest price generic	100.0%	2.82	
Phenobarbitone	15mg	cap/tab	Lowest price generic	76.7%		
Phenytoin	100mg	cap/tab	Lowest price generic	90.0%	3.81	0.1

Jordan, May 2004

a. public sector procurement

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Diazepam	5mg	cap/tab	Originator brand	n/a	1.98	n/a
Phenytoin	100mg	cap/tab	Originator brand	n/a	6.54	n/a
Carbamazepine	200mg	cap/tab	Lowest price generic	n/a	0.74	n/a

b. public sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	5.6%		
Phenytoin	100mg	cap/tab	Originator brand	27.8%	13.76	0.9
Carbamazepine	200mg	cap/tab	Lowest price generic	66.7%	1.97	0.6
Diazepam	5mg	cap/tab	Lowest price generic	55.6%	4.49	

c. private sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	75.0%	27.01	8.4
Diazepam	5mg	cap/tab	Originator brand	80.0%	94.45	
Phenytoin	100mg	cap/tab	Originator brand	65.0%	21.51	1.4
Carbamazepine	200mg	cap/tab	Lowest price generic	60.0%	13.37	4.1
Diazepam	5mg	cap/tab	Lowest price generic	60.0%	15.00	

Kazakhstan, November 2004

a. public sector procurement

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	n/a	8.68	n/a
Carbamazepine	200mg	cap/tab	Lowest price generic	n/a	3.95	n/a

b. private sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	70.0%	19.48	10.1
Carbamazepine	200mg	cap/tab	Lowest price generic	70.0%	11.30	5.9
Phenytoin	100mg	cap/tab	Lowest price generic	20.0%	12.29	1.4

Kenya, November 2004

a. public sector procurement

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Lowest price generic	n/a	0.39	n/a
Diazepam	5mg	cap/tab	Lowest price generic	n/a	0.23	n/a
Phenytoin	100mg	cap/tab	Lowest price generic	n/a	0.45	n/a

b. public sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Lowest price generic	88.7%	2.07	1.2
Diazepam	5mg	cap/tab	Lowest price generic	83.0%	10.58	
Phenytoin	100mg	cap/tab	Lowest price generic	34.0%	4.31	0.5

c. private sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	58.6%	44.69	26.5
Diazepam	5mg	cap/tab	Originator brand	31.0%	112.95	
Phenytoin	100mg	cap/tab	Originator brand	39.7%	43.20	5.5
Carbamazepine	200mg	cap/tab	Lowest price generic	81.0%	6.16	3.7
Diazepam	5mg	cap/tab	Lowest price generic	82.8%	7.07	
Phenytoin	100mg	cap/tab	Lowest price generic	67.2%	4.31	0.5

Kuwait, June 2004

a. public sector procurement

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	n/a	4.09	n/a
Phenytoin	100mg	cap/tab	Originator brand	n/a	5.26	n/a
Diazepam	5mg	cap/tab	Lowest price generic	n/a	17.90	n/a

b. public sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	80.0%		
Diazepam	5mg	cap/tab	Originator brand	20.0%		
Phenytoin	100mg	cap/tab	Originator brand	36.0%		

c. private sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	84.0%	13.09	10.1
Phenytoin	100mg	cap/tab	Originator brand	84.0%	7.45	1.2

Kyrgyzstan, February 2005

a. public sector procurement

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Lowest price generic	n/a	1.99	n/a
Diazepam	10mg	cap/tab	Lowest price generic	n/a	1.08	n/a

b. private sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Lowest price generic	70.0%	6.81	9.9
Diazepam	10mg	cap/tab	Lowest price generic	53.3%	7.63	
Phenytoin	100mg	cap/tab	Lowest price generic	10.0%		

Lebanon, February 2004

a. public sector procurement

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Phenytoin	100mg	cap/tab	Originator brand	n/a	5.81	n/a
Carbamazepine	200mg	cap/tab	Lowest price generic	n/a	2.55	n/a

b. public sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Lowest price generic	10.0%		

c. private sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	97.5%	9.26	4.5
Diazepam	5mg	cap/tab	Originator brand	72.5%	47.34	
Phenytoin	100mg	cap/tab	Originator brand	85.0%	9.35	1.0
Carbamazepine	200mg	cap/tab	Lowest price generic	27.5%	4.51	2.2
Phenytoin	100mg	cap/tab	Lowest price generic	5.0%		

Malaysia, October 2004

a. public sector procurement

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	n/a	3.22	n/a
Phenytoin	100mg	cap/tab	Originator brand	n/a	1.45	n/a
Diazepam	5mg	cap/tab	Lowest price generic	n/a	2.35	n/a

b. public sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	95.0%		
Diazepam	5mg	cap/tab	Originator brand	15.0%		
Phenytoin	100mg	cap/tab	Originator brand	80.0%		
Carbamazepine	200mg	cap/tab	Lowest price generic	5.0%		
Diazepam	5mg	cap/tab	Lowest price generic	55.0%		

c. private sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	40.6%	40.82	12.8
Phenytoin	100mg	cap/tab	Originator brand	43.8%	54.66	3.7
Carbamazepine	200mg	cap/tab	Lowest price generic	28.1%	12.09	3.8
Phenytoin	100mg	cap/tab	Lowest price generic	12.5%	18.00	1.2

Mali, March 2004

a. public sector procurement

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Diazepam	5mg/ml	inj	Lowest price generic	n/a	0.89	n/a
Phenobarbitone	100mg	cap/tab	Lowest price generic	n/a	0.89	n/a

b. public sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Diazepam	5mg/ml	inj	Lowest price generic	100.0%	4.86	
Phenobarbitone	100mg	cap/tab	Lowest price generic	14.3%		

c. private sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Diazepam	5mg/ml	inj	Originator brand	55.0%	15.14	
Phenobarbitone	100mg	cap/tab	Originator brand	55.0%	60.27	3.0
Diazepam	5mg/ml	inj	Lowest price generic	50.0%	8.33	

Mongolia, November 2004

a. public sector procurement

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Lowest price generic	n/a	1.98	n/a
Diazepam	5mg	cap/tab	Lowest price generic	n/a	7.04	n/a

b. public sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Lowest price generic	100.0%	6.36	3.1
Diazepam	5mg	cap/tab	Lowest price generic	75.0%		

c. private sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Lowest price generic	80.0%	11.03	5.3
Diazepam	5mg	cap/tab	Lowest price generic	20.0%	31.59	

Morocco, April 2004

a. public sector procurement

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	n/a	6.31	n/a
Diazepam	5mg	cap/tab	Originator brand	n/a	8.76	n/a
Valproric acid	200mg	cap/tab	Originator brand	n/a	1.33	n/a
Carbamazepine	200mg	cap/tab	Lowest price generic	n/a	5.20	n/a

b. public sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	50.0%		
Diazepam	5mg	cap/tab	Originator brand	60.0%		
Valproric acid	200mg	cap/tab	Originator brand	15.0%		
Carbamazepine	200mg	cap/tab	Lowest price generic	25.0%		

c. private sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	100.0%	24.39	3.9
Diazepam	5mg	cap/tab	Originator brand	65.0%	36.91	
Phenytoin	100mg	cap/tab	Originator brand	45.0%	27.11	0.9
Valproric acid	200mg	cap/tab	Originator brand	100.0%	5.63	7.8

Nicaragua, July 2008

a. public sector procurement

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Lowest price generic	n/a	0.62	n/a
Diazepam	5mg	cap/tab	Lowest price generic	n/a	1.74	n/a
Phenytoin	100mg	cap/tab	Lowest price generic	n/a	1.96	n/a

b. public sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	0.0%		
Diazepam	5mg	cap/tab	Originator brand	0.0%		
Phenytoin	100mg	cap/tab	Originator brand	0.0%		
Carbamazepine	200mg	cap/tab	Lowest price generic	83.3%		
Diazepam	5mg	cap/tab	Lowest price generic	80.0%		
Phenytoin	100mg	cap/tab	Lowest price generic	83.3%		

c. private sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	41.9%	77.91	21.1
Diazepam	5mg	cap/tab	Originator brand	6.5%		
Phenytoin	100mg	cap/tab	Originator brand	3.2%		
Carbamazepine	200mg	cap/tab	Lowest price generic	71.0%	19.39	5.2
Diazepam	5mg	cap/tab	Lowest price generic	25.8%	55.81	
Phenytoin	100mg	cap/tab	Lowest price generic	51.6%	68.01	3.9

Nigeria, September 2004

a. public sector procurement

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Lowest price generic	n/a	1.74	n/a
Diazepam	5mg	cap/tab	Lowest price generic	n/a	1.56	n/a

b. public sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	9.5%	20.70	21.1
Diazepam	5mg	cap/tab	Originator brand	31.0%	37.20	
Phenytoin	100mg	cap/tab	Originator brand	2.4%		
Carbamazepine	200mg	cap/tab	Lowest price generic	11.9%	8.13	8.3
Diazepam	5mg	cap/tab	Lowest price generic	54.8%	5.58	
Phenytoin	100mg	cap/tab	Lowest price generic	4.8%		

c. private sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	36.4%	24.36	24.9
Diazepam	5mg	cap/tab	Originator brand	40.9%	49.60	
Phenytoin	100mg	cap/tab	Originator brand	9.1%	45.53	10.0
Carbamazepine	200mg	cap/tab	Lowest price generic	15.9%	4.06	4.1
Diazepam	5mg	cap/tab	Lowest price generic	29.5%	9.30	
Phenytoin	100mg	cap/tab	Lowest price generic	25.0%	22.76	5.0

Oman, October 2007

a. public sector procurement

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	n/a	4.64	n/a
Diazepam	5mg	cap/tab	Lowest price generic	n/a	15.86	n/a

b. public sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	100.0%		
Diazepam	5mg	cap/tab	Lowest price generic	86.7%		

c. private sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	90.6%	23.81	5.2
Diazepam	5mg	cap/tab	Originator brand	12.5%	89.47	
Carbamazepine	200mg	cap/tab	Lowest price generic	3.1%		

Pakistan, July 2004

a. public sector procurement

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Lowest price generic	n/a	0.65	n/a
Diazepam	5mg	cap/tab	Lowest price generic	n/a	0.21	n/a

b. public sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Diazepam	5mg	cap/tab	Lowest price generic	60.0%		

c. private sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	85.4%	8.97	6.9
Diazepam	5mg	cap/tab	Originator brand	64.6%	10.13	
Carbamazepine	200mg	cap/tab	Lowest price generic	33.3%	5.96	4.6
Diazepam	5mg	cap/tab	Lowest price generic	31.3%	8.66	
Phenytoin	100mg	cap/tab	Lowest price generic	10.4%	5.05	0.8

Peru, September 2005

a. public sector procurement

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Lowest price generic	n/a	0.69	n/a
Diazepam	5mg	cap/tab	Lowest price generic	n/a	2.24	n/a
Phenytoin	100mg	cap/tab	Lowest price generic	n/a	4.96	n/a

b. public sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Lowest price generic	80.8%	1.98	0.7
Diazepam	5mg	cap/tab	Lowest price generic	84.6%	5.44	
Phenytoin	100mg	cap/tab	Lowest price generic	42.3%	13.80	1.0

c. private sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	45.8%	42.70	14.5
Diazepam	5mg	cap/tab	Originator brand	6.3%	272.44	
Phenytoin	100mg	cap/tab	Originator brand	50.0%	55.23	4.0
Carbamazepine	200mg	cap/tab	Lowest price generic	86.5%	6.58	2.2
Diazepam	5mg	cap/tab	Lowest price generic	78.1%	36.32	
Phenytoin	100mg	cap/tab	Lowest price generic	33.3%	18.42	1.3

Philippines, February 2005

a. public sector procurement

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	n/a	11.50	n/a
Diazepam	5mg	cap/tab	Originator brand	n/a	36.43	n/a
Diazepam	5mg	cap/tab	Lowest price generic	n/a	39.22	n/a

b. public sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	34.6%	55.80	8.7

c. private sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	64.7%	62.55	9.7
Carbamazepine	200mg	cap/tab	Lowest price generic	3.9%		

São Tomé and Príncipe, June 2008

a. public sector procurement

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Lowest price generic	n/a	0.67	n/a
Diazepam	5mg	cap/tab	Lowest price generic	n/a	1.67	n/a

b. public sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	3.1%		
Carbamazepine	200mg	cap/tab	Lowest price generic	28.1%	1.15	3.6
Diazepam	5mg	cap/tab	Lowest price generic	56.2%	6.14	
Phenytoin	100mg	cap/tab	Lowest price generic	6.2%		

c. private sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Diazepam	5mg	cap/tab	Lowest price generic	11.1%	31.42	

South Africa, Gauteng Province, November 2004

a. public sector procurement

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Lowest price generic	n/a	1.38	n/a
Diazepam	5mg	cap/tab	Lowest price generic	n/a	2.17	n/a
Phenytoin	100mg	cap/tab	Lowest price generic	n/a	12.18	n/a

b. private sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	66.7%	49.30	4.3
Diazepam	5mg	cap/tab	Originator brand	50.0%	226.43	
Phenytoin	100mg	cap/tab	Originator brand	80.0%	93.87	1.8
Carbamazepine	200mg	cap/tab	Lowest price generic	80.0%	28.98	2.5
Diazepam	5mg	cap/tab	Lowest price generic	80.0%	12.17	
Phenytoin	100mg	cap/tab	Lowest price generic	20.0%	17.67	0.3

Sudan, North Kordofan State (February 2006), Gadarif State (February 2006), Northern State (February 2006), Khartoum State (June 2005)

a. public sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Lowest price generic	44.3%	11.64	4.4
Diazepam	5mg	cap/tab	Lowest price generic	73.5%	26.87	
Phenytoin	100mg	cap/tab	Lowest price generic	19.7%	18.40	1.5

Syria, December 2003

a. public sector procurement

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	n/a	6.96	n/a
Diazepam	5mg	cap/tab	Originator brand	n/a	11.07	n/a
Carbamazepine	200mg	cap/tab	Lowest price generic	n/a	1.90	n/a
Diazepam	5mg	cap/tab	Lowest price generic	n/a	3.32	n/a
Phenytoin	100mg	cap/tab	Lowest price generic	n/a	1.68	n/a

b. private sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	94.7%	21.12	10.7
Diazepam	5mg	cap/tab	Originator brand	100.0%	37.30	
Carbamazepine	200mg	cap/tab	Lowest price generic	98.2%	8.55	4.3
Diazepam	5mg	cap/tab	Lowest price generic	100.0%	15.74	
Phenytoin	100mg	cap/tab	Lowest price generic	98.2%	7.72	0.8

Tajikistan, February 2005

a. public sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Diazepam	5mg	cap/tab	Lowest price generic	5.0%		

b. private sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	5.0%		
Carbamazepine	200mg	cap/tab	Lowest price generic	5.0%		
Diazepam	5mg	cap/tab	Lowest price generic	10.0%		

Tanzania, September 2004

a. public sector procurement

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Lowest price generic	n/a	0.69	n/a
Diazepam	5mg	cap/tab	Lowest price generic	n/a	0.18	n/a
Phenytoin	100mg	cap/tab	Lowest price generic	n/a	0.83	n/a

b. public sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Lowest price generic	34.4%	2.11	1.8
Diazepam	5mg	cap/tab	Lowest price generic	53.1%	3.22	
Phenytoin	100mg	cap/tab	Lowest price generic	65.6%		

c. private sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	14.6%	42.25	36.5
Diazepam	5mg	cap/tab	Originator brand	2.1%		
Phenytoin	100mg	cap/tab	Originator brand	2.1%		
Carbamazepine	200mg	cap/tab	Lowest price generic	37.5%	10.57	9.1
Diazepam	5mg	cap/tab	Lowest price generic	66.7%	4.84	
Phenytoin	100mg	cap/tab	Lowest price generic	8.3%	8.88	1.6

Thailand, October 2006

a. public sector procurement

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	n/a	4.26	n/a
Phenytoin	100mg	cap/tab	Originator brand	n/a	6.68	n/a
Carbamazepine	200mg	cap/tab	Lowest price generic	n/a	1.67	n/a
Diazepam	5mg	cap/tab	Lowest price generic	n/a	1.20	n/a
Phenytoin	100mg	cap/tab	Lowest price generic	n/a	1.45	n/a

b. public sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	25.0%	16.42	3.2
Phenytoin	100mg	cap/tab	Originator brand	55.0%	28.11	1.2
Carbamazepine	200mg	cap/tab	Lowest price generic	80.0%	7.28	1.4
Diazepam	5mg	cap/tab	Lowest price generic	100.0%	14.64	
Phenytoin	100mg	cap/tab	Lowest price generic	40.0%	10.22	0.4

c. private sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	76.2%	25.53	5.0
Phenytoin	100mg	cap/tab	Originator brand	66.7%	25.57	1.1
Carbamazepine	200mg	cap/tab	Lowest price generic	28.6%	8.20	1.6
Diazepam	5mg	cap/tab	Lowest price generic	14.3%		
Phenytoin	100mg	cap/tab	Lowest price generic	28.6%	10.22	0.4

Tunisia, March 2004

a. public sector procurement

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Diazepam	5mg	cap/tab	Originator brand	n/a	6.44	n/a
Phenytoin	100mg	cap/tab	Originator brand	n/a	4.46	n/a
Carbamazepine	200mg	cap/tab	Lowest price generic	n/a	1.41	n/a
Diazepam	5mg	cap/tab	Lowest price generic	n/a	2.89	n/a

b. public sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Diazepam	5mg	cap/tab	Originator brand	23.8%		
Phenytoin	100mg	cap/tab	Originator brand	61.9%		
Carbamazepine	200mg	cap/tab	Lowest price generic	100.0%		
Diazepam	5mg	cap/tab	Lowest price generic	47.6%		

c. private sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Diazepam	5mg	cap/tab	Originator brand	53.7%	28.62	
Phenytoin	100mg	cap/tab	Originator brand	80.5%	16.20	0.7
Carbamazepine	200mg	cap/tab	Lowest price generic	95.1%	5.18	1.0
Diazepam	5mg	cap/tab	Lowest price generic	14.6%	16.26	

Uganda, April 2004

a. public sector procurement

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Lowest price generic	n/a	0.75	n/a
Diazepam	5mg	cap/tab	Lowest price generic	n/a	0.67	n/a
Phenytoin	100mg	cap/tab	Lowest price generic	n/a	0.70	n/a

b. public sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Lowest price generic	40.0%		
Diazepam	5mg	cap/tab	Lowest price generic	70.0%		
Phenytoin	100mg	cap/tab	Lowest price generic	60.0%		

c. private sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	20.0%	119.09	45.6
Carbamazepine	200mg	cap/tab	Lowest price generic	80.0%	15.87	6.1
Diazepam	5mg	cap/tab	Lowest price generic	80.0%	14.54	
Phenytoin	100mg	cap/tab	Lowest price generic	75.0%	22.27	1.8

Ukraine, 2007

a. public sector procurement

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Diazepam	5mg	cap/tab	Lowest price generic	n/a	4.75	n/a

b. public sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Diazepam	5mg	cap/tab	Lowest price generic	50.0%		

c. private sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Diazepam	5mg	cap/tab	Lowest price generic	3.7%		

United Arab Emirates, December 2006

a. public sector procurement

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	n/a	4.64	n/a
Phenytoin	100mg	cap/tab	Originator brand	n/a	6.15	n/a
Carbamazepine	200mg	cap/tab	Lowest price generic	n/a	2.38	n/a
Diazepam	5mg	cap/tab	Lowest price generic	n/a	26.26	n/a

b. public sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	50.0%		
Diazepam	5mg	cap/tab	Originator brand	22.2%		
Phenytoin	100mg	cap/tab	Originator brand	33.3%		
Carbamazepine	200mg	cap/tab	Lowest price generic	5.6%		
Diazepam	5mg	cap/tab	Lowest price generic	100.0%		

c. private sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	100.0%	11.91	8.7
Diazepam	5mg	cap/tab	Originator brand	78.3%	57.87	
Phenytoin	100mg	cap/tab	Originator brand	78.3%	7.20	1.1
Carbamazepine	200mg	cap/tab	Lowest price generic	17.4%	5.22	3.8
Diazepam	5mg	cap/tab	Lowest price generic	17.4%	21.33	

Uzbekistan, December 2004

a. public sector procurement

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Lowest price generic	n/a	4.18	n/a

b. private sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Lowest price generic	55.0%	17.94	18.3

Yemen, July 2006

a. public sector procurement

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Lowest price generic	n/a	0.70	n/a
Phenytoin	100mg	cap/tab	Lowest price generic	n/a	0.50	n/a

b. public sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Lowest price generic	5.0%		
Diazepam	5mg	cap/tab	Lowest price generic	15.0%		

c. private sector

Medicine	Strength	Form	Medicine type	Availability	Adjusted MPR	Affordability
Carbamazepine	200mg	cap/tab	Originator brand	95.0%	7.97	9.3
Diazepam	5mg	cap/tab	Originator brand	55.0%	54.89	
Phenytoin	100mg	cap/tab	Originator brand	50.0%	10.21	2.6
Carbamazepine	200mg	cap/tab	Lowest price generic	100.0%	2.35	2.7
Diazepam	5mg	cap/tab	Lowest price generic	80.0%	12.68	

Chapter 5

Quantifying the impoverishing effects of purchasing medicines: a cross-country comparison of the affordability of medicines in the developing world

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Summary

Background

Increasing attention is being paid to the affordability of medicines in low- and middle income countries (LICs and MICs) where medicines are often highly priced in relation to income levels. The impoverishing effect of medicine purchases can be estimated by determining pre- and postpayment incomes, which are then compared to a poverty line. Here we estimate the impoverishing effects of four medicines in 16 LICs and MICs using the impoverishment method as a metric of affordability.

Methods and Findings

Affordability was assessed in terms of the proportion of the population being pushed below US$1.25 or US$2 per day poverty levels because of the purchase of medicines. The prices of salbutamol 100 mcg/dose inhaler, glibenclamide 5 mg cap/tab, atenolol 50 mg cap/tab, and amoxicillin 250 mg cap/tab were obtained from facilitybased surveys undertaken using a standard measurement methodology. The World Bank's World Development Indicators provided household expenditure data and information on income distributions. In the countries studied, purchasing these medicines would impoverish large portions of the population (up to 86%). Originator brand products were less affordable than the lowest-priced generic equivalents. In the Philippines, for example, originator brand atenolol would push an additional 22% of the population below US$1.25 per day, whereas for the lowest priced generic equivalent this demographic shift is 7%. Given related prevalence figures, substantial numbers of people are affected by the unaffordability of medicines.

Conclusions

Comparing medicine prices to available income in LICs and MICs shows that medicine purchases by individuals in those countries could lead to the impoverishment of large numbers of people. Action is needed to improve medicine affordability, such as promoting the use of quality assured, low priced generics, and establishing health insurance systems.

Introduction

In developing countries the cost of medicines accounts for a relatively large portion of total healthcare costs (1–4). As the majority of people in developing countries do not have health insurance (5) and medicines provided free through the public sector are often unavailable (4), medicines are often paid for out of pocket at the time of illness. Consequently, where medicine prices are high, people may be unable to procure them and therefore forego treatment or they may go into debt. For this reason, the World Health Organization (WHO) has designated affordable prices as a determinant of access to medicines (together with rational selection and use, sustainable financing, and reliable health and supply systems) (6). In several international treaties, access to healthcare has been established as a right (7,8). States have a legal obligation to make essential medicines available to those who need them at an affordable cost. Determining the degree of affordability of medicines, especially in low- and middleincome countries (LICs and MICs), is an important, yet complex undertaking as affordability is a vague concept.

Medicine affordability has been investigated in terms of the days' wages that a country's lowest paid unskilled government worker (LPGW) needs to spend on a standard course of treatment (4,9). However, this metric is limited because it does not provide insight into the affordability of medicines for the often large sections of the population that earn less than the LPGW (4,10). Recently, Niëns et al. have proposed two alternative methods to gain insight into the affordability of medicines in the developing world (11). A first method focuses on the catastrophic impact of expenditures on medicines, while the second approach consists of studying the impoverishing effect of these expenditures. Here we discuss the application of the latter approach and present the results of a cross-country analysis of the affordability of four medicines in 16 developing countries.

Methods

Our measurement of the affordability of medicines is based on the approach taken by Van Doorslaer et al. (3), who reassessed poverty estimates in 11 Asian countries after taking into account household expenditures on health care.

The impoverishment approach has also been used in other fields of study such as housing affordability (12,13) and health insurance (14). The impoverishing effect of a medicine is defined in terms of the percentage of the population that would be pushed below an income level of US$1.25 or US$2 per day when having to purchase the medicine. Although different income levels have been used/proposed (3,15), the US$1.25 and US$2 poverty lines were chosen because they are the most recent widely recognized pov-

erty indicators as used by the World Bank (16). Thus, the approach essentially compares households' daily per capita income before and after (the hypothetical) procurement of a medicine. If the prepayment income is above the US$1.25 (or US$2) poverty line and the postpayment income falls below these lines, purchasing the medicine impoverishes people. We used this method to generate "impoverishment rates," which denote the percentage of the population that would become impoverished. The unaffordability of a medicine then refers to the percentage of the population that either already is or would fall below the poverty line when having to procure the medicine. First we consider the affordability of medicines in the total population at risk of becoming ill. We also indicate, using prevalence rates for the three chronic diseases, the expected number of patients actually affected.

Data

To conduct the first analysis, three types of data were required per country: medicine prices, aggregated income data, and information on the income distribution. In calculating expected numbers of patients affected, prevalence data are also required. Medicine prices were taken from standardized surveys using the WHO/Health Action International (HAI) price measurement methodology, which report median patient prices for a selection of commonly used medicines in the private sector, for both originator brand (OB) and lowest priced generic (LPG) products (17). We focused on the private sector because the availability of essential medicines in the public sector is much lower (4). In the countries studied here, therefore, many people will depend on the private sector for their medicines.

The World Bank's World Development Indicators (WDIs) provided Household Final Consumption Expenditure (HHFCE) data and information on income distribution (18). Although WDIs have shortcomings (highlighted in the Discussion section), they have the advantage of being available for a wide range of countries. Moreover, in this context commonly used household surveys are often not available on a yearly basis and are not conducted in a standardized way, limiting the comparability of results across countries and over time (3,19). Here we use an affordability measure that can be quite easily applied in LICs and MICs where the use of more detailed household survey data may be limited.

HHFCE was selected as an aggregate income measure rather than gross domestic product (GDP) per capita as it better reflects households' resources (19), while GDP also includes consumption, gross investment, and net trade. Because the WDI did not provide any information on HHFCE for Nigeria and Yemen, the Economist Intelligence Unit (EIU) nominal private consumption figure was used for these countries (20). For simplicity, we refer to "income" as measured by HHFCE or nominal private consumption.

Apart from average income, the WDIs also provide some information on a country's income distribution by listing the proportion of total income earned in seven income groups; five income quintiles, with the poorest and richest quintiles split into deciles.

At the time of analysis, medicine price surveys were available for 53 countries. In large countries such as India and China, price surveys were carried out on a state or provincial level (4). Because the WDIs do not provide state-level income distributions, HHFCE, and population figures, these countries were excluded from the current study. To ensure cross-country comparability, the analysis was limited to countries where income distributions (WDI data) were available from the year 2000 onwards. We used WDI income data from the same year as the WHO/HAI price data. Data on income distributions for the same year were used when possible, if not, the most recent income distribution data prior to the year of the price and income data were used.

Table 1 provides an overview of all countries and data used in this study. When discussing results, countries were grouped into LICs and MICs according to the 2008 World Bank's classification (21). Sixteen countries were selected on the basis of the availability of WHO/HAI data. They are not representative of the developing world as a whole. However, as these countries vary substantially in terms of economic development, health care infrastructure, and medicine prices, they provide an interesting sample to study affordability of medicines.

We selected four medicines for which price data were available for the majority of countries and for which treatment regimens are relatively standard across countries. While these may not lead to results that are in a strict sense generalisable, they provide valuable insight into the affordability of common medicines in the selected countries. Table 2 lists the medicine, the ill health conditions for which these medicines are used, the total number of units per treatment course, and the treatment duration in days (17). Three of the four study medicines are used to treat chronic conditions (asthma, diabetes, and hypertension). For each of these, we also calculated the expected numbers of patients becoming impoverished, using the prevalence data shown in Table S1. We could not do this for adult respiratory infection because of unavailability of comparable prevalence data.

The emphasis on medicines for chronic disease is justified by the fact that these conditions require ongoing, usually lifelong expenditures, making it more difficult for households to use financing strategies like borrowing and selling assets (22). Table 2 shows that the treatment duration for these medicines was set at 30 d to represent the monthly treatment costs. The affordability of one acute condition (adult respiratory infection) treated with a 7-d treatment course of amoxicillin was also studied. Recently, the WHO increased the guidelines for treatment of adult respiratory infection with amoxicillin to

a daily regimen of three times 500 mg amoxicillin. This change implies that the affordability of this medicine is likely to be lower than reported here (23).

Calculation methods

Our method of estimating the impoverishing effect of procuring medicines was based on the method used by Van Doorslaer et al. (3). However, using aggregate data requires some simplifying assumptions about the income distribution across population groups. For a detailed discussion of the method used to calculate the impoverishing effect of medicines, we refer to Niëns et al. (11). The basic idea is to compare poverty estimates before and after a (potential) purchase of the medicines listed in Table 1. Average per capita income within each income group is estimated by combining information on the proportion of total income earned across income groups with data on the HHFCE (as provided by the WDIs). As only data on average income in the different quintiles and deciles were available, we assumed linearity of the income distribution within these relevant groups in which the US$1.25 and US$2 poverty lines were located in calculating poverty and impoverishment. The proportion of the population that would earn less than US$1.25 or US$2 per day after buying a medicine but not before would therefore be impoverished because of purchasing medicines. The medicine is deemed affordable for the proportion of the population that would remain above the poverty line after having purchased it. We also estimated the actual number of patients with one of the three chronic illnesses for which the medicine is unaffordable. To make this estimation, we used prevalence rates from various data sources and again assume that the respective disease is evenly spread over the income distribution.

Because HHFCE is measured in current US$, we recalculated the US$1.25 and US$2 poverty lines to US$ values for the WHO/HAI survey year. WHO/HAI medicine prices were expressed in US$ for the same year.

Results

Table 3 presents the percentages of the population that are pushed below the poverty line owing to the purchasing of each of the four study medicines, both LPG and OB products.

For each country, Table 3 first highlights the proportion of the population already below the US$1.25 and US$2 poverty lines without purchasing these medicines. These poverty estimates correlate highly with the commonly used (household-survey based) estimates from the United Nations Development Program with Pearson correlation coefficients (24) equal to 0.90 for the proportion of the population below the US$1.25 poverty line, and 0.86 for the proportion below the US$2 poverty line. Table 3 also shows the proportion of the population earning less than the LPGW, which varies wide-

ly across countries; from only 1% in Tajikistan to 96% in Tanzania. This cross-country variability represents one of the limitations of the LPGW metric as used by the WHO/HAI methodology (9).

Comparing the proportion of the population below the US$1.25 and US$2 poverty lines before and after procurement of medicines gives insight into the impoverishing effect of medicine procurement. By adding the proportion of the population already living below the US$1.25 and US$2 poverty lines to the group that would fall below these poverty lines when procuring the medicines, we get the proportion of the population for which the four medicines are unaffordable.

The results in Table 3 illustrate that the impoverishing effect of medicines varies substantially between OB and LPG products. For example in Yemen, a LIC where 7% of the population lives on a prepayment income of less than US$1.25 a day, OB glibenclamide purchased in the private sector would impoverish an additional 22% of the population versus 3% for the LPG equivalent. In Nigeria, a LIC where 56% of the population lives below US$1.25 per day, purchasing amoxicillin from the private sector would impoverish an additional 23% if the OB is bought and 12% if buying the LPG.

Rather than showing proportions of the population, Table 4 presents both the absolute number of individuals that would be pushed into poverty owing to the cost of buying medicines from the private sector ("Impoverished" column) and the number of people for which medicines are unaffordable ("Unaffordable" column). Besides absolute figures, in Table 5 we present the relative change of the poverty estimates for the total population studied as well as for the patient population. So, if 40% of the population is initially above the poverty line, while only 30% would remain above after purchasing medicines, this proportion is 25% (10% out of 40% are impoverished). These numbers are listed for all four medicines, both OB and LPG. The total population of the 16 countries analyzed amounts to over 775 million people, of which approximately 126 million live on less than US$1.25 and 209 million on less than US$2 per day, respectively. Table 4 illustrates that across this set of 16 developing countries, for respectively almost one-fourth and two-fifths of the total population, essential medicines are unaffordable using the US$1.25 and US$2 poverty line.

The upper half of Table 4 shows the proportions of the total population for which medicines would be unaffordable when having to procure them. The actual number of people affected by this unaffordability (in terms of experiencing the disease) depends on the prevalence of diseases as well. Therefore, the lower half of Table 4 also shows the expected absolute number of patients affected by the unaffordability of medicines using the prevalence rates listed in Table S1. As the prevalence rates of hypertension are substantially higher than those of asthma and diabetes, the impoverishing effect,

and therefore also the unaffordability, of atenolol is substantially higher than that for the other medicines. In this approach, given the height and distribution of income, impoverishment is determined by both medicine prices and prevalence rates for the relevant diseases.

Discussion

The results illustrate that substantial proportions of the population would be pushed into poverty as a result of medicine procurement, implying that in many countries affordability of these treatments is low. In the private sector, LPGs were generally substantially more affordable than OB products. Thus, increasing the use of quality-assured generics could reduce the impoverishing effect of medicines. This use of generics, in turn, could bring about improvements in the health status of these populations by avoiding low compliance to recommended dosages or duration of treatment, resulting in problems such as sustained hypertension, elevated blood glucose levels, or the promotion of bacterial resistance due to too short courses of antibiotics.

Our calculation method has the advantage of allowing for comparisons of medicine-induced impoverishment across time and across countries using widely available aggregate data. The method, therefore, is useful and generalisable for studying the affordability of a wide range of goods and health care services. The use of such data also brings some limitations, which are discussed in further detail in Niëns et al. (11). First, dividing HHFCE by total population to get an estimate of income per capita assumes that each household is the same size. However, poor households are generally larger than their richer counterparts (25). This discrepancy causes the average income per capita to be overestimated in the lower income groups, making our affordability estimates rather conservative. Second, the assumption of linearity of the income distribution between income groups is also likely to lead to an overestimation of average incomes across the income distribution and therefore to a downward bias in our results. We also assumed a linear distribution of illness over the income distribution to calculate expected numbers of affected people. Although, in general, disease may be more prevalent in low income groups, which would imply conservative estimates of unaffordability, this also depends on the exact diseases studied. Moreover, it is clear that considering only medicine costs, for four medicines independently, merely demonstrates the larger problem of medicine and health care affordability. The treatment of chronic conditions often requires a combination of medicines and is therefore likely to be even more unaffordable than what is reported here (4). For chronic asthma patients, for example, appropriate management of their disease requires use of both salbutamol and beclometasone inhalers for treatment

and prevention (17). Due to the lack of available price information on beclometasone inhalers (because of poor availability), it was not possible to include this medicine in the analysis. As such, the true affordability of asthma treatment is likely to be lower than reported in Tables 3 and 4. Having said this, the medicines studied in this paper are commonly used to treat ill health conditions from which considerable proportions of the population in the developing world suffer, as is also illustrated in Table S1 (26). As such, low affordability of these medicines is likely to signal a more general problem of low affordability of medicines in LIC and MIC. Further, it should be noted that comparability of impoverishment rates for acute and chronic conditions may be limited. If people suffer from an adult respiratory infection, on average three times per year, and are able to shift resources over time, the impoverishment rates for amoxicillin should be interpreted with caution. Further research is needed on this issue, for example by calculating affordability for standardized time periods taking into account the relevant incidence rates of respiratory infections.

Notwithstanding these limitations, this study provides useful insights into the affordability of these four medicines in the developing world. When medicine prices are known, the methods used, as they rely on easily obtainable aggregated data, can be used to compare affordability of medicines across countries and over time. Clearly, medicines represent only a part of the costs associated with the management of an illness. Other costs, such as for diagnostics, physician consultations, transport costs to clinics, lost work time, etc., place an additional burden on household finances in developing countries. However, given the relatively large share of health care costs for medicines in developing countries (1–4), medicine affordability is likely to be an important determinant to access to treatment.

This study shows high medicine costs can push large groups of patients into poverty. These results call for action, both by governments, civil society organizations, and others, to make access to essential medicines a priority, and not only to ensure access to necessary medicines, but also as a component in the context of reducing poverty. Possible lines of action include developing, implementing, and enforcing sound national and international price policies. In the short term these policies could encompass, for example, restrictions on supply chain mark-ups, tax exemptions, and regulating prices for end-users. Promoting the use of quality-assured, low-cost generics, for example, through preferential registration procedures, is also an important strategy (4). In the public sector, ensuring availability of essential medicines at little or no charge to the poor is critical. In the longer term, establishing health insurance systems with outpatient medicine benefits seems crucial to avoid poverty due to health shocks (and poor health due to poverty). Innovative approaches, such as using private distribution systems to supply subsidized medicines to chronic disease patients, should also be considered. For medicines that are

still subject to patent restrictions, pharmaceutical companies should be encouraged to differentially price these products, as is the case with antiretrovirals (27). Countries also have the option of using compulsory licensing to oblige patent holders to grant its use to the state or others (28), as was recently done by Thailand (29,30).

When resources are limited, those in greatest need, such as people suffering from chronic disease who earn less than US$1.25 per day, should benefit from state and/or donor actions. The price in terms of health losses due to unaffordable medicines is something we cannot afford.

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Tables and Figures

Table 1. Overview of countries studied and years of data sources used

Countries	Medicine price survey and WDI income data	WDI data on income distribution
Low-income		
Kyrgyzstan	2005	2003
Mali	2004	2001
Nigeria	2004 [a]	2003
Pakistan	2004	2002
Tajikistan	2005	2004
Tanzania	2003	2000
Uganda	2004	2002
Uzbekistan	2004	2003
Yemen	2006 [a]	2005
Middle- income		
El Salvador	2006	2002
Indonesia	2004	2002
Jordan	2004	2002
Mongolia	2004	2002
Peru	2005	2003
Philippines	2005	2003
Tunisia	2004	2000

[a] *Nominal private consumption from EIU was used.*

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Table 2. Description of studied medicines

Medicine name	Ill health condition	Medicine strength per dose	Total *n* of doses per treatment	Dosage form	Treatment duration (d)
Salbutamol inhaler	Asthma	100 mcg	200	inhaler	30 (1 inhaler)
Glibenclamide	Diabetes	5 mg	60	capsule/ tablet	30
Atenolol	Hypertension	50 mg	30	capsule/ tablet	30
Amoxicillin	Adult Respiratory Infection	250 mg	21	capsule/ tablet	7

Table 3. Percentage of the population below the poverty line before procurement of the medicines and the population drawn below the poverty line by expenditures on these medicines

Percentage of population below poverty lines and LPGQW wage, before medicine purchase					Percentage of the population below poverty line after medicine purchase															
					Salbutamol inhaler				Glibenclamide				Atenolol				Amoxicillin			
Country	GDP/cap (current US$)[b]	US$1.25	US$2	LPGW wage	US$1.25		US$2		US$1.25		US$2		US$1.25		US$2		US$1.25		US$2	
					OB	LPG	OB	LPG	OB	LPG	OB	LPG	OB	LPG	OB	LPG	OB	LPG	OB	LPG
LIC																				
Kyrgyzstan	478	0	14	10	8	5	22	18	[a]	2	[a]	2	[a]	1	[a]	15	[a]	12	[a]	26
Mali	422	37	61	85	51	50	67	69	66	53	76	65	[a]	[a]	[a]	[a]	[a]	[a]	[a]	[a]
Nigeria	639	56	77	90	71	[a]	77	[a]	71	71	79	79	67	63	83	81	79	68	80	84
Pakistan	644	-	8	46	0	[a]	13	[a]	0	0	13	12	1	0	17	12	4	4	21	21
Tajikistan	354	10	32	1	[a]	19	[a]	40	[a]	11	[a]	33	[a]	12	[a]	34	[a]	28	[a]	50
Tanzania	286	50	77	96	[a]	60	[a]	82	[a]	58	[a]	81	[a]	57	[a]	80	[a]	61	[a]	82
Uganda	305	52	73	90	59	54	77	74	[a]	53	[a]	74	72	53	85	74	74	54	86	74
Uzbekistan	465	17	38	68	28	24	50	46	[a]	22	[a]	43	[a]	19	[a]	41	[a]	35	[a]	58
Yemen	882	7	22	87	14	10	31	26	29	10	47	26	20	9	38	25	[a]	12	[a]	28
MIC																				
El Salvador	3,067	7	11	59	9	9	14	14	17	11	21	16	15	12	19	17	21	[a]	26	[a]
Indonesia	1,187	-	4	71	11	[a]	20	[a]	13	0	36	6	15	0	38	12	20	0	43	9
Jordan	2,157	-	1	58	0	0	4	2	0	0	6	3	1	0	8	4	19	3	26	10
Mongolia	721	2	13	81	[a]	7	[a]	20	[a]	6	[a]	19	[a]	4	[a]	19	[a]	8	[a]	13
Peru	2,852	2	9	64	7	5	14	11	[a]	5	[a]	11	13	4	20	10	27	7	33	14
Philippines	1,156	5	21	88	16	12	32	28	23	13	38	29	27	12	41	28	23	17	37	32
Tunisia	2,832	-	1	73	0	[a]	2	[a]	0	0	5	2	[a]	0	[a]	3	[a]	[a]	[a]	[a]

The sum of both gives the proportion of the population for which the medicine is unaffordable.

[a] *No reliable medicine price estimate was possible due to lack of data.*

[b] *Source: WDI (18).*

Table 4. Absolute impoverishment and unaffordability estimates of medicines procured in the private sector for the total and chronic patient populations across of 16 countries (rounded to millions)

Medicine	Under USD1.25				Under USD2			
	OB		LPG		OB		LPG	
	Impoverished	Unaffordable	Impoverished	Unaffordable	Impoverished	Unaffordable	Impoverished	Unaffordable
Total population								
Salbutamol inhaler	64	190	16	142	71	280	23	233
Glibenclamide	72	198	36	162	112	321	35	244
Atenolol	79	206	20	146	133	343	50	259
Amoxicillin	111	237	46	172	144	354	72	281
Chronic patient population								
Salbutamol inhaler	3	9	1	7	2	13	1	12
Glibenclamide	3	8	2	6	5	14	2	11
Atenolol	19	58	6	44	29	92	10	73

Impoverished, the number of people that would be pushed below the USD$1.25 and USD$2 poverty lines if the total population had to buy the respective medicine.
Unaffordable, the total number of people for which the respective medicine can be considered unaffordable.

Table 5. The relative change of the poverty estimates (i.e., the impoverished population expressed as a proportion of the population initially above the poverty line)

	Medicine	Additional percentage under US$1.25		Additional percentage under US$2	
		OB	LPG	OB	LPG
Total population	Salbutamol inhaler	10	2	13	4
	Glibenclamide	11	6	20	6
	Atenolol	12	3	23	9
	Amoxicillin	17	7	25	13
Chronic patient population	Salbutamol inhaler	10	2	10	3
	Glibenclamide	10	5	18	5
	Atenolol	12	4	21	7

Chapter 6

Switching from originator brand medicines to generic equivalents in selected developing countries: how much could be saved?

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Summary

Objectives

In low- and middle-income countries, patients and reimbursement agencies that purchase medicines in the private sector pay more for originator brands when generic equivalents exist. We estimated the savings that could be obtained from a hypothetical switch in medicine consumption from originator brands to lowest-priced generic equivalents for a selection of medicines in 17 countries.

Methods

In this cost minimization analysis, the prices of originator brands and their lowest-priced generic equivalents were obtained from facilitybased surveys conducted by using a standard methodology. Fourteen medicines most commonly included in the surveys, plus three statins, were included in the analysis. For each medicine, the volume of private sector consumption of the originator brand product was obtained from IMS Health, Inc. Volumes were applied to the median unit prices for both originator brands and their lowest-priced generics to estimate cost savings. Prices were adjusted to 2008 by using consumer price index data and were adjusted for purchasing power parity.

Results

For the medicines studied, an average of 9% to 89% could be saved by an individual country from a switch in private sector purchases from originator brands to lowest-priced generics. In public hospitals in China, US $ 370 million could be saved from switching only four medicines, saving an average of 65%. Across individual medicines, average potential savings ranged from 11% for beclometasone inhaler to 73% for ceftriaxone injection.

Conclusions

Substantial savings could be achieved by switching private sector purchases from originator brand medicines to lowest-priced generic equivalents. Strategies to promote generic uptake, such as generic substitution by pharmacists and increasing confidence in generics by professionals and the public, should be included in national medicines policies.

Introduction

In low- and middle-income countries (LMICs), a significant proportion of the population lack access to essential medicines (1). While many LMICs provide medicines for free or at low cost in public sector facilities, availability is often low (2). Furthermore, while social health insurance schemes are expanding in LMICs, overall coverage in low-income countries remains poor (3) and many schemes do not provide medicines benefits or do so with substantial co-payments (4,5). As a result, medicines are still primarily purchased through out-of-pocket payments in the private sector (6) where high prices can be a barrier to access (2,6–11). Given the important and often dominant role of the private sector in supplying medicines in LMICs (12), national medicines policies (NMPs) often include efforts to manage the performance of this sector so as to make medicines available at an affordable cost (13,14). The majority of LMICs have an NMP (14), a primary objective of which is securing the population's access to medicines necessary to achieve major public health goals (15).

The use of generic medicines is often promoted as a measure to reduce medicine costs and increase consumer access and can be included in NMPs as part of strategies to encourage the cost-effective use of medicines by health professionals and consumers (16). In LMICs, originator brand medicines that have come off patent generally cost substantially more than do their generic equivalents. Patients purchasing medicines in the private sector pay, on average, 2.6 times more for originator brands than for their lowestpriced generic equivalent (2). In some countries, this price differential is more than 10-fold. When higher-cost originator brands are the only products available at a given dispensing point, patients may be forced to forgo treatment or may be pushed into poverty as a result of medicine purchases. A study of the impoverishing effect of purchasing medicines in 16 LMICs found that an additional 10% to 17% of the population would be pushed under the $1.25/d poverty line as a result of purchasing individual medicines as originator brands (17). If the same medicines were purchased as lowest-priced generic equivalents, the impoverishin effect was substantially lower (2%–7%). The magnitude of price differential between brands can be influenced by the presence/absence and nature of price regulations and reimbursement policies; for example, restricting reimbursement to the price of lower-cost products was found to reduce and stabilize retail prices in Kyrgyzstan (18). In unregulated markets, price differentials will be influenced by patients' willingness to pay for higher-priced products (15).

The organization of a country's health system can have implications for medicine prices and overall spending. In fully public systems, medicines are financed, procured, and distributed by a centralized government unit at the national or state/provincial level; in mixed systems, public funding from central budgets or social health insurance is used

to reimburse patients or private pharmacies, or medicines are supplied through government medical stores and health facilities but paid for by patient fees; in fully private systems, patients or private insurance systems pay the entire cost of medicines purchased from private pharmacies and drug sellers. Most countries utilize a combination of two or more of these approaches (13). The organization of the pharmaceutical sector, including the presence/absence of price regulations, will influence overall spending, which is a function of both price levels and consumption volumes. Among Organization for Economic Cooperation and Development countries, for example, Switzerland and Denmark have among the highest price levels but the lowest per-capita spending, while France and Spain have among the lowest prices but the highest per-capita spending due to high consumption volumes (19).

Market factors will also have an impact on pharmaceutical price levels. Pharmaceutical markets are subject to several failures that prevent the production of socially optimal amounts of medicines over time. A main source of failure is the information asymmetry that exists between prescribers, dispensers, and consumers regarding the quality, safety, efficacy, and value for money of individual medicines, which allows prescribers/dispensers to give misleading advice to increase profits (13,20). Market failures may also occur because of lack of competition, for example, monopoly power due to patent protection or barriers to market entry of generic competitors, leading to higher prices than would be expected in a competitive market (13,20). A further failure occurs because of the externality of certain medicines used to treat communicable diseases, where the benefits of treatment extend beyond the individual consuming the medicine. In a free market, the consumption of these products will be less than optimal from a societal perspective (13). In countries where medicines are covered under health insurance benefits, market failure may also occur because of moral hazard. That is, consumers are inclined to overconsume because they do not directly bear the cost of consumption (20). Another potential source of market failure is the underinvestment for particular diseases (20). As a result of these failures, pharmaceutical markets are usually extensively regulated, far more so than the markets for most other goods (13). Government regulations are often related to patents, marketing authorization, and pricing and reimbursement (20). Additional measures include information and training for health professionals and consumers, regulation of promotional practices to prevent the provision of biased or inaccurate information, substitution of brand products with generic equivalents by dispensers, and subsidization of products with externalities (13). The nature of government interventions in pharmaceutical markets vary substantially between countries; for example, EU member states use a range of approaches that address both supply-side and demand-side issues (20).

In discussing the possible overreliance on higher-priced originator brands once patents have expired and generic competitors have entered the market, the market failure of primary concern is that caused by information asymmetry. Because of a limited understanding of the characteristics of individual products, consumers often purchase a different medicine than they would if they were better informed (21). To compensate for this lack of information, consumers frequently rely on prescribers and/or dispensers for advice on what to buy ("agency relationship"). Prescribers and/or dispensers, however, often advise on the basis of their own incentives rather than the buyer's interests. For example, when wholesaler/retailer margins are a fixed percentage of the price, there is the incentive to stock and sell more expensive products to obtain a greater profit (15). Physicians' prescribing behavior can also be influenced by pharmaceutical companies through a variety of measures ranging from high-end education programs to cash payment for prescriptions (15). As a result of these incentives, patients are often encouraged to use higherpriced originator-branded products instead of equally effective, lower-cost generics (21).

There is a wide variability in the uptake of generic medicines across high-income countries. For example, in Japan, generic medicines represent only 16% of the prescription medicines market by volume, compared with 60% to 70% in the United Kingdom, Canada, and Germany (22). Efforts have been made to increase the uptake of generics in developing countries, and in some cases, to quantify the cost savings achieved from these efforts. For example, the cost savings to UK's National Health Service of a campaign to promote the most cost-effective use of medicines through strategies such as generic substitution have been estimated at £1 billion a year (23). A review of European pricing and reimbursement systems reported on the budgetary impact of generic substitution (allowing/requiring pharmacists to dispense a generic equivalent in place of the prescribed originator brand) in Finland based on evaluations conducted by the Finnish Social Insurance Institution (24). Savings were estimated at €25.7 million in 2005, corresponding to an average saving of €15.80 per substitution. When medicine price reductions brought on by price competition were also included, the total cost savings were estimated at €88.3 million. Another analysis found that in the 3 years following the introduction of generic substitution at patent expiry in Sweden, the accumulated savings in the pharmaceutical budget were about €760 million (25). Overall pharmaceutical prices decreased by 15%, with the highest decrease observed for statins (71%).

While results from high-income countries indicate that the cost savings of increased use of generic medicines can be substantial, little is known about the economic impact of increased generic uptake in LMICs. This study estimates the potential savings that could be obtained by switching purchases from originator brand medicines to the lowest-priced generic equivalents for a selection of multisource products (i.e., medicines pro-

duced by more than one manufacturer, including both the originator brand and generic equivalents) in developing countries. This information is important for governments in considering which policy interventions could be undertaken to achieve the goals of an NMP. Because such policies have many possible components and resources for implementation are limited, it is important to understand where possible investments have the potential to achieve the goal of improved access to quality medicines.

Methods

To estimate the maximum cost savings that could be generated if the originator brand products consumed were purchased as lowest- priced generics, final (retail) prices of both originator brands and their lowest-priced generic equivalents were applied to the volume of originator brand product consumed. Medicine price data were obtained from surveys conducted by using a validated (26) methodology developed by the World Health Organization (WHO) and Health Action International (HAI) (27), while medicine consumption data were obtained from IMS Health, Inc., a pharmaceutical market intelligence company (www.imshealth.com/). In the WHO/HAI surveys, the median unit prices (e.g., price per tablet, mililiter) of approximately 50 medicines are calculated from data collected in a sample of public and private sector facilities.For each medicine, data are collected on both the originator brand first authorized worldwide for marketing (normally as a patented product) on the basis of the documentation of its efficacy, safety, and quality, according to requirements at the time of authorization, and the lowest-priced generic equivalent found at each facility. In WHO/HAI surveys, generic medicines are defined as pharmaceutical products intended to be interchangeable with the originator brand product, manufactured without a license from the originator manufacturer, and marketed after the expiry of patent or other exclusivity rights (27). Only registered products distributed through regulated channels (e.g., licensed pharmacies) are included, thereby reducing the risk that the generics surveyed are of substandard quality or counterfeit. Data are collected on the same medicine formulation (e.g., capsule(cap)/tablet (tab) and slow release tablet) and strength for originator brands and their generic equivalents, because such treatment costs are directly comparable.

The survey method does not collect price data on medicines provided free of charge or for a fixed fee. Discounted prices that are offered to all patients are recorded. The WHO/HAI method is standardized across surveys through the use of a common survey manual and tools such as training resources. The survey manual has been translated into five languages and provides guidance on methodological adaptations to account for contextual issues (e.g., geography). WHO/HAI survey data have been used to generate

national-level reports (28), to conduct secondary analyses (2,9,17,29), and as an information source for international monitoring activities (30,31). IMS collects pharmaceutical consumption data from wholesalers, hospitals, and/or dispensing outlets such as pharmacies or drugstores (32). The methodology employed varies by country and is dependent on the nature of each health system.

The 40 countries for which WHO/HAI pricing data were available were compared with countries for which IMS Health consumption data were also available. A set of 17 developing countries, as designated by the United Nations system (33), was identified for which both data sets would be available to enable the analysis. Ukraine was also included even though it is not categorized by the United Nations system as either a developed or developing country because it is a country of the Commonwealth of Independent States in Europe. In each of the 17 countries, price data are based on a national survey, with the exceptions of China and South Africa, where surveys were conducted on a subnational level. While data from South Africa represent a single province (Gauteng), in China results from two surveys (Shandong and Shanghai) were averaged without weighting as has been done in previous studies (2). Weighting by population size was considered as a potential method to account for price variations that might occur as a result of differences in consumption volumes. However, as a previous study showed only a very limited relationship between medicine price and volume purchases (34), the decision was made to use an unweighted average. All surveys were conducted at a single point in time, with survey dates ranging from 2004 to 2008. Next, the medicines included in the price and availability surveys in these 17 countries were compared to identify the 15 most commonly surveyed medicines for inclusion in the analysis. This method, which has been previously applied (2), was used to increase the comparability of study medicines across the countries. In addition to the 15 most frequently surveyed medicines, 3 statins were also included in the analysis given the high price differential between originator brands and generics for these medicines and the large volumes consumed.

For each study medicine, the originator brands included in each price and availability survey was cross-checked against those collected through IMS Health to ensure matched data on price and volume for the same product. The volume of originator brand medicines supplied through the retail sector in each country in 2009 was then extracted in IMS standard units. Exceptions are China, where data were available from public hospitals only, and Malaysia, where data were available only for the combined private hospital and retail sectors. For one of the selected medicines (hydrochlorothiazide 25 mg cap/tab), no consumption of the originator brand product was reported by IMS Health in any of the study countries; it was therefore excluded from the analysis. The total volumes for each medicine (specific dosage form and strength corresponding to price data) as well as for the therapeutic class (IMS Anatomical Therapeutic Chemical classification

level 3) represented by each medicine were also obtained to estimate the consumption of each medicine as a proportion of total consumption for its therapeutic class, as well as the consumption of the originator brand product as a proportion of total medicine consumption (all products, i.e., brands and generics) for that molecule.

The private sector median unit prices of each medicine, for both originator brand and lowest-priced generic products, were applied to the volume of originator brand product consumed in 2009 to estimate the cost savings that could be generated if all the originator brand products consumed were purchased as lowestpriced generics. For China, where consumption data were available only for public hospitals, public sector prices were used. Prices were adjusted to 2008 by using consumer price index data for each country and were converted from national currency units to US dollars by using gross domestic product purchasing power parities (35). The year 2008 was used because this was the most recent year for which consumer price index and purchasing power parity data were available at the time of analysis. Results for individual countries and individual medicines are reported as average savings, total savings, and per-capita savings, with population for the latter taken from a standard international source (36).

Results

Table 1 lists the 17 countries included in the analysis with key indicators of pharmaceutical expenditures. In the majority of the countries under study, private sector spending represents the majority of total pharmaceutical expenditure. In countries such as the Philippines, private sector spending is primarily out of pocket, because the social health insurance system does not currently include an outpatient medicines benefit. In Thailand, Ukraine, and Pakistan, the large majority of pharmaceutical spending comes from the public sector.

The 17 medicines included in the analysis are listed in Table 2. With the exception of the three statins, all study medicines were included in at least 80% of WHO/HAI surveys, thereby maximizing the price data available for the analysis. Average medicine consumption (all products, including originator brand and generics) as a proportion of therapeutic class (Anatomical Therapeutic Chemical classification level 3) ranged from more than 90% for salbutamol 100mcg/dose inhaler and co-trimoxazole 8+40 mg/mL suspension to 7% for lovastatin 20 mg cap/tab. Across all individual medicines in all the countries studied, the average market share (by volume) of the originator brand product was 39%, indicating that for these multisource products the originator brands still hold a substantial proportion of the market. Large differences, however, were observed across individual medicines, ranging from 100% for amitryptilline 25 mg cap/tab to 3% for

omeprazole 20 mg cap/tab. For amitryptilline, it should be noted that originator brand volume data were available only for four countries; the presence of WHO/HAI price data for generic amitryptilline in other study countries confirms the presence of generic equivalents though volumes are unknown.

The average, total, and per-capita potential cost savings that could be obtained from switching consumption from switching consumption from originator brands to lowest-priced generics are shown in Table 3 for the basket of medicines studied in each country. While 17 medicines were included in the study, the absence of volume and/or price data for individual medicines limited the number of medicines analyzed in each country, ranging from 12 medicines in Ecuador and the United Arab Emirates to 3 medicines in Tunisia. Across the countries studied, an average of 60% could be saved from a switch in private sector purchases from originator brands to lowest-priced generic equivalents. Notably high cost savings of more than 80% were obtained in Colombia and Indonesia, while more than three quarters of current spending could be saved in Peru, South Africa, and Thailand. While Pakistan and the Philippines had lower-than-average percentage savings (51% and 57%, respectively), large consumption volumes resulted in the high observed absolute savings in private sector purchases (more than Int$ 38 million in both countries). Similarly in public hospitals in China, high consumption volumes resulted in potential savings of about Int$ 370 million from switching only four medicines, saving patients an average of 65%. While these results illustrate the magnitude of potential savings in high-volume markets, absolute savings across countries cannot be compared because of differences in population size and medicine usage patterns. Per-capita potential cost savings range from less than Int$ 0.05 in Kuwait and the Ukraine to Int$ 2.16 in the United Arab Emirates; however, it should be underscored that in these results medicine consumption from the private sector only is being applied to the total population who access medicine from public, private, and often other sectors (e.g., nongovernment organization hospitals and dispensing doctors). In China, if the savings from four public hospitals, which represent a relatively small proportion of overall consumption, are calculated on a percapita basis, savings of nearly 30 cents per person are still possible.

Table 4 shows the total potential cost savings and average percentage savings that could be obtained from switching consumption from originator brands to lowest-priced generics, by individual medicine. Average percentage savings range from 11% for beclometasone 50 mcg/dose inhaler to 73% for ceftriaxone 1 g/vial injection. For the latter medicine, this percentage savings would amount to Int$ 275 million across the six countries for which data were available.

To illustrate the country-level savings that could be incurred from switching from brands to generics for a single medicine, individual results for omeprazole 20 mg cap/tab, ciprofloxacin 500 mg cap/tab, and atenolol 50 mg cap/tab are shown for individual countries in Table 5. With the exception of Kuwait, savings of at least 50% could be obtained for all three medicines in every country for which data were available. Average cost savings ranged from about Int$ 1.9 million for atenolol to Int$ 4.7 million for omeprazole, with relatively similar average percentage savings for the three medicines (65%–71%). For omeprazole, a savings of 80% or more could be obtained in half the countries through a switch in private sector consumption from the originator brand to the lowest-priced generic product. In Colombia and Peru, more than 90% savings could be achieved for omeprazole though the absolute savings in these two countries are relatively small (approximately Int$ 582,000 and 89,000, respectively) due to low volumes consumed. A much higher absolute saving is obtained in public hospitals in China (Int$ 43.6 million) owing to both the large volumes consumed and a substantial price differential between the originator brand and lowest-priced generic products.

Discussion

The above analysis shows that cost savings of more than 50% could be generated in all but two of the countries studied if the consumption of the studied medicines shifted from originator brand products to the lowest-priced generic equivalents available at medicine outlets in the private sector. Results varied substantially across individual countries, ranging from average percent savings of more than 80% in Colombia and Indonesia to only 9% in Kuwait. Differences in the percent savings across countries can be due to market factors (e.g., size of market and number of competitors) and/or national policies, such as price regulations, that influence the prices of originator brands and generic equivalents. The countries in this study vary in their degree of pharmaceutical price regulation as well as in their methods of application. In countries such as Indonesia, Malaysia, and Ukraine, medicine prices are not subject to regulations (37–39), while in countries such as Jordan, Lebanon, and Morocco, prices are regulated using a variety of methods (40–42). In South Africa, price controls are applied to medicine at various stages in the supply chain (43), while in Pakistan only selections of medicines are subject to price controls (44). In Kuwait, the results of the WHO/HAI survey show that the low price differential between originator brands and their generic equivalents observed in this country is the result of high-priced generics and not low-priced originator brands (45). Across the 29 medicines surveyed in Kuwait, generics and originator brandswere priced at 15.7 and 17.5 times international reference prices, respectively. In Kuwait, the retail prices of medicines in the private sector are set by the government. The small price

difference between originator brand and generic medicines is probably an indication of generic medicines having their selling price based onthe selling price of the brand medicine rather than on the actual costs of manufacture (45). In such cases, price regulations may be having an unintended effect of keeping generic prices higher than what would be achieved through market competition and should be revisited. Unfortunately, evidence is lacking on the presence or absence of price regulations on pharmaceutical price levels and on the impact of different types of price regulations. It should be noted that to improve the comparability of results across countries, total cost savings have been adjusted for purchasing power parity, which changed the results substantially for most countries. Unadjusted cost savings, while not comparable across countries, would better reflect national-level savings and are available in the Appendix.

Cost savings also varied across individual medicines, though most medicines had an average percent savings in the range of 50% to 70%. Reasons for variations across individual medicines could include time since patent expiry, with greater competition occurring in products that have been off patent for a longer period of time. Indeed, omeprazole and ciprofloxacin, which have been off patent for a shorter period than other study medicines (less than 10 years), had among the highest potential cost savings (71% and 70%, respectively). Given that all the study medicines have been off patent for several years and that multiple generic equivalents exist on the international market for each, the impact of time since patent expiry on price levels has probably not been fully captured. Interestingly, the two products with the lowest savings were inhalers, namely, beclometasone (11% average savings) and salbutamol (38% average savings). The technology required to produce inhalers compared with that required to produce tablets may be such that generics are priced at levels closer to those of originator brands.

The results of this study are illustrative only and are subject to certain limitations. First, the choice of countries included in the analysis is dependent on the availability of both price data from WHO/HAI surveys and volume data from IMS Health. They have not been selected according to the level of generic penetration or other characteristics. Second, the results of this analysis are largely dependent on the selection of medicines used in the analysis. They have been selected on the basis of their frequency of inclusion in WHO/HAI surveys to increase comparability across countries. These medicines, however, may not reflect the products with the highest national consumption overall, or those with the largest consumption of brands in relation to generics. National treatment practices as well as availability of alternative treatments influence the volume share that each study medicine holds in its therapeutic class; however, volume shares of 20% or more for all but two medicines show that the study medicines are common treatment choices. A further limitation is that for each medicine included in the analysis, volume data as well as price data for both the originator brand and the lowest-priced generic

product were needed to allow an estimation of cost savings. In no country studied were all data available for all 17 target medicines, and in China, Tunisia, and Ukraine fewer than 5 medicines had sufficient price data to enable the cost savings estimate to be made. The generalizability of the study results is also limited by the fact that medicine prices collected between 2004 and 2008 were applied to consumption data from 2009 and therefore do not take into account price changes that could have occurred as a result of policy changes, market fluctuations, or other factors. It should be noted, however, that while individual surveys were conducted over a 4-year period, country-level prices of originator brands and generics were collected at the same time and are therefore comparable. A further limitation lies in the fact that in China and South Africa, price data were available only for a small number of provinces (2 and 1, respectively) and as such may not be representative of the country as a whole. In a study conducted by Wang in 2006 (46), it was noted that the purchase patterns and prices of medicines procured by hospitals in China may differ by hospital size, a factor that may translate into differences in prices charged to patients. A study of Hubei province, China, using similar methods found consistent results in terms of a high price differential between originator brands and generics; however, it was also noted that brands were not widely available in this rural province where patients cannot afford them (47).

Despite these limitations, this study demonstrates the potential for improving the cost-effective use of medicines through greater use of quality assured lower-cost generics. Even when they are not the principal payer, governments may consider intervening in this area to improve access to affordable medicines and realize the policy objectives laid out in their NMP. Government intervention should be aimed at supporting buyers who would make different purchase decisions if equipped with information about the range of products available. In the context of private sector pharmaceutical markets in LMICs, this represents the majority of purchasers and an even greater proportion of the low-income population who are less likely to have information and more likely to be pushed into financial hardship as a result of medicine purchases (48). It should be recognized, however, that there is also a segment of the population who are informed of the treatment options available and are willing to pay higher prices to purchase brands.

In implementing NMPs, governments in LMICs have a range of possible interventions to choose from, targeting issues of quality and safety, selection, procurement, supply and distribution, and use. The information provided in this article suggests that in LMICs, promoting the use of generic medicines for off-patent products may be an important strategy for improving access to medicines for the poor. Countering the information asymmetries that act as a barrier to the use of generic medicines requires both interventions to ensure that 1) patients and consumers are informed of the existence of these

products and 2) prescribers and dispensers have incentives (or at least do not have disincentives) to supply these products. Possible interventions include the following:

- Increasing confidence in generics and promoting their acceptance by professionals, patients, and the general community;
- Encouraging/requiring prescribers to prescribe generic medicines;
- Generic substitution by pharmacists;
- Incentives for wholesalers and retailers to supply generic medicines, for example, regressive mark-up schemes that allow greater margins for lower-priced products; and
- Selective financing of generic medicines, for example, by reimbursing all equivalent/similar medicines at the same price (27,49).

A multipronged strategy that employs a range of interventions is likely to be more successful, recognizing that an essential precondition to any strategy promoting generic uptake is a well-functioning regulatory system that can ensure that medicines are of assured quality. In Australia, a reimbursement policy by which patients were reimbursed only at the cost of the lowest-priced generics found that after 4 years these products represented only 17% of prescriptions dispensed. When generic substitution was added, the market share of these products increased to 54% (50). In most developed countries, policies and strategies that address prescribing and dispensing practices are used alongside those that address supply-side issues, such as market entry and penetration of generics, and pricing and reimbursement policies (49). Examples of the use of these policy tools in developing countries are limited. A WHO survey in 2007 found that generic substitution was permitted in 75% of LMICs (14). Incentives for private pharmacies to dispense generics was practiced in 30% and 27% of low- and middle-income countries, respectively, and the prescription of generic medicines in the private sector was mandatory in 22% and 28% of low- and middle-income countries, respectively. There are also examples of regressive mark-up schemes from countries such as Iran, Lebanon, Syria, South Africa, and Tunisia (51). While the existence of such policies is a positive step toward promoting generic medicine use, effective implementation is likely to be challenging in resource-constrained settings. While there may also be a role for generic manufacturers in promoting the use of their products, objective information from a neutral third-party is needed to address the information asymmetries that characterize pharmaceutical markets and prevent consumers from making informed choices.

Substandard and counterfeit medicines are a valid concern, particularly in countries that lack a stringent regulatory authority, and can undermine prescribers' and patients'

confidence in generics as a whole. However, prescribers and dispensers who benefit from the sale of higher-cost medicines (e.g., when margins are set as a percentage of the price) may also encourage the perception that generics are less effective and/or unsafe and that originator brand products are superior (15). When medicines provided through official channels are highly priced, it pushes patients to purchase medicines in unregulated sectors (e.g., street markets) where substandard and counterfeit medicines are most often found (52). It is therefore particularly important that low-cost, quality-assured generics be made available through regulated channels (both public and private). If a generic product has been shown to be therapeutically equivalent, for example, through in vivo bioequivalence testing or other methods, it can be considered interchangeable with the originator brand product in terms of safety and efficacy (53), though other product characteristics, such as taste, smell, or packaging, may differ. The issue of interchangeability of brands and generics is the subject of debate in certain disease areas (e.g., epilepsy) where some treatments have a narrow therapeutic index, and therefore a higher risk of loss of efficacy and/or toxicity (54,55). Stringent regulatory control including the capacity to ensure quality is particularly important in these cases to allow the most cost-effective medicines to be used while ensuring patient safety. The issue of changing patients' treatment to take advantage of lower prices and its impact on adherence could also be a concern. While data are limited, one study of hypertensive patients in the Netherlands showed that generic substitution of antihypertensive drugs did not lead to lower adherence, more discontinuation of treatment, or higher cardiovascular disease–related hospitalizations compared with brand-name therapy (56).

It should be emphasized that the generic medicines used in this study represent the lowest-priced products registered in the country and available in regulated facilities at the time of the survey. Lower-priced products are often available through unregulated channels (e.g., street vendors); however, because the quality of these products cannot be assured, they did not factor into this analysis. Conversely, the use of higher priced generic equivalents, such as branded generics, would not produce as high a saving. In addition, the estimates in the study reflect a total shift in consumption from originator brand products to their generic equivalents, which does not represent a feasible scenario under real world conditions. A study that investigated the impact of generic substitution in Sweden in the first year of implementation found that the actual savings achieved were on average 60% of the total possible savings and largely depended on the extent to which pharmacies kept the cheapest brand in stock (57). However, countries such as Denmark, Czech Republic, Turkey, and Poland have achieved generic medicine consumption of more than 50% of the total pharmaceutical market by volume (58), and the market share of generic medicines has risen over each of the past 5 years in the United States and now accounts for 78% of all prescriptions dispensed (59). Opportu-

nities may therefore exist for LMICs to im-prove generic uptake and by consequence, improve the affordability of treatment for their populations.

The data presented in this article reflect a static analysis of prices and consumption volumes, which themselves are not static and will vary over time. Policies to change consumption toward lower-price generics may affect price levels as well as total consumption volumes. For example, the increased use of lowestpriced generics could induce originator brand manufacturers to reduce their prices, thereby reducing cost savings. One study of generic substitution in Finland found that a substantial amount of cost savings was attributable to price competition generated by substitution, as opposed to substitution itself (60). The potential impact of the increased use of lowest-priced generics on consumption is difficult to predict because of a lack of data on the price elasticity of demand for medicines in LMICs. While price elasticity of individual demand may be lower for pharmaceuticals than for other health services (61), and is generally low (15). Given that lower-income consumers are generally more price sensitive (61), however, promoting the use of lower-priced generics may result in an increase in overall demand or a shift in demand from the informal sector to the formal private sector.

Recognizing the dynamic nature of pharmaceutical markets, this study serves to illustrate the potential to improve cost-effective medicine use through a shift in consumption from originator brands to lowest-priced generics in a selection of developing countries. While such estimates have been previously conducted in developed countries, to the authors' knowledge it is the first time that such an analysis has been conducted in developing countries. Further research into the determinants of the relative market shares of originator brands and generics in developing countries, the price elasticity of demand for medicines in these countries, the effects of pharmaceutical price regulations and strategies to promote generic medicine use, and the possible effects of shifts in consumption from originator brands to generics on price levels would help to refine the estimates of cost savings that could be achieved.

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Tables

Table 1. Countries included in the analysis (both IMS-Health medicine consumption data and WHO/HAI medicine price data were available), with pharmaceutical expenditure indicators*

Country (WHO/HAI survey year)	Year of pharmaceutical expenditure data	Per capita total pharmaceutical expenditure (TPE) (constant year, 2005), USD PPP	TPE as % of GDP	TPE as % of Total Health Expenditure (THE)	Pharmaceutical private spending as % TPE	Per capita public pharmaceutical spending (constant year, 2005), USD PPP	Per capita private pharmaceutical spending (constant year, 2005), USD PPP
China[§] (2004, 2006)	2006	77.6	1.7	36.2	73.5	32.6	57.0
Colombia (2008)	2006	87.0	1.4	19.3	77.9	19.2	67.7
Ecuador (2008)	2006	128.9	1.9	35.1	77.6	28.8	100.0
Indonesia (2004)	2006	22.6	0.7	28.3	94.0	1.4	21.2
Jordan (2004)	2001	101.0	2.9	30.1	81.5	18.7	82.3
Kuwait (2004)	2006	126.0	0.3	13.6	ND	76.7	ND
Lebanon (2004)	1998	251.7	3.0	25.4	94.4	14.2	237.6
Malaysia (2004)	2005	71.3	0.6	14.7	66.0	24.2	47.0
Morocco (2004)	2006	54.6	1.4	27.1	ND	ND	ND
Pakistan (2004)	2001	18.1	1.0	43.7	41.5	10.6	7.5
Peru (2005)	2006	68.5	1.0	22.4	77.2	15.7	52.9
Philippines (2005)	2006	47.7	1.6	41.1	90.1	4.7	43.0
South Africa[†] (2004)	2006	100.5	1.2	14.5	ND	ND	ND
Thailand (2006)	2006	110.3	1.5	42.9	12.3	96.7	13.5
Tunisia (2004)	2006	229.9	3.5	67.6	ND	69.0	ND
Ukraine (2007)	2006	111.5	1.8	26.5	40.0	66.9	44.6
United Arab Emirates (2006)	2006	208.8	0.4	15.4	---	ND	ND

** Source: Lu Y, Hernandez P, Abegunde D, Edejer T. Medicine expenditures annex to Medicine Expenditures. In: The World Medicines Situation 2011. 3rd Edition. Geneva: World Health Organization, 2011. Available: http://www.who.int/medicines/areas/policy/world_medicines_situation/en/index.html. Accessed 08 November 2011.*

[§] Medicine price data based on two sub-national surveys conducted in Shandong Province (2004) & Shanghai (2006)

[†] Medicine price data based on a sub-national survey conducted in Gauteng Province

Abbreviations: USD - United States Dollar; PPP - Purchasing Power Parity; GDP - Gross domestic product; ND - no data.

Table 2. Medicines included in the analysis

Medicine	Medicine category	% of WHO/ HAI surveys that included medicine	Mean % consumption as proportion of therapeutic class (ATC level 3) (min, max)	Mean % consumption of originator brand product as a proportion of medicine consumption (min, max)
Aciclovir 200mg cap/tab	Antiviral	89	60.1 (16.1 95.6)	28.8 (0.7, 100)
Amitryptilline 25mg cap/tab	Antidepressant	94	25.0 (0.2, 71.6)	100 (100, 100)
Atenolol 50mg cap/tab	Cardiovascular	94	30.9 (1.7, 62.0)	36.3 (1.9, 93.0)
Atorvastatin 10mg cap/tab	Cardiovascular	11	30.5 (8.2, 55.1)	60.6 (2.8, 100)
Beclometasone 50mcg/dose inhaler	Antiasthmatic	89	37.8 (0.0, 99.2)	39.3 (0.0, 95.7)
Captopril 25mg cap/tab	Cardiovascular	100	23.9 (0.0, 88.8)	31.9 (0.0, 100)
Carbamazepine 200mg cap/tab	Antiepileptic	83	20.0 (0.0, 42.1)	62.3 (15.0, 100)
Ceftriaxone 1g/vial injection	Antibacterial	100	52.4 (2.0, 96.4)	20.1 (0.0, 74.0)
Ciprofloxacin 500mg cap/tab	Antibacterial	94	57.9 (1.6, 85.2)	11.1 (0.2, 25.0)
Co-trimoxazole susp 8 + 40 mg/ml	Antibacterial	94	99.3 (93.4, 100)	24.4 (0.0, 77.4)
Fluoxetine 20mg cap/tab	Antidepressant	100	14.8 (5.6, 27.5)	27.3 (0.8, 90.8)
Glibenclamide 5mg cap/tab	Antidiabetic	100	49.0 (4.6, 91.6)	34.6 (0.8, 93.3)
Lovastatin 20 mg cap/tab	Cardiovascular	44	6.9 (0.0, 52.5)	65.5 (30.9, 100)
Omeprazole 20mg cap/tab	Antiulcerant	100	32.5 (9.2, 66.5)	3.4 (0.0, 20.8)
Ranitidine 150mg cap/tab	Antiulcerant	100	21.8 (6.4, 43.8)	25.5 (0.0, 93.2)
Salbutamol 100mcg/ dose inhaler	Antiasthmatic	100	95.3 (56.8, 100)	71.0 (0.0, 100)
Simvastatin 20mg cap/tab	Cardiovascular	50	30.6 (2.1, 70.8)	12.6 (0.2, 57.9)
		AVERAGE (MIN, MAX)	40.5 (6.9, 99.3)	38.5 (3.4, 100)

Table 3. Total potential cost savings and average percentage savings that could be obtained from switching private sector consumption from originator brands to lowest-priced generics, by county

Country* (n= number of medicines)	Average percentage savings across individual medicines (%) (95% CI) (min, max) [§]	Total potential cost savings, 2008 Int$
China, public hospitals (n=4)[†]	65 ± 26 (38, 93)	369,889,300
Colombia (n=9)	89 ± 4 (76, 97)	7,757,442
Ecuador (n=12)	63 ± 10 (40, 90)	4,813,935
Indonesia (n=9)	84 ± 6 (65, 95)	15,259,172
Jordan (n=11)	56 ± 8 (33, 78)	1,810,218
Kuwait (n=6)	9 ± 8 (-5, 25)	44,785
Lebanon (n=8)	68 ± 9 (51, 85)	4,035,033
Malaysia, private hospital and retail sectors (n=10)	67 ± 8 (45, 85)	16,682,860
Morocco (n=6)	52 ± 18 (18, 78)	8,338,820
Pakistan (n=9)	51 ± 19 (0, 86)	38,830,406
Peru (n=11)	79 ± 11 (33, 92)	5,141,464
Philippines (n=9)	57 ± 9 (24, 69)	38,183,032
South-Africa (n=7)[‡]	79 ± 13 (41, 93)	6,601,871
Thailand (n=7)	76 ± 13 (44, 93)	3,997,118
Tunisia (n=3)	26 ± 13 (14, 36)	758,853
Ukraine (n=5)	52 ± 39 (-10, 95)	1,287,355
United Arab Emirates (n=12)	53 ± 6 (31, 74)	8,787,523
AVERAGE	**60**	**31,301,717**

** Results refer to the private sector unless otherwise indicated.*
[§] Simple average of the percentage savings for individual medicines.
[†] Price data is from the public sector and is based on 2 surveys conducted in Shanghai (2006) and Shandong (2004) provinces.
[‡] Price data based on a survey conducted in Gauteng province (2004).
Abbreviations: Abbreviations: Int$ - International Dollars; min – minimum; max - maximum.

Table 4. Total potential cost savings and average percentage savings that could be obtained from switching private sector consumption from originator brand to lowest-priced generic, by medicine

Medicine* (n=number of countries)	Average percentage savings across countries (95% CI) (min, max)§	Total potential cost savings, 2008 Int$
Aciclovir 200mg cap/tab (n=11)	70 ± 13 (18, 89)	2,567,350
Atenolol 50mg cap/tab (n=13)	65 ± 12 (6, 85)	24,300,804
Atorvastatin 10mg cap/tab (n=2)	69 ± 32 (53, 85)	2,197,993
Beclometasone 50mcg/dose inhaler (n=2)	11 ± 41 (-10, 33)	28,687
Captopril 25mg cap/tab (n=12)	57 ± 17 (-5, 92)	8,742,552
Carbamazepine 200mg cap/tab (n=10)	64 ± 11 (41, 91)	6,479,659
Ceftriaxone 1g/vial injection (n=5)	73 ± 18 (51, 93)	275,060,435
Ciprofloxacin 500mg cap/tab (n=9)	70 ± 17 (9, 95)	21,856,907
Co-trimoxazole susp 8 + 40 mg/ml (n=10)	61 ± 15 (14, 95)	5,697,460
Fluoxetine 20mg cap/tab (n=10)	72 ± 14 (28, 97)	9,488,476
Glibenclamide 5mg cap/tab (n=11)	60 ± 15 (8, 93)	18,987,737
Lovastatin 20 mg cap/tab (n=1)	57 (57, 57)	213,152
Omeprazole 20mg cap/tab (n=12)	71 ± 13 (12, 97)	56,484,455
Ranitidine 150mg cap/tab (n=15)	67 ± 12 (24, 92)	23,206,566
Salbutamol 100mcg/dose (n=8)	38 ± 13 (0, 58)	18,946,479
Simvastatin 20mg cap/tab (n=7)	53 ± 14 (20,76)	57,870,474

**Amitryptilline 25 mg cap/tab is not included as no country in the study had all the necessary data to estimate cost savings.*

§ Simple average of the percentage savings for individual countries.

Abbreviations: Int$ - International Dollars; min – minimum; max – maximum.

Table 5. Potential cost savings and average percentage savings that could be obtained from switching private sector consumption from originator brands to lowest-priced generics for 3 individual medicines

	Omeprazole 20mg cap/tab		Ciprofloxacin 500mg cap/tab		Atenolol 50mg cap/tab	
Country*	**Potential cost savings, 2008 Int$**	**Percentage savings (%)**	**Potential cost savings, 2008 Int$**	**Percentage savings (%)**	**Potential cost savings, 2008 Int$**	**Percentage savings (%)**
China, public hospitals[§]	43,621,073	81	ND	ND	ND	ND
Colombia	582,296	97	ND	ND	603,316	85
Ecuador	6,240	84	ND	ND	441,646	50
Indonesia	2,659,927	82	ND	ND	2,262,877	73
Jordan	10,607	61	162,176	78	230,505	60
Kuwait	11,602	12	369	9	472	6
Lebanon	ND	ND	865,732	72	785,874	80
Malaysia, private hospital and retail sectors	1,122,190	76	3,454,603	85	1,509,044	72
Morocco	1,929,864	78	ND	ND	ND	ND
Pakistan	4,672,532	80	ND	ND	14,240,335	62
Peru	88,576	92	ND	ND	446,825	84
Philippines	1,203,861	63	11,707,674	65	1,426,862	69
South-Africa[†]	ND	ND	2,755,157	76	450,242	78
Thailand	ND	ND	711,602	93	1,308,148	78
Ukraine	ND	ND	196,809	95	ND	ND
United Arab Emirates	575,686	52	2,002,784	58	594,658	52
Total potential cost savings	56,484,455		21,856,907		24,300,804	
Average cost savings	4,707,038	71	2,428,545	70	1,869,293	65

** Results refer to the private sector unless otherwise indicated. Tunisia is not included as cost savings estimates were not available for these three medicines due to lack of data.*

[§] Price data is from the public sector and is based on 2 surveys conducted in Shanghai (2006) and Shandong (2004) provinces.

[†] Price data based on a survey conducted in Gauteng province (2004).

Abbreviations: Int$ - International Dollars; ND - no data.

Appendix

Table A1. Total potential cost savings that could be obtained from switching private sector consumption from originator brands to lowest-priced generics, without PPP adjustments, by county

Country* (n= number of medicines)	Total potential cost savings (2008 USD)
China, public hospitals (n=4)†	86,492,276
Colombia (n=9)	2,876,453
Ecuador (n=12)	3,023,151
Indonesia (n=9)	6,405,597
Jordan (n=11)	887,262
Kuwait (n=6)	64,261
Lebanon (n=8)	4,397,432
Malaysia, private hospital and retail sectors (n=10)	7,419,942
Morocco (n=6)	3,175,435
Pakistan (n=9)	12,606,083
Peru (n=11)	2,520,356
Philippines (n=9)	9,415,319
South-Africa (n=7)‡	3,461,600
Thailand (n=7)	1,348,669
Tunisia (n=3)	280,001
Ukraine (n=5)	458,892
United Arab Emirates (n=12)	10,671,587
AVERAGE	**9,147,313**

** Results refer to the private sector unless otherwise indicated.*
† Price data is from the public sector and is based on 2 surveys conducted in Shanghai (2006) and Shandong (2004) provinces.
‡ Price data based on a survey conducted in Gauteng province (2004).
Abbreviations: PPP - Purchasing Power Parity. USD - United States Dollars.

Table A2. Total potential cost savings that could be obtained from switching private sector consumption from originator brand to lowest-priced generic, without PPP adjustments, by medicine

Medicine* (n=number of countries)	Total potential cost savings (2008 USD)
Aciclovir 200mg cap/tab (n=11)	1,138,597
Atenolol 50mg cap/tab (n=13)	9,695,977
Atorvastatin 10mg cap/tab (n=2)	1,047,610
Beclometasone 50mcg/dose inhaler (n=2)	16,549
Captopril 25mg cap/tab (n=12)	2,818,529
Carbamazepine 200mg cap/tab (n=10)	3,149,571
Ceftriaxone 1g/vial injection (n=5)	64,549,677
Ciprofloxacin 500mg cap/tab (n=9)	9,639,515
Co-trimoxazole susp 8 + 40 mg/ml (n=10)	2,126,684
Fluoxetine 20mg cap/tab (n=10)	4,786,995
Glibenclamide 5mg cap/tab (n=11)	7,146,653
Lovastatin 20 mg cap/tab (n=1)	69,199
Omeprazole 20mg cap/tab (n=12)	16,493,621
Ranitidine 150mg cap/tab (n=15)	9,705,842
Salbutamol 100mcg/dose (n=8)	6,339,098
Simvastatin 20mg cap/tab (n=7)	16,780,201

**Amitryptilline 25 mg cap/tab is not included as no country in the study had all the necessary data to estimate cost savings.*
Abbreviations: USD - United States Dollars.

Table A3. Potential cost savings that could be obtained from switching private sector consumption from originator brands to lowest-priced generics for 3 individual medicines, without PPP adjustments

Country*	Potential cost savings (2008 USD)		
	Omeprazole 20mg cap/tab	Ciprofloxacin 500mg cap/tab	Atenolol 50mg cap/tab
China, public hospitals[§]	11,345,033	ND	ND
Colombia	215,915	ND	223,709
Ecuador	3,919	ND	277,354
Indonesia	1,116,602	ND	949,926
Jordan	5,199	79,489	112,980
Kuwait	16,648	ND	677
Lebanon	ND	943,486	856,456
Malaysia, private hospital and retail sectors	499,110	1,536,485	671,169
Morocco	734,895	ND	ND
Pakistan	1,516,912	ND	4,623,048
Peru	43,420	ND	219,034
Philippines	296,853	2,886,923	351,841
South-Africa[†]	ND	1,444,629	236,078
Thailand	ND	245,633	451,550
Ukraine	ND	70,155	ND
United Arab Emirates	699,115	2,432,185	722,154
Total potential cost savings	16,493,621	9,638,985	9,695,977
Average cost savings	$1,374,468	1,204,873	745,844

** Results refer to the private sector unless otherwise indicated. Tunisia is not included as cost savings estimates were not available for these three medicines due to lack of data.*

[§] Price data is from the public sector and is based on 2 surveys conducted in Shanghai (2006) and Shandong (2004) provinces.

[†] Price data based on a survey conducted in Gauteng province (2004).

Abbreviations: Abbreviations: USD - United States Dollars; ND - no data.

Chapter 7

Discussion

This concluding chapter discusses the usefulness of national data on medicine price and availability to inform our understanding of access to medicines at the supra national level as a tool for evidence-based advocacy and policy making. The findings of this thesis are placed in a broader perspective, opportunities and limitations related to aggregating national data on the pharmaceutical sector are described, and the policy and programmatic implications of the study findings are presented. Finally, areas for future research are identified that could improve our understanding of access to medicines at a global level.

Using country-level data to report on global trends in medicine prices and availability—what can it tell us?

As described in the introduction of this thesis, prior to the late 1990s very little data was available regarding the prices of medicines in low- and middle-income countries (LMICs). While there may have been a perception that prices were unaffordable, the absence of concrete evidence made it challenging to advocate for interventions to lower medicine prices. Supported by a resolution of WHO Member States (1), in 2001 WHO and Health Action International (HAI) initiated a project to address the lack of transparency around medicine prices with a specific focus on measuring and reporting on medicine prices and availability in LMICs. This project has been successful in generating a critical mass of data on medicine prices and availability from over 70 countries across the globe. While primarily used at national level to examine the country situation towards identifying issues and possible policy responses, the hypothesis of this thesis was that this data could also be aggregated and analysed in a variety of ways that could improve our general understanding of access to medicines in LMICs and identify trends. Throughout the chapters of the thesis, this hypothesis is investigated through various analyses of price, availability, and affordability as an extension of price, to understand what insights could be gained in terms of access to medicines.

As a first step, a comprehensive secondary analysis of national-level data was undertaken to provide a global overview of the price and availability of commonly-available medicines. The secondary analysis presented in **Chapter 2** was the first time that medicine prices, availability and affordability were reported for as large a group of LMICs. Since its publication in January 2009 through July 2012, it had been cited in 118 peer-reviewed publications (2), suggesting a strong demand for published evidence on this topic. It has, and continues to be, a valuable resource for those interested in reporting on the price and availability of medicines. The methods applied in this study were seminal

in that they set a standard for aggregation of country-level price data that was acceptable to the scientific community and to which subsequent secondary analysis would be evaluated. This included several steps to improve the comparability of results across countries, namely limiting the analysis to a subset of frequently-surveyed medicines, and adjusting for survey year, inflation and purchasing power parity. Results were presented for all countries, as well as broken down by WHO Region and World Bank Income Groups to investigate whether results varied by geographic area and/or income level.

This study showed that overall, medicine availability is generally low and prices are frequently high, with much scope for improvement. Specifically, mean availability of a basket of 15 commonly-used medicines was 38.4% in the public sector and 64.2% in the private sector. Private sector patient prices ranged from 9 to 25 times international reference prices for lowest-priced generic products across WHO regions, which suggests that even generics may be high-priced in the private sector. However results varied significantly across countries, sectors, and medicines, which is likely the result of the interaction of the multiplicity of factors including the policies and structure that govern the pharmaceutical sector. For example, while private sector prices were generally high, public sector procurement prices were, on average, reasonable (on par with international reference prices). This refutes the conventional wisdom that procurement inefficiencies are largely to blame for low public sector availability. In fact, many countries are procuring at very competitive prices, suggesting that a lack of financing could be a stronger factor in the observed low availability. However, in countries where patients pay for medicines in the public sector, the prices of even the lowest-priced generics can still be high. For the basket of 15 medicines studies, public sector patient prices ranged from 3.18 times international reference prices in the Americas to 11.95 times in Western Pacific countries. The observed mark-ups applied in some public sectors (e.g. cumulative mark-ups of over 80% from cost, insurance and freight (CIF) price to final patient price in Ethiopia and Mali) suggests that some public sectors may be generating revenue from medicine sales to subsidize other parts of the health care system. For example, in China it is estimated that approximately 41% of the total institutions' revenue in the public sector comes from sales of medicines (3), and three sub-national surveys conducted using the WHO/HAI methodology found public sector patient prices that were higher than those in the private sector (4). The use of medicine sales as a revenue generating mechanism places an inequitable financial burden on patients who require medicines as part of their health care compared to those who do not.

This paper included a breakdown of the components of medicine prices in selected countries, which is essential for understanding the underlying determinants of high prices. For example, without knowing whether high patient prices are caused by high procurement prices, supply chain markups or other factors, it is difficult to design ap-

propriate policy interventions. In the private sector, wholesale mark-ups ranged from 2% to 380%, whereas retail mark-ups ranged from 10% to 552%, suggesting that supply chain charges can contribute substantially to final medicine prices. As this analysis focuses on the downstream supply chain, it could be usefully supported by additional research to elucidate medicine production cost structures and assess how these contribute to manufacturer's selling prices.

While investigating medicine prices and availability across a range of medicines is useful in identifying overarching issues and trends, individual therapeutic areas can be studied across a range of countries to elucidate whether any disease-specific factors may be influencing price and/or availability. Two additional studies on individual diseases – cardiovascular diseases and epilepsy (**Chapters 4.1 and 4.2,** respectively) – demonstrate the value in such analyses. For example, for both cardiovascular disease (CVD) medicines and epilepsy medicines availability of generics in the public sector was low (average of 26.3% for CVD medicines and availability of < 50% for nearly all antiepileptics). While the findings are similar, for epilepsy the low availability of generics is likely to be caused in part by the narrow therapeutic index of antiepileptics and the resulting risk of loss of efficacy and/or toxicity that may make prescribers reluctant to switch from originator brands to generics. Stringent regulatory control and the capacity to ensure quality and ensure prescribers are aware of quality-assured options are therefore likely to be key areas of focus in efforts to improve access. Similar studies have also been conducted by others to examine the price and availability of medicines for individual disease areas (5,6).

The low availability of essential medicines reported in **Chapter 2**, particularly in the public sector, raises questions regarding access to medicines for those seeking care in this sector. While it is important to identify low overall availability, it is also of value to understand whether medicines for certain disease areas have particularly low availability. This question was explored in **Chapter 3**, specifically by investigating whether availability is consistently low or whether certain disease areas have better/worse availability than others. A previous study had reported that medicines used for chronic diseases such as cardiovascular disease, diabetes and asthma had low availability in a small sample of developing countries (7). Building from this study and the results from **Chapter 2**, data on medicine availability at public and private sector facilities from a wide range of countries was used to compare the availability of medicines used for acute and chronic conditions. Results showed that while medicine availability is generally low, there can be variation across disease areas, with some disease areas being strong drivers of low availability overall. Specifically, medicines for chronic conditions were substantially less available than generic medicines for acute conditions in both the public sector (36.0% availability versus 53.5%) and the private sector (54.7% versus 66.2%). Of the chronic diseases studied, antiasthmatics, antiepileptics and antidepres-

sants had lower availability than antiulcerants and oral antidiabetics. Another key finding from this study was that the availability gap between acute and chronic disease medicines was inversely related to country income level (i.e. lowest income countries had the largest gap in availability), particularly in the public sector. This is an important finding in that it implies that the public health systems of lower income countries are not adapting as needed to the epidemiological shift taking place from acute to chronic illnesses (8,9). While these countries may still have a substantial burden of acute illness and may in fact be experiencing a "double burden of disease" where they need to address both acute and chronic illnesses simultaneously, priority must be given to transitioning health systems towards better management of chronic illnesses in order to address the growing burden of these conditions.

While price is an important component of medicine access, it is important to understand how price translates into affordability to better understand the relationship between price levels and access. Affordability has been defined as "concerned with securing some given standard of a commodity (or different standards) at a price … which does not impose, in the eyes of a third party (usually government) an unreasonable burden on household incomes" (10). **Chapter 2** reported on the affordability of medicines by comparing mean medicine prices to the daily wage of the lowest-paid government worker to estimate the number of days wages needed to purchase a course of treatment. In the private sector, standard treatments frequently cost over a days' wage even when lowest-priced generics were used. This is particularly concerning for chronic diseases that require ongoing medicine purchases which are less amenable to short-term financial coping strategies such as borrowing or selling assets. In **Chapter 5**, a deeper investigation into medicine affordability is conducted by accounting for consumers ability to pay using household expenditure data and information on income distributions as proxies. These metrics were used in combination with medicine price to determine the proportion of a population that would be pushed under the international poverty lines as a result of medicine purchases. This builds on the methods of Wagstaff and Van Doorslaer (11) which are underpinned by the principle that "no one ought to be pushed into poverty – or further into poverty – because of health care expenses".

In the 17 countries studied, purchasing a month's supply of generic glibenclamide, for example, would push an additional 6% of populations below the US $1.25/day poverty line. The affordability results from **Chapters 2 and 5** show that while the concept of affordability is difficult to measure and quantify, it may be a better proxy for access than price alone as it takes into account the income levels of consumers. **Chapter 5** also showed that substantially greater proportions of people would be pushed into poverty through the consumption of originator brands as compared with their generic equivalents (e.g. for salbutamol an additional 10% of the population would fall below

the US $1.25/day poverty line by purchasing the originator brand vs. 2% with the lowest priced generic). **Chapter 6** explored this finding in greater depth by estimating the potential cost savings that could be achieved by switching private sector consumption from originator brands to their lowest-price generic equivalents. From a methodological perspective, this analysis demonstrated how price data can be combined with other data on the pharmaceutical sector, in particular consumption volumes, to explore potential options for improving access. The analysis showed that a savings of approximately 60% could be achieved by switching private sector consumption from originator brands to lowest-priced generics. These results suggest that, as part of national medicines policies, governments should consider including strategies to promote cost effective generic medicine use in the private sector as a strategy for improving access.

The body of work described in Chapters 2-6 confirms the hypothesis that medicine price and availability data can be used in a variety of ways to improve our understanding of access to medicines in LMICs and to support evidence-based advocacy and policy making. While results vary across individual countries, global and regional trends are observed that raise concerns regarding access to medicines in these contexts. These include the low availability of medicines in the public sectors in many countries, which raises questions about the levels of financing being allocated to supply medicines in public health facilities. High private sector prices as compared to international reference prices, particularly for originator brands but also for generics in some cases, is particularly concerning given the low availability in the public sector where medicines are usually provided for free or at low cost. Given the trends observed and their implications for medicine access more generally, presenting global and regional results can be seen as highly valuable in terms of improving transparency on medicine price and availability issues, raising awareness of medicine access issues globally, and stimulating global health players to take action. Important policy issues have also been illuminated, namely the need for increased attention to the management of chronic diseases in low income countries, and promoting cost-effective medicine use in the private sector as a measure to improve access. While an investigation of national-level results is needed to design appropriate policy interventions, this body of work suggests that important policy areas requiring attention from both policy makers and other national and international stakeholders, can also be elucidated by looking at results across countries.

Methodological issues in measuring medicine price, availability and affordability

The capacity to use national-level data to accurately report on medicine prices, availability and affordability at the global level depends on two key factors:

1. the strength of the underlying methodology used to collect data at the country level and the resulting quality of the data reported;

2. the comparability of the data across countries and the reliability of the methods used to aggregate data at the regional and global level.

Historically, very little information has been available about the availability and especially the price of medicines in LMICs. Beginning in the late 1990s, some initial efforts were made to collect medicine prices and compare then across LMICs (12-15). However these studies were relatively small and did not use consistent methodologies that would allow comparative data to be generated. The WHO/HAI Project on Medicine Prices and Availability attempted to address these issues by developing a standardized methodology for surveying medicines availability and prices in facilities. The project supported the application of the survey method in a large number of countries, and contributed to price transparency by making the data publicly available. Today, the landscape of medicine pricing data has changed in that there are many sources of medicine price data available (16). Efforts include websites that provide information on reimbursement prices such as the Common European Drug Database (17), the publication of procurement prices on a regional basis such as the WHO Western Pacific Region Price Information Exchange (18), databases of prices paid by international donors such as the Global Price Reporting Mechanisms for HIV, Tuberculosis and Malaria (19), and reports on patient price levels for individual disease areas (20). IMS Health (www.imshealth.com/), a pharmaceutical market intelligence company, also collects data on pharmaceutical prices in a wide range of countries though the methodologies employed vary by country (21). While this data is generally only available at a fee, recently efforts have been made to make this data available for research purposes (22). While other data sources exist, the data from WHO/HAI surveys are the most comprehensive in terms of both number of countries surveyed and therapeutic categories of medicines studied. A major strength of the WHO/HAI method is the standardized approach that promotes a consistent approach across individual surveys, thereby making individual results more comparable. Considerable efforts have been made to develop and refine a methodology that could easily be reproduced in a standardized and reliable way. This included the development of a draft methodology (23), pilot testing in 9 countries (24), and refinement of the original method based on the learnings acquired in conducting the survey

in a variety of settings and health systems. Currently a standardized survey guide and tools, available in multiple languages, is reinforced by regional training workshops that promote a common approach. In addition, an automated survey workbook is used that generates a standardized analysis (25). A second key strength of the WHO/HAI method is the multiple quality control steps that are applied to identify and correct errors. Three tiers of quality control checks are conducted during data collection, followed by a double entry of data into the survey workbook to identify any data entry errors. Once data is entered, an automated data checking program is run which highlights outlier data for further verification. Finally, before any data is entered into the centralized database of survey results, a thorough manual verification of data is undertaken. These multiple steps ensure that any data available in the global database are reliable.

Another key issue in the reliability of country-level data is the degree to which data are nationally representative. In the WHO/HAI surveys, data are collected from a relatively small number of medicine outlets in six geographic or administrative regions of the country (for each sector, a minimum of 5 outlets are sampled per region) (26). It should be noted that this sampling frame is recommended as a minimum, and several countries have sampled a larger number of facilities. A validation study conducted in Peru showed that this sampling frame does yield a nationally representative sample (27), however validation studies from additional countries would be useful to further support this finding. In very large countries this sampling frame may not be sufficient to generate a nationally representative sample, and as such the survey method is applied on a sub-national basis with sampling conducted for a single province or state. The extent to which subnational surveys are representative of the country situation is likely to vary according to the country situation. While availability tends to be more variable, results from state- and provincial-level surveys in India, China and Sudan indicate that price results can be fairly consistent. For example, median price ratios for lowest priced generics in the private sector ranged from 0.51 to1.77 in China (3 surveys), from 4.35 to 5.31 in Sudan (4 surveys), and from 1.54 to 2.83 in India (8 surveys) (28). However, this may not hold in all circumstances and large countries should attempt to elucidate any regional disparities which may exists by conducting subnational surveys. This is especially relevant in countries where health care in managed at the state/provincial level, and/or in cases where geography or security risks may render access to medicines particularly difficult.

As described above, the WHO/HAI method has several strengths which are supportive of its use as a reputable data source for international reporting on medicine prices and availability. However, the methods also have some limitations which have been described in detail in the various chapters of this thesis and must be borne in mind when analysing and interpreting aggregate data. In terms of the availability metric, this represents avail-

ability of an individual product on the day of data collection and may not always be reflective of average availability over time. However, from the perspective of a person who is visiting a facility to obtain a medicine, what matters most is that the product is available on the day that it is needed. In this respect the WHO/HAI method is an accurate reflection of what a patient finds when visiting a health facility. In addition, medicine availability is specific to an individual strength and dosage form, for example, amoxicillin 250mg may not be available while amoxicillin 500mg would be available but is not part of the surveyed medicines. In the study described in **Chapter 3** which specifically investigates medicine availability, an attempt was made to address this issue by combining alternate strengths of the same medicine to account for country-level differences in medicine use. That is, the availability of amoxicillin represents the combined availability of any surveyed strength at each individual facility; if either the 250mg or the 500mg strength was available, the medicine was recorded as available. Equivalent treatments in other therapeutic classes may also be available but not captured in the survey, e.g. captopril is surveyed and is not available but enalapril is available but was not surveyed. An attempt is made to overcome this issue through the targeted selection of survey medicines to reflect what is recommended in national treatment guidelines and what is commonly found at the facility level. The extent to which countries factor this into their survey determines the extent to which availability is accurately captured. While these efforts improve the availability estimates generated in WHO/HAI surveys, surveys that capture the availability of the full range of therapeutic alternatives for a given disease area (e.g. ACT Watch) (20), may be a more accurate reflection of availability.

The price data that is collected through WHO/HAI surveys is also subject to certain limitations. Firstly, while efforts are made to standardize the pack sizes for which data are collected, economies of scale resulting from larger pack sizes might cause price differences across individual facilities. Another issue may arise in countries where prices are not clearly labelled on medicine packages and sellers adjust the retail price based on their perception of what the buyer is willing to pay ("price discrimination") (29). A further limitation relates to the use of a set of international prices as a comparator to the local price. In WHO/HAI surveys, such median price ratios (MPR) are reported. The comparator is generally the list of international reference prices compiled and reported by Management Sciences for Health (MSH) (30). These have been selected as the most useful standard as they are updated annually, are always available and are relatively stable (26). MSH prices represent recent procurement prices offered by both not-for-profit and for-profit suppliers to developing countries for multi-source products. As MSH prices are purchase prices the goal for retail prices is not to obtain a ratio of 1 but rather a ratio that accounts for reasonable local distribution costs. The use of MPRs is useful in that it provides a reference by which to evaluate local prices. For example, it is difficult to know if a certain price for a certain medicine is high or low. However, if you

know that the local price is five times the international price, this is more indicative of a high price as local distribution costs should not be contributing substantially to such a high differential. However, using a set of comparator prices means that any limitations in this price data are carried over into the national price results. For example, in the MSH data set most, but not all, prices reported are Ex-works which is the cost of the medicine at the factory gate excluding any transportation or related costs (30). Variations in the types of prices reported by MSH, e.g. with or without additional costs such as international shipping or insurance, may have a small impact on the resulting price ratios for individual medicines. In addition, the number of price points for individual medicines varies and can be as low as one. If a price ratio is calculated based on a single reference price that is particularly high or low, it will skew the result. This was the reason for which results on losartan were not able to be reported in **Chapter 4.1**. A final implication in the use of a set of comparator prices is the fact that all survey medicines must have a comparator price to allow calculation of the price ratio and inclusion into aggregate results. This may result in the exclusion of medicines with significant local importance into aggregate results, though the prices of these medicines can still be reported in local currency or in international dollars (26).

Affordability is not measured as such in the WHO/HAI survey but rather is an extension of the price data that is collected. That is, median local prices and the daily wage of the lowest-paid government worker are used to estimate the number of days needed to purchase a course of treatment. As described in Chapter 5, this measure has certain limitations and can really only be seen as a broad indication of medicine affordability. Certainly, in many LMICs a substantial proportion of the population earns less than the lowest-paid government worker (31). In addition, the need for other non-discretionary expenditures (eg, food or housing), seasonal fluctuations in income, the number of dependants who live on this wage, and the full costs of treatment that includes consultation fees, diagnosis, etc., are not accounted for. However, on a broader level, true affordability is a difficult concept to conceptualize and measure as it depends on an individuals' values and judgements about what they are able to pay for a certain good or service (32,33). Household surveys are one method to try to elucidate the concept of affordability, for example Wagner et al used data from the World Health Survey to estimate the economic burden of healthcare expenditures including medicines in 70 countries (34). However, the WHO/HAI metric has value in that it presents price data in a way that is more relevant to national and global stakeholders. For example, if a policy maker is told that a certain medicine costs $0.50 per treatment course, this may have very little meaning. However, if the same policy maker is told that a low-paid worker would need to spend half his monthly salary to purchase a treatment course, this may resonate more as a public health issue which warrants intervention.

Notwithstanding the limitations of the WHO/HAI survey methodology in measuring medicine prices and availability, it is a reliable source of national data with sufficient global coverage to enable regional and global analyses. Regardless of the data source used, a significant methodological challenge lies in how to aggregate national data reliably to produce global and regional results. Comparing medicine prices across countries is an inherently complex and challenging task given that consumption patterns, quality and patent status differ across countries as do the dosages forms, strengths and pack sizes of individual products (35-37). Certainly a key means of improving comparability is to limit analyses to a set of identical products across countries. For this purpose, the WHO/HAI method recommends that all surveys include a common set of 14 medicines which have been shown to be widely used in a large number of countries (26). Regional lists of medicines that are commonly used in certain geographic areas are also provided and recommended for use in selecting survey medicines. However, even when individual products are analysed across countries, several issues influence their price and availability and can limit comparability across countries. For example, final retail prices will differ according to local distribution costs which were shown in **Chapter 2** to differ substantially across countries. Such factors are likely account to some degree for the price ranges observed in most of the aggregate results reported in this thesis. A further issue is that in WHO/HAI surveys, a specific generic product from an individual manufacturer is not surveyed. Rather, data is collected on the lowest priced generic equivalent found at each facility (26). This limits the ability to compare exact identical products (i.e. brand and manufacturer) across countries given that even within a single country, the individual generic medicine surveyed differ across facilities. However, it has the advantage of providing an estimate of the lowest prices available across facilities irrespective of the brands being supplied and sold in individual outlets.

Additional issues in aggregating the WHO/HAI national datasets is the fact that surveys have been conducted in different years with countries subject to diverse inflation rates. A set of data adjustments has been applied to the data to account for these variations. Similarly, the retail buying power of individual currencies varies depending on the wealth of the respective countries (38). For this reason, retail price data are also adjusted for purchasing power parity (PPP), or "the rate at which the currency of one country needs to be converted into that of a second country to ensure that a given amount of the first country's currency will purchase the same volume of goods and services in the second country as it does in the first" (38). Procurement data are not adjusted for PPP as they reflect prices paid on the international markets and are therefore not subject to variations in the purchasing power of individual currencies (26). Since the application of these sets of adjustments for procurement and retail prices as part of the secondary analysis presented in **Chapter 2**, they have become a standard part of the WHO/HAI survey method and are recommended to others who wish to conduct international price

comparisons. However in applying PPP adjustments it was observed that national results were modified substantially in some cases. As such PPP adjustments, while important to improve the comparability of data across countries, may limit the local relevance of the findings. To address this issue, it is important to provide unadjusted national data as a supplement to the adjusted aggregate data wherever possible.

Implications of the findings : supporting efforts to improve price, availability and affordability of medicines

The ultimate goal of studying medicine prices and availability is to identify where issues of low availability, high prices, and/or poor affordability exist and develop policy and programmatic interventions that can be applied to rectify the problems and ultimately improve access. While this ultimately happens at the national level for medicines purchase through domestic or donor funding, providing supra national results can support evidence-based policy making in several ways. Firstly, for the numerous international agencies and NGOs advocating for improved access to medicines in LMICs, global results can help direct advocacy efforts to specific issues and can provide the evidence necessary to substantiate advocacy messages. For example, until recently there has been very little attention paid by the international community to chronic, non-communicable diseases (39). When a UN Summit was eventually convened on this topic in 2011 (40), it was debatable whether access to medicines would feature on the agenda. The results of the study described in Chapter 3 were used to argue in favour of access to medicines as a key issue in the management of chronic diseases in LMICs, which was subsequently added to the agenda. The potential cost-savings of increased use of generic medicines, which was reported in WHO's World Health Report 2011 on Universal Coverage (41), has also been quoted in speeches by the Director-General of WHO to support efforts to promote increased use of generic medicines as a means of improving access (42). Global results can also be used to monitor and report on international efforts to improve access to medicines in LMICs, as demonstrated by the inclusion of WHO/HAI survey data and analyses in the yearly publication reporting on progress towards attaining MDG 8 (43-46). Finally and certainly most importantly, such findings can be used to encourage national policy-makers to undertake policy and programmatic interventions towards improving access to medicines for their populations. Following this, regular monitoring is required to ensure that any actions taken are having the desired effect.

However, the international community faces significant challenges in supporting countries in designing interventions to increase medicine availability and/or manage prices

and ultimately improve access. A key difficulty lies in the fact that the factors that influence pharmaceutical prices and availability are multiple and complex and final prices can therefore be seen as the sum of a range of influences (26, 47,48). Any intervention must therefore be based on a clear understanding of the underlying issues in the national context. Manufacturer's pricing strategies, while outside the scope of this thesis, will clearly have a direct impact on final prices. These include monopoly pricing whereby prices are set which maximize the manufacturer's profit, and differential pricing whereby drug prices are adapted to the purchasing power of consumers in different geographical or socio-economic segments (48,49). International-level factors such as free trade agreements, global financing mechanisms (e.g. Global Fund), and regional negotiation and/or pooled procurement mechanisms, also have an influence. At the national level, policies that govern the pharmaceutical sector as well as broader health sector policies can both impact on price levels, as can national policies outside the health sector. Non-health sector policies impacting on pharmaceutical prices include intellectual property legislation, taxation policy, trade and procurement policies, and competition law. The overall structure of the healthcare system, including reimbursement systems, will also have an impact on pharmaceutical prices. Within the pharmaceutical sector, policies and practices governing the selection, procurement and supply of medicines, including the regulatory and quality assurance system, can have a strong influence on price levels. Finally, policies with the most direct impact on prices are those that regulate pharmaceutical prices specifically.

In an unregulated environment, market forces will also exert influence on price levels. However, as described **in Chapter 6**, pharmaceutical markets are subject to a range of failures that prevent the production of socially optimal amounts of medicines over time. One of the most important sources of failure in pharmaceutical markets is the information asymmetries that prevent consumers and others from making informed decisions about treatment choices (50,51). For example, when consumers have limited information sellers may recommend products based on their advantages (e.g. higher profit market, offloading of slow-moving products) but which may not reflect the most cost effective treatment option for the patient (50,51). As reported in this chapter, overall savings of up to 60% could be achieved through greater use of lowest-priced generic medicines in place of their equivalent originator brands. While some consumers might be making an informed decision about paying more to obtain a brand name product, many do not have the information needed to make educated choices. Information asymmetries can also lead to perverse incentives in the supply chain. As reported in **Chapter 2**, wholesale and retail mark-ups as high as 380% and 552%, respectively, have been observed and can contribute substantially to the final price of medicines. Supply chain agents can therefore have an incentive to stock and sell higher priced products to obtain a higher margin.

Several methods of price regulation are available and applied, and many high income countries use a combination of approaches (52). Price regulation methods include cost-plus pricing, whereby prices are based on the cost of production and profit, plus margins to cover distribution costs (53); external reference pricing, or price setting/negotiation based on a comparison with reference countries (54); and value-based pricing in which pricing and/or reimbursement decisions are based on an assessment of the added value of one medicine over another, with value usually assessed as clinical effectiveness and cost effectiveness (55). Sub-components of pharmaceutical prices, such as supply-chain mark-ups, can also be regulated. Each of these policies has its own pros and cons, and uses methods which are technically challenging and resource intensive to implement and enforce. Further, pricing policies can have unintended negative effects. For example, regulating supply chain margins as a fixed percentage of the price provides an incentive for supply chain agents to stock and sell higher-priced products to obtain a higher absolute margin (56). Setting retail prices too low, regardless of the price-setting method used, can result in manufacturers exiting the market. For this reason, pricing policies must be carefully designed and closely monitored. Policies to promote the use of lower-priced generics can also be seen as an indirect method of influencing prices. Again, a range of approaches can be used including regulations that facilitate market entry following patent expiration, insurance policies that only reimburse at the level of the generic price, and strategies to influence prescribing and dispensing patterns (57,58).

Medicine availability can also be influenced by a number of factors. Certainly availability of sustained financing is a key factor influencing medicine availability in the public sector. Other factors can include poor demand quantification and forecasting, inefficient procurement practices, and inefficiencies in supply and distribution, including leakage of medicines for resale through unofficial channels (26). There is also interplay between price and availability that occurs. For example, if a government's pricing policies result in prices that are not attractive to the manufacturer, they may choose to stop supplying a particular product. In the United States, shortages of life-saving medicines have been reported recently, said to be caused in part by lack of interest of pharmaceutical companies to supply medicines due to low profits (59,60). Supply shortages can in turn result in increased prices as sellers benefit from a situation where demand outstrips supply. Conversely if prices are too high for patients to be able to purchase medicines, retailers may choose not to stock these items due to low demand. Policy makers must be cognizant of the relationship that exists between price and availability and aim to achieve prices which are affordable but which do not encourage manufacturers to exit the market, thereby causing availability issues.

As there are often several contributing causes of high prices/low availability, the most appropriate response will likely be multi-faceted and will vary depending on the sector,

whether the medicine is imported or locally manufactured and whether it is a single-source originator brand product or a multi-source generic product, as well as other country-specific factors. (47) The choice of strategy will also depend on resource availability, enforcement capacity, pharmaceutical market structure, health and industrial policies, and sector to be targeted (public, private, NGO).

Given the complexity of inter-related factors influencing prices and availability, providing technical guidance to national policy makers that want to improve access through better availability and improved price management is a challenging task. The body of research presented in this thesis does not assist entirely in this regard. While an inventory of possible policy and programmatic interventions can be provided considered to address issues of high price and low availability, as was done in **Chapter 2**, it is less feasible to provide targeted policy guidance based on regional or global aggregates. However, identifying issues related to price and availability can already go a long way towards diagnosing issues that national policy makers can consider in the context of their own systems toward eventual action. Unfortunately, there is a dearth of evidence on the actual impact of such policies, even in high income countries (54,56,58). High income countries generally use a mix of policies and strategies to manage pharmaceutical prices (51), and as such disentangling the impact of individual policies is inherently challenging. Furthermore, countries that are operating in the context of reimbursement systems have an important lever for influencing prices than many LMICs do not have. For example, restricting reimbursement to the price of lower-cost products was found to reduce and stabilize retail prices in Kyrgyzstan (61). An added complicating factor is that it is likely not the policy itself, but rather the method of application, which will determine its impact. For example, if a country is setting up an external reference pricing system, the choice of countries to be used as comparators will be critical to the outcome, as will the determination of the "reference point", e.g. lowest price, average price, etc. Indeed, there is substantial heterogeneity in the application of this method among European countries (62). Until such time when evidence becomes available as to the effects of individual pricing policies, it will be difficult for international bodies to provide optimal guidance to LMICs. However, as more LMICs begin to implement policies of their own, it is imperative that the necessary operational research be conducted to better understand the impact of these policies and benefit from the lessons learned. This will require that monitoring systems be established that allow prices and availability to be tracked over time.

Opportunities for future research

Price and availability can be used in a variety of ways to improve our understanding of access to medicines in LMICs. However, as both of these measures are dependent on a range of factors including market conditions as well as national policies, a deeper understanding of the underlying determinants of price and availability are needed in order to identify policy interventions that can be effective. For example, while this body of work included an examination of the add-on costs applied in the supply chain, a more comprehensive examination of medicine price structures, including production costs, would help to identify where savings might be possible. Looking at the prices of medicines overall provides an indication of potential problems, e.g. price setting policy that is having an unintended negative effect on availability, but more insights can be gathered by looking more in-depth in individual disease areas. This approach can provide greater insights into specific problems such as lack of competition for certain medicines, or concerns about bioequivalence which can lead to reliance on higher-priced, originator brand products. Ultimately, measuring price and availability levels should be seen as a first step towards designing appropriate policy interventions to improve access. A necessary second step will be additional work to understand the underlying determinants of high prices, low availability or poor affordability, which may necessitate additional research. It is only through an understanding of these underlying causes that appropriate policy interventions can be developed.

While the work presented in this thesis aimed to explore how national level data could be analysed in different ways to generate global findings on access to medicines, it also identified additional areas where further exploration would be useful. Firstly, as described in **Chapter 2**, time series data on medicine prices and availability is needed to investigate trends over time and understand the impact of interventions in these areas. For example, routine price monitoring in Kenya was useful in showing the dramatic increase in the availability of the recommended first-line treatment for malaria (artemether lumefantrine) as a result of increased funding provided through the Global Fund to Fight HIV, TB and Malaria (43). The development of tools for routine monitoring of medicine prices and availability would therefore be a useful complement to the WHO/HAI survey method. With respect to the latter, operational research on the effects of various policies to improve access to medicines through improved availability and prices, by means of longitudinal time series, is also needed. As an increasing number of LMICs embark on policy reforms in this area, an opportunity to understand the effects of different strategies in these contexts should be capitalized upon. More specifically, research on the price elasticity of demand for medicines in LMICs would be valuable in better understanding what degree of price reductions would be required to actually improve access. Finally, there is also a need to conduct more in depth investigations of medicine

affordability to patients using both quantitative and qualitative methods, in order to better understand the impact of price on access.

While facility-level availability and prices can provide important insights into levels of access to medicines at the local level, these alone are insufficient to understand the range of complex factors that determine true access. Other factors, such as geographical proximity to a dispensing point, should also be investigated in the context of a broader framework for understanding true access. Certainly one key limitation of facility-level data in describing access issues is that is does not account for the segment of the population who do not visit such facilities for reasons of geographic isolation or extreme poverty. These populations are facing a different set of access issues which can only be investigated through alternative research methods such as focus household surveys (63). Supplementing facility-based surveys through qualitative data obtained through exit interviews, focus groups or household surveys would enhance our understanding of true levels of access to medicines.

Conclusion

Alongside targeted efforts to promote access to medicines for individual disease areas such as HIV, TB and malaria, ensuring access to affordable essential medicines more broadly is a key priority for the international health community and has been included as a target of the Millennium Development Goals (43). When the Director General of WHO was re-elected to her second term in office in May 2012, her acceptance speech referred to poor access to essential medicines, especially affordable generic products, as one of the "biggest problems facing health systems" (64). Such a strong statement from the head of the leading international health agency sends a very clear message to national policy makers, international agencies, donors and other stakeholders: increased access to affordable medicines is strongly needed and should be a priority. In 2012 statements such as these are possible as they have, as their foundation, a solid evidence base. They confirm that reporting on trends in medicine price, availability and affordability has a place alongside more specific analysis of national-level situations in order to bring medicine access issues to the foreground of international health arenas. Each serves a unique and valuable purpose; the former to inform the advocacy and programmatic priorities at a broad level, the latter to help design effective interventions at the country level. Both serve to redress the information asymmetries that characterize pharmaceutical markets and to empower stakeholders at all levels to work towards equitable access to appropriate, affordable treatment.

The body of work presented in this thesis has demonstrated that national-level data can be used to report on trends in medicine access using price and availability as proxy indicators, and can also highlight important policy issues that warrant attention. It complements the work of Waning in 2011 (65), which explored various aspects of access to medicines using the purchase transactions of international donors, by shedding light on non-donor funded medicines. While in the past policy makers had limited information upon which to make policy and programmatic decisions, evidence-based decision making is becoming increasingly possible. Going forward, additional efforts are needed to continue to monitor these indicators to ensure that national policy makers and the global health community continue to have access to up-to-date information upon which to target advocacy efforts, investments, and policy and programmatic support.

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Summary

Chapter 1 of *Understanding access to medicines in low- and middle-income countries through the use of price and availability indicators* begins by noting the difficulty in defining and measuring « access to medicines », a concept promoted by many global stakeholders including donors, UN agencies and NGOs. One definition is provided, namely "having medicines continuously available and affordable at public or private health facilities or medicine outlets that are within one hour's walk from the homes of the population". This definition highlights two key elements of access, availability and affordability, the latter of which is an extension of price and is itself a difficult concept to define. It is suggested that, given its complexity, an overall picture of the degree of access to essential medicines can only be generated using a range of proxy indicators that provide data on medicine availability and price in both the public and the private sectors, in combination with key policy indicators. However, prior to 2001, very little empirical evidence was available on medicine availability, and particularly price, in low- and middle-income countries. In 2001, following a resolution endorsed by the Member States of the World Health Organization, the WHO/Health Action International (HAI) Project on Medicine Prices and Availability was launched. To address the lack of evidence on medicine availability and prices in LMICs, the project focused primarily on the development and application of a standard survey methodology for measuring medicine prices, availability, affordability and price components.

The chapter goes on to describe the survey methodology, in which data on the price and availability of approximately 50 medicines are collected in a sample of medicine outlets in the public and private sector. To estimate affordability, median local prices are combined with the daily wage of the lowest-paid government worker to determine the number of days needed to purchase a course of treatment. Price components, or add-on costs in the distribution chain, are also collected in the survey. It is noted that the WHO/HAI survey methodology has been applied in over 70 countries, generating a critical mass of data on medicine price and availability across a range of national contexts. While its primary use has been to inform and influence policies and programs at the national level, it is suggested that the data also have utility in understanding access to medicines on a broader level and can be used to support evidence-based advocacy and policy-making at both supra national and national levels. The advantages of this data source for global reporting are presented, including a validated methodology, standardization across countries, multiple quality control checks, and broad geographic coverage. In addition, while the medicines surveyed in each country varies, data is available for a subset of common medicines, thereby allowing direct comparisons across individual products and groups of identical products.

It is argued that information on the price and availability of essential medicines is strongly needed to inform the access to medicines debate at the global level and inform global funding, advocacy and programmatic efforts. The hypothesis of the thesis is presented, namely that national medicine price and availability data can be analysed in a variety of ways that can contribute to our global understanding of access to medicines in low- and middle-income countries, and can support evidence-based advocacy and policy-making. In Chapters 2-6, this hypothesis is explored through the use of different methods and analyses that elucidate various aspects of medicine price and/or availability and draw global-level conclusions.

In **Chapter 2**, WHO/HAI survey data on medicine price and availability is aggregated on a global level, taking several steps to improve the comparability of national results, to examine whether any overall conclusions can be drawn on medicine prices and availability in low- and middle-income countries. The secondary analysis presented in this chapter was the first time that medicine prices, availability and affordability were reported for as large a group of LMICs. Since its publication in January 2009 through July 2012, it had been cited in 118 peer-reviewed publications (2), suggesting a strong demand for published evidence on this topic. The methods applied in this study were seminal in that they set a standard for aggregation of country-level price data that was acceptable to the scientific community and to which subsequent secondary analysis would be evaluated.

This study showed that overall, medicine availability is generally low and prices are frequently high, with much scope for improvement. Specifically, mean availability of a basket of 15 commonly-used medicines was 38.4% in the public sector and 64.2% in the private sector. Private sector patient prices ranged from 9 to 25 times international reference prices for lowest-priced generic products across WHO regions, which suggests that even generics may be high-priced in the private sector. This paper included a breakdown of the components of medicine prices in selected countries, which is essential for understanding the underlying determinants of high prices. In the private sector, wholesale mark-ups ranged from 2% to 380%, whereas retail mark-ups ranged from 10% to 552%, suggesting that supply chain charges can contribute substantially to final medicine prices.

In **Chapter 3**, price and availability results are examined for groups of medicines in different therapeutic areas, specifically by comparing medicine availability for medicines used for acute vs. chronic conditions. It was found that medicines for chronic conditions were substantially less available than generic medicines for acute conditions in both the public sector (36.0% availability versus 53.5%) and the private sector (54.7% versus 66.2%). Of the chronic diseases studied, antiasthmatics, antiepileptics and antidepressants had lower availability than antiulcerants and oral antidiabetics.

Another key finding from this study was that the availability gap between acute and chronic disease medicines was inversely related to country income level (i.e. lowest income countries had the largest gap in availability), particularly in the public sector. This is an important finding in that it implies that the public health systems of lower income countries are not adapting as needed to the epidemiological shift taking place from acute to chronic illnesses.

While Chapter 1 investigated medicine prices and availability across a range of medicines to identify overarching issues and trends, in **Chapter 4** similar data are analysed for two therapeutic areas—cardiovascular disease (**Chapter 4.1**) and epilepsy (**Chapter 4.2**)—to elucidate whether any disease-specific factors may be influencing price and/or availability. It was found that for both cardiovascular disease (CVD) medicines and epilepsy medicines, availability of generics in the public sector was low (average of 26.3% for CVD medicines and availability of < 50% for nearly all antiepileptics). While the findings are similar, for epilepsy the low availability of generics is likely to be caused in part by disease-specific factors such as the narrow therapeutic index of antiepileptics that may make prescribers reluctant to switch from originator brands to generics. Stringent regulatory control and the capacity to ensure quality and ensure prescribers are aware of quality-assured options are therefore likely to be key areas of focus in efforts to improve access.

While price is an important component of medicine access, it is important to understand how price translates into affordability to better understand the relationship between price levels and access. Affordability has been defined as "concerned with securing some given standard of a commodity (or different standards) at a price … which does not impose, in the eyes of a third party (usually government) an unreasonable burden on household incomes". In **Chapter 5**, an investigation into medicine affordability is conducted by combining medicine price data with consumers' ability to pay, with the latter estimated using household expenditure data and information on income distributions as proxies. From these, the proportion of a population that would be pushed under the international poverty lines as a result of medicine purchases is estimated for a selection of treatments. For example, in the 17 countries studied, purchasing a month's supply of generic glibenclamide would push an additional 6% of populations below the US $1.25/day poverty line. The affordability results from Chapters 2 and 5 show that while the concept of affordability is difficult to measure and quantify, it may be a better proxy for access than price alone as it takes into account the income levels of consumers.

In Chapter 2 it is reported that originator brand medicines consistently cost substantially more than their generic equivalents. **Chapter 6** explored this finding in greater depth by estimating the potential cost savings that could be achieved by switching private sector

consumption from originator brands to their lowest-price generic equivalents. From a methodological perspective, this analysis demonstrated how price data can be combined with other data on the pharmaceutical sector, in particular consumption volumes, to explore potential options for improving access. The analysis showed that a savings of approximately 60% could be achieved by switching private sector consumption from originator brands to lowest-priced generics. These results suggest that, as part of national medicines policies, governments should consider including strategies to promote cost effective generic medicine use in the private sector as a strategy for improving access.

The concluding chapter of this thesis contains a discussion of the usefulness of national data on medicine price and availability to inform our understanding of access to medicines at the supra national level and to support evidence-based advocacy and policy-making **(Chapter 7)**. Key findings from Chapters 2 through 6 are presented to support the hypothesis that medicine price and availability data can be used in a variety of ways to improve our understanding of access to medicines in LMICs and to support evidence-based advocacy and policy making. Key trends observed across countries include the low availability of medicines in the public sectors in many countries, and high private sector prices as compared to international reference prices, particularly for originator brands but also for generics in some cases. Given the trends observed and their implications for medicine access more generally, presenting global and regional results can be seen as highly valuable in terms of improving transparency on medicine price and availability issues, raising awareness of medicine access issues globally, and stimulating global health players to take action. The chapter also summarizes the important policy issues illuminated in Chapters 2-6, for example the need for increased attention to the management of chronic diseases in low income countries, and promoting cost-effective medicine use in the private sector as a measure to improve access. While an investigation of national-level results is needed to design appropriate policy interventions, this body of work suggests that important policy areas requiring attention from both policy makers and other national and international stakeholders, can also be elucidated by looking at results across countries.

Chapter 7 then goes on to describe the limitations of aggregating national data on the pharmaceutical sector. It is noted that the capacity to use national-level data to accurately report on medicine prices, availability and affordability at the global level depends on two key factors: 1) the strength of the underlying methodology used to collect data at the country level and the resulting quality of the data reported; and 2) the comparability of the data across countries and the reliability of the methods used to aggregate data at the regional and global level.

This section notes that while several new sources of data on medicine price and availability have emerged in recent years, data from WHO/HAI surveys are the most comprehensive in terms of both number of countries surveyed and therapeutic categories of medicines studied. However, this data source also has certain limitations which should be borne in mind when conducting secondary analyses. This includes the fact that availability represents availability of an individual product on the day of data collection and is specific to an individual strength and dosage form. In terms of prices, results may be influenced by economies of scale resulting from larger pack sizes, and by sellers adjusting the retail price based on their perception of what the buyer is willing to pay. For affordability, a key consideration is that in many LMICs a substantial proportion of the population earns less than the lowest-paid government worker. The chapter goes on to describe the methodological challenge of aggregating national data reliably to produce global and regional results, regardless of the data source used. Given that medicine consumption patterns, quality and patent status differ across countries as do the dosages forms, strengths and pack sizes of individual products, a key means of improving comparability is to limit analyses to a set of identical products across countries. Data adjustments are also suggested to account for differences in survey year and purchasing power parity across the countries being analyzed.

Chapter 7 then describes the policy and programmatic implications of the study findings. It is suggested that trends in medicine price, availability and affordability can help direct global advocacy efforts to specific issues and can provide the evidence necessary to substantiate advocacy messages. However, the international community faces significant challenges in supporting countries in designing interventions to increase medicine availability and/or manage prices and ultimately improve access. A key difficulty lies in the fact that the factors that influence pharmaceutical prices and availability are multiple and complex, and include both national policies and market conditions. As a result, the most appropriate response will likely be multi-faceted and will vary depending on the sector, product characteristics, as well as other country-specific factors. It is noted that while regional or global aggregates can be used to generate an inventory of possible policy and programmatic interventions to address issues of high price and low availability, they are less useful in providing targeted policy guidance. However, identifying issues related to price and availability can already go a long way towards diagnosing issues that national policy makers can consider in the context of their own systems toward eventual action.

Finally, areas for future research are identified that could improve our overall understanding of access to medicines. In particular, additional investigations into both the underlying determinants of price and availability and additional in-depth studies of individual disease areas are needed in order to design effective policy interventions. In

addition, operational research on the effects of various policies to improve access to medicines through improved availability and prices is also needed. Chapter 7 concludes by confirming the original hypothesis that national-level data can be used to report on trends in medicine access using price and availability as proxy indicators, and can also highlight important policy issues that warrant attention. It is suggested that going forward, additional efforts are needed to continue to monitor these indicators to generate up-to-date information upon which to target advocacy efforts, investments, and policy and programmatic support.

Samenvatting

In dit proefschrift is onderzocht in hoeverre gegevens over prijzen en beschikbaarheid van geneesmiddelen, verzameld op lokaal niveau in lage en midden inkomenslanden, een bijdrage kunnen leveren aan een beter begrip van toegang tot geneesmiddelen. **Hoofdstuk 1** begint met de vaststelling dat toegang tot geneesmiddelen een moeilijk te definiëren en meten maar veel gebruikt concept is. Toegang tot geneesmiddelen wordt wereldwijd door vele partijen zoals internationale donoren, gespecialiseerde organisaties van de Verenigde Naties en non-gouvernementele organisaties (NGOs) gepromoot. Een van de definities voor toegang tot geneesmiddelen is "het continue beschikbaar en betaalbaar zijn van geneesmiddelen in zowel publieke als private gezondheidscentra of verkooppunten van geneesmiddelen, die vanaf de woonplaats van elke persoon binnen een uur te voet bereikbaar zijn". In deze definitie zijn twee belangrijke elementen van toegang opgenomen, namelijk beschikbaarheid en betaalbaarheid. Betaalbaarheid hangt samen met de prijs van geneesmiddelen en is zelf ook een moeilijk definieerbaar concept. Omdat toegang tot geneesmiddelen zo'n complex begrip is, wordt wel gezegd dat de mate van toegang tot essentiële geneesmiddelen in de publieke en private sector alleen kan worden vastgesteld door gebruik te maken van afgeleide indicatoren, zoals beschikbaarheid en prijs van geneesmiddelen, in combinatie met andere beleidsindicatoren. Tot 2001 waren er bijzonder weinig empirische gegevens beschikbaar over beschikbaarheid en vooral prijzen in lage en midden inkomenslanden. In 2001 werd een resolutie aangenomen door de lidstaten van de Wereldgezondheidsorganisatie (WHO), waarna het WHO/Health Action International (HAI) project werd gestart. Dit project richtte zich in eerste instantie op het ontwikkelen en toepassen van een gestandaardiseerde onderzoeksmethode om prijzen en prijscomponenten, beschikbaarheid en betaalbaarheid van geneesmiddelen te meten, om zo tegemoet te komen aan het ontbreken van goed wetenschappelijk bewijs op dit gebied in lage en midden inkomenslanden.

In dit hoofdstuk wordt de WHO/HAI onderzoeksmethode beschreven. Gegevens over prijzen en beschikbaarheid van circa 50 geneesmiddelen zijn verzameld in een steekproef van verkooppunten van geneesmiddelen in de publieke en private sector. Om de betaalbaarheid van geneesmiddelen te kunnen bepalen zijn lokale prijzen gecombineerd met gegevens over het loon van de laagstbetaalde ambtenaar. Zo kan het aantal werkdagen dat nodig is om een behandeling te kunnen betalen worden ingeschat. Prijscomponenten of extra kosten in de distributieketen zijn eveneens onderzocht als onderdeel van dit onderzoek. De WHO/HAI methodologie is inmiddels toegepast in meer dan 70 landen, waardoor er voldoende gegevens beschikbaar zijn voor een grote diversiteit aan landen. Het primaire doel van het verzamelen van deze gegevens was het informeren en beïnvloeden van nationaal beleid en nationale programma's. De gegevens kunnen echter ook mogelijk

worden gebruikt om het algemene inzicht in toegang tot geneesmiddelen te vergroten en om het noodzakelijke bewijs aan te leveren voor het onderbouwen van belangenbehartiging en het ontwikkelen van beleid op nationaal en internationaal niveau. De voordelen van het gebruik van deze gegevens omvatten de gevalideerde methodologie, de toegepaste standaardisatie, de vele kwaliteitscontroles en de brede geografische dekking. Hoewel de onderzochte geneesmiddelen kunnen variëren tussen individuele landen, is er een groep veel gebruikte geneesmiddelen die in elk land is onderzocht. Hierdoor is het mogelijk om directe vergelijkingen tussen (groepen van) individuele producten te maken.

De informatie over prijzen en beschikbaarheid van essentiële geneesmiddelen is van belang om het mondiale debat over toegang tot geneesmiddelen goed te kunnen voeren en om inspanningen op het gebied van financiering, belangenbehartiging en het opzetten van (gezondheids)programma's en beleid te kunnen ondersteunen. De hypothese van dit proefschrift is dat de beschikbare gegevens hiervoor op verschillende manieren kunnen worden gebruikt. In hoofdstukken 2-6 worden daarom verschillende methoden en analysetechnieken toegepast om verscheidene aspecten van prijzen en/of beschikbaarheid van geneesmiddelen op te helderen.

In **hoofdstuk 2** zijn de data die verkregen zijn met behulp van de WHO/HAI methodologie geaggregeerd om te onderzoeken of het mogelijk is om zo op mondiaal niveau uitspraken te doen over prijzen en beschikbaarheid van geneesmiddelen in lage en midden inkomenslanden. Dit onderzoek was het eerste grootschalige onderzoek op dit gebied in lage en midden inkomenslanden.

Uit het onderzoek bleek dat de beschikbaarheid van geneesmiddelen over het algemeen laag was en hun prijzen veelvuldig relatief hoog waren. De mediane beschikbaarheid van 15 vaak gebruikte geneesmiddelen was slechts 38.4% in de publieke sector ten opzichte van 64.2% in de private sector. De laagste prijzen (voor generieke geneesmiddelen) voor patiënten waren in de private sector 9-25 keer hoger dan de internationale referentieprijzen. Dit resultaat laat zien dat zelfs prijzen voor generieke geneesmiddelen hoog zijn in deze sector. Om te kunnen begrijpen waarom prijzen hoog zijn, is het van belang om de opbouw van prijzen in kaart te brengen. Uit het onderzoek bleek dat de marges voor de groothandel varieerden van 2 tot 380% en voor de verkoper van 10% tot 552%. Kosten in de distributieketen dragen dus aanzienlijk bij aan de hoge prijzen van geneesmiddelen. Dit onderzoek is sinds de publicatie in januari 2009 tot aan juli 2012 118 keer geciteerd in andere, *peer-reviewed* publicaties. Dit grote aantal geeft aan dat er een grote behoefte is aan wetenschappelijk bewijs op dit gebied. De gebruikte methoden hebben tevens een norm gesteld voor het samenvoegen van landelijke prijsdata die acceptabel was voor de wetenschappelijke gemeenschap en die als vergelijking voor toekomstig onderzoek op dit gebied dient.

In **hoofdstuk 3** wordt ingegaan op de beschikbaarheid en prijzen van geneesmiddelen voor verschillende therapeutische gebieden, waarbij specifiek de beschikbaarheid van geneesmiddelen voor acute en chronische aandoeningen werd vergeleken. Geneesmiddelen voor chronische ziekten bleken aanzienlijk minder vaak beschikbaar dan geneesmiddelen voor acute aandoeningen. Dit gold zowel voor de publieke sector (beschikbaarheid 36.0% versus 53.5%) als voor de private sector (54.7% versus 66.2%). Binnen de groep van chronische aandoeningen was de beschikbaarheid van geneesmiddelen bij astma (private sector 43.1%, publieke sector 30.1%), epilepsie (private sector 40.3%, publieke sector 29.4%) en depressie (private sector 45.1%, publieke sector 27.8%) lager dan van zuurremmende geneesmiddelen (private sector 82.9%, publieke sector 51.7%) en orale antidiabetica (private sector 65.0%, publieke sector 49.5%). Een andere belangrijke bevinding van dit onderzoek was dat het verschil in beschikbaarheid van geneesmiddelen voor acute versus chronische aandoeningen omgekeerd evenredig was met het inkomen van de onderzochte landen, dat wil zeggen dat het verschil in beschikbaarheid het grootste was in de landen met de laagste inkomens. Deze belangrijke bevinding toont aan dat de publieke zorgsector van dergelijke landen nog onvoldoende aangepast is aan de behoeften die ontstaan door de huidige verschuiving van ziektelast van acute naar chronische ziekten.

Waar in hoofdstuk 2 in grote en algemene lijnen is gekeken naar prijzen en beschikbaarheid van geneesmiddelen, richt **hoofdstuk 4** zich op twee therapeutische gebieden - cardiovasculaire aandoeningen (**hoofdstuk 4.1**) en epilepsie (**hoofdstuk 4.2**) – om zo te bestuderen of ziektespecifieke factoren de prijzen en beschikbaarheid van geneesmiddelen beïnvloeden. De beschikbaarheid van generieke geneesmiddelen in de publieke sector was voor beide aandoeningen laag (gemiddeld 26.3% voor cardiovasculaire geneesmiddelen en gemiddeld < 50% voor bijna alle anti-epileptica). De betaalbaarheid van cardiovasculaire geneesmiddelen werd uitgedrukt in het salaris van de laagstbetaalde ambtenaar. Gemiddeld kostte het een dergelijke ambtenaar 1.8 dagen van zijn loon om cardiovasculaire geneesmiddelen voor één maand te kopen. Dit aantal is vergelijkbaar met de 1-2.6 dagen die het de laagstbetaalde ambtenaar kost om voor 30 dagen fenytoïne te kopen. Carbamazepine was echter veel minder betaalbaar (2.7-16.2 dagen van het loon). Uit beide onderzoeken bleek dat lage inkomenslanden hogere prijzen hebben dan hoge inkomenslanden. Ziektespecifieke factoren die van invloed kunnen zijn op de prijzen en beschikbaarheid zijn in beide studies besproken. Een voorbeeld is de nauwe therapeutische breedte bij anti-epileptica; hierdoor zijn voorschrijvers wellicht minder geneigd om te switchen naar een ander product, waardoor het aandeel van generieke producten lager is.

De prijzen van geneesmiddelen maken onderdeel uit van de toegang tot geneesmiddelen. Om beter inzicht te krijgen in de relatie tussen prijzen en toegang tot geneesmiddelen,

is het van belang om eerst inzicht te hebben in de relatie tussen prijzen en betaalbaarheid van geneesmiddelen. Betaalbaarheid is gedefinieerd als "zich bezighoudend met het veiligstellen van een bepaalde standaard (of verschillende standaarden) van goederen voor een prijs … die geen onredelijke last drukt op het huishoudinkomen in de ogen van een derde partij (meestal de overheid)". In **hoofdstuk 5** wordt de betaalbaarheid van geneesmiddelen verder onderzocht door gegevens over prijzen van geneesmiddelen te combineren met gegevens over de mogelijkheden van patiënten om voor deze geneesmiddelen te betalen. Gegevens hierover zijn gebaseerd op gegevens over huishoudduitgaven en informatie over inkomensverdelingen. Op basis van deze gegevens is voor een aantal behandelingen uitgerekend welk deel van de bevolking onder de internationale armoedegrens terecht komt door het moeten kopen van geneesmiddelen. In de 17 landen in het onderzoek zou bijvoorbeeld 6% van de bevolking onder de internationale armoedegrens van $1.25 per dag terechtkomen, als ze glibenclamide – een middel bij suikerziekte – voor één maand kopen. Merkgeneesmiddelen waren daarbij minder betaalbaar dan de laagst geprijsde generieke geneesmiddelen. In de Filipijnen zou bijvoorbeeld 22% van de bevolking onder de internationale armoedegrens van $1.25 per dag terechtkomen, als ze het merkgeneesmiddel van atenolol zouden kopen ten opzichte van 7% als ze het laagst geprijsde generieke atenolol zouden kopen. Het concept van betaalbaarheid is moeilijk te meten en kwantificeren. De resultaten in hoofdstuk 2 en 5 laten echter zien dat betaalbaarheid een betere voorspeller is voor toegang tot geneesmiddelen dan prijzen alleen, omdat ook het inkomen van consumenten hierin wordt meegenomen.

De resultaten uit hoofdstuk 2 toonden aan dat merkgeneesmiddelen stelselmatig duurder zijn dan hun generieke equivalenten. In **hoofdstuk 6** wordt dieper op dit onderwerp ingegaan. In dit hoofdstuk is de omvang van de besparingen ingeschat die zouden kunnen worden behaald, als in de private sector zou worden overgestapt van merkgeneesmiddelen naar de laagst geprijsde generieke equivalenten. Vanuit een methodologisch perspectief laten deze analyses zien hoe gegevens met betrekking tot prijzen van geneesmiddelen kunnen worden gecombineerd met andere gegevens uit de farmaceutische sector, met name gegevens over de omvang van gebruik van geneesmiddelen, om mogelijkheden te verkennen voor het verder verbeteren van toegang tot geneesmiddelen. In de onderzochte landen en voor de onderzochte geneesmiddelen bleek dat in de private sector ongeveer 60% van de geneesmiddelkosten kan worden bespaard met een dergelijke overstap. De resultaten varieerden van 9% tot 89% voor de verschillende landen. In publieke ziekenhuizen in China zou bijvoorbeeld 370 miljoen US dollar (65%) kunnen worden bespaard. Voor individuele geneesmiddelen varieerden de mogelijke besparingen van 11% voor een inhalator met beclometason tot 73% voor injecties met ceftriaxon. Deze resultaten geven aan dat overheden het hanteren van strategieën om het gebruik van generieke geneesmiddelen in de private sector te bevorderen zouden moeten

overwegen, bijvoorbeeld als onderdeel van hun nationale geneesmiddelenbeleid, om zo de toegang tot geneesmiddelen verder te bevorderen.

Het afsluitende hoofdstuk van dit proefschrift, **hoofdstuk 7**, beschrijft de belangrijkste resultaten van hoofdstukken 2 tot en met 6. Dit proefschrift toont aan dat de verzamelde gegevens over prijzen en beschikbaarheid van geneesmiddelen op verschillende manieren ons inzicht in toegang tot geneesmiddelen in lage en midden inkomenslanden kunnen vergroten en gebruikt kunnen worden voor het opkomen voor belangen van patiënten en het maken van beleid. Belangrijke trends die in vrijwel alle landen werden gezien waren de slechte beschikbaarheid van geneesmiddelen in de publieke sector en de hoge prijzen voor geneesmiddelen in de private sector, zowel voor merkgeneesmiddelen als in sommige landen voor generieke geneesmiddelen. Deze trends en hun implicaties voor toegang tot geneesmiddelen onderstrepen het belang van het presenteren van mondiale en regionale gegevens op dit gebied; verbeteren van inzichtelijkheid van prijzen en beschikbaarheid van geneesmiddelen, vergroten van de bewustwording van de mondiale toegang tot geneesmiddelen en stimuleren van betrokken partijen binnen de gezondheidssector om verdere actie te ondernemen. Ook worden de belangrijkste punten voor het beleid die uit hoofdstukken 2 tot en met 6 naar voren zijn gekomen in dit hoofdstuk samengevat. Zo is er bijvoorbeeld meer aandacht nodig voor het omgaan met chronische ziekten in lage inkomenslanden en zou het gebruik van kosteneffectieve geneesmiddelen in de private sector moeten worden gestimuleerd om toegang tot geneesmiddelen te verbeteren.

Ook worden de beperkingen van het samenvoegen van landelijke gegevens in de farmaceutische sector in dit hoofdstuk bediscussieerd. Hoewel er de laatste jaren verschillende nieuwe bronnen met gegevens over prijzen en beschikbaarheid van geneesmiddelen bij zijn gekomen, zijn de gegevens uit de WHO/HAI onderzoeken het meest veelomvattend wat betreft het aantal onderzochte landen en het aantal en type onderzochte geneesmiddelen. Ook deze dataset kent echter een aantal beperkingen, waaronder het feit dat het de beschikbaarheid voor een individueel product (met een specifieke sterkte en formulering) op de dag van de dataverzameling betreft. Daarnaast kunnen de prijsresultaten beïnvloed zijn door schaalvoordelen bij grotere verpakkingen en door het bijstellen van prijzen door verkopers op basis van hun inschatting wat kopers zouden willen betalen. Voor betaalbaarheid geldt dat een aanzienlijk deel van de beroepsbevolking in veel lage inkomenslanden minder verdient dan de laagstbetaalde ambtenaar. In dit hoofdstuk worden tevens methodologische uitdagingen besproken die betrekking hebben op het op een betrouwbare manier samenvoegen van landelijke gegevens, ongeacht de gebruikte dataset. Omdat gebruikspatronen, kwaliteit, patentstatus, doseringen, formuleringen en doosjesgroottes van individuele geneesmiddelen variëren tussen landen, is het van essentieel belang om bij het onderzoek uit te gaan van een identieke set van

geneesmiddelen om zo de vergelijkbaarheid te kunnen waarborgen. Aanpassingen van de data zijn daarnaast nodig om te kunnen corrigeren voor verschillen in kalendertijd en koopkracht tussen de landen in het onderzoek.

De resultaten van dit proefschrift hebben ook belangrijke implicaties voor gezondheidsbeleid en –programma's. De gevonden trends in prijzen, beschikbaarheid en betaalbaarheid van geneesmiddelen kunnen helpen om richting te geven aan de mondiale inspanningen op het gebied van belangenbehartiging van patiënten en geven het wetenschappelijke bewijs dat nodig is om belangrijke boodschappen op dit gebied te staven. Het ondersteunen van het ontwerpen van goede interventies is echter uitdagend, omdat de factoren die de prijs en beschikbaarheid van geneesmiddelen beïnvloeden velerlei en complex zijn en betrekking hebben op zowel het landelijke beleid als de marktomstandigheden. Daarom zal de meest doelmatige aanpak zeer waarschijnlijk multifactorieel zijn en afhankelijk zijn van de sector, de productkenmerken en andere factoren die specifiek zijn voor het betreffende land.

Tot slot wordt stil gestaan bij toekomstig onderzoek dat ons inzicht in toegang tot geneesmiddelen verder zou kunnen vergroten. Aanvullend onderzoek naar de determinanten van prijzen en beschikbaarheid van geneesmiddelen en diepgaand onderzoek naar specifieke ziektegebieden zijn met name nodig om effectieve beleidsmaatregelen te kunnen ontwerpen. Daarnaast is onderzoek nodig naar de effecten van beleid om de toegang tot geneesmiddelen te vergroten door beschikbaarheid en prijzen van geneesmiddelen te verbeteren. Hoofdstuk 7 eindigt met de conclusie dat landelijke gegevens gebruikt kunnen worden voor het rapporteren van trends in toegang tot geneesmiddelen, waarbij prijzen en beschikbaarheid als indicatoren worden gebruikt, en voor het identificeren van belangrijke beleidspunten die verdere aandacht behoeven. In de toekomst zijn aanvullende inspanningen nodig om deze indicatoren te blijven monitoren, zodat ze actuele informatie blijven genereren waarop behartiging van belangen van patiënten, financiële investeringen, beleid en programmaondersteuning kunnen worden afgestemd.

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Alexandra Cameron obtained an Honours Bachelor of Science degree in Biochemistry from McMaster University in Hamilton, Ontario, Canada in 1997. Upon graduation she worked for several years with the Ministry of Health and Long-Term Care in Ontario, Canada. The majority of this time was spent as a policy analyst with the Ontario Women's Health Council, an advisory body to the Minister on women's health issues and policies. In 2003, she completed a Masters of International Public Health from the University of Sydney, Australia. From there she went on to work at the World Health Organization in Geneva, Switzerland in several technical positions related to chronic diseases and medicines. Her principal role was as a Technical Officer in the department of Essential Medicines and Pharmaceutical Policies where she undertook work related to pharmaceutical pricing research and policy. It was through this position that she joined the Utrecht WHO Collaborating Centre for Pharmacoepidemiology and Pharmaceutical Policy Analysis in the Netherlands under which umbrella the work presented in this thesis was conducted. In 2011 Alexandra assumed the role as Technical Officer, Market Dynamics at UNITAID, a WHO-partnership based in Geneva where she undertakes market research related to medicines, diagnostics and preventive commodities.