Allocating scarce financial resources for HIV treatment: benchmarking prices of antiretroviral medicines in Latin America

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Accepted 29 November 2011

Public sector price analyses of antiretroviral (ARV) medicines can provide relevant information to detect ARV procurement procedures that do not obtain competitive market prices. Price benchmarks provide a useful tool for programme managers and policy makers to support such planning and policy measures. The aim of the study was to develop regional and global price benchmarks which can be used to analyse public-sector price variability of ARVs in low- and middle-income countries using the procurement prices of Latin America and the Caribbean (LAC) countries in 2008 as an example.

We used the Global Price Reporting Mechanism (GPRM) data base, provided by the World Health Organization (WHO), for 13 LAC countries’ ARV procurements to analyse the procurement prices of four first-line and three second-line ARV combinations in 2008. First, a cross-sectional analysis was conducted to compare ARV combination prices. Second, four different price ‘benchmarks’ were created and we estimated the additional number of patients who could have been treated in each country if the ARV combinations studied were purchased at the various reference (‘benchmark’) prices.

Large price variations exist for first- and second-line ARV combinations between countries in the LAC region. Most countries in the LAC region could be treating between 1.17 and 3.8 times more patients if procurement prices were closer to the lowest regional generic price. For all second-line combinations, a price closer to the lowest regional innovator prices or to the global median transaction price for lower-middle-income countries would also result in treating up to nearly five times more patients.

Some rational allocation of financial resources due, in part, to price benchmarking and careful planning by policy makers and programme managers can assist a country in negotiating lower ARV procurement prices and should form part of a sustainable procurement policy.

Keywords Antiretroviral medicines, prices, benchmarks, procurement, cross-country comparison
KEY MESSAGES

- In terms of HIV infection, the Latin American and Caribbean (LAC) region is the third most affected region after sub-Saharan Africa and South and South-East Asia, with over 2.2 million people living with HIV.
- There exists very wide variation of prices for antiretroviral medicines (ARVs) between countries in the LAC region, indicating opportunities for extensive cost savings with respect to procurement of these essential medicines.
- Regional and global price referencing (i.e. benchmarking) provides a useful method for programme managers and policy makers to understand the need for lower ARV procurement prices.
- Referencing to the number of ‘extra’ patients which could be treated with ARVs if they are procured at the reference (benchmark) prices illustrates the implications of obtaining lower prices for the countries’ ARV programmes.

Introduction

The public procurement of medicines in an efficient manner in both high-income and low/middle-income countries is a laudable goal, but it requires execution of a complex process. This process is often bureaucratic, lacking in essential information on price/supply, and plagued with long lead times caused by lack of capacity and/or indecision (Seiter 2010). In 2009, one-third of all 144 countries reporting to the World Health Organization had one or more cases of treatment interruptions due to problems in the pharmaceutical supply chain, including procurement (WHO 2010a). Effective and efficient public procurement systems can make an important contribution to sustainable development, required for the achievement of the Millennium Development Goals (MDGs) (Organization for Economic Cooperation and Development 2006). Public money is spent through budgets that are converted into services largely through the government’s purchase of goods (e.g. medicines) and services (Organization for Economic Cooperation and Development 2006). Strengthening medicines procurement capacity in countries in a sustainable manner should be a necessary feature of programmes designed to meet international commitments related to access to medicines.

Efficient procurement can be defined in various ways: paying a reduced price per item, receiving an improved quality at the same price as one of less quality, reduced procurement process costs, shorter lead times. For the purpose of this paper we focus on price per item as a marker of procurement ‘efficiency’. Evaluating the procurement processes and their associated costs is complex and data are not easy accessible.

Price analyses of antiretroviral (ARV) medicines could be an important tool to detect procurement inefficiencies. Methods of accomplishing this would be of importance to policy makers and programme managers who are interested in allocating these increasingly scarce donor resources. To use such analyses for these purposes requires at least two components. The first component is comparative price analysis. Clearly, if prices are everywhere approximately the same, then the need to compare the prices of ARV procurements against each other becomes irrelevant and a waste of valuable resources. If price differences between countries are found, the second component can be a ‘benchmarking’ analysis. Benchmarking measures performance using a specific indicator (cost per unit of measure, productivity per unit of measure, cycle time of x per unit of measure and the like) resulting in a metric of performance that is then compared with others as a reference.

There are several existing and applied methods of benchmarking medicine prices, the most common being ‘reference’ pricing used for price regulation. Briefly, in this context, reference prices are defined according to the price charged at various points in the supply chain of medicines: for instance, the costs of production, the price the manufacturer charges the wholesaler, the maximum price at which the medicine is reimbursed by insurance and the retail price. One example of a ‘reference’ price is the maximum retail price which is used to regulate prices in the private sector.

For example, South Africa fixes reference prices for pharmaceuticals sold in the private sector using prices in a basket of comparator countries selected from South Africa itself and other countries including Australia, Canada, New Zealand or Spain (Department of Public Health, South Africa 2006). The price of originator medicines in each of the benchmark countries is obtained and converted into rands. The lowest price from amongst the benchmark countries is then used to obtain the reference price (if the South African lowest price is the lowest then the price will remain the same). This type of external reference pricing is also used extensively in 24 European Union countries (Kanavos et al. 2011)

‘Internal’ reference pricing is a method using prices of medicines from inside the country of interest and is most often used for reimbursement purposes. In the most widely understood practice, prices above a ‘reference’ level will not be reimbursed. If a patient wants a medicine which is at a price above the internally-generated reference level, they will bear the additional cost out-of-pocket. The goal of referencing for this purpose is the control of third-party expenditure on prescription drugs (Lopez-Casanovas and Puig-Junoy 2000). Several European countries implement internal reference pricing in various forms (Kanavos et al. 2008). In the United States, the ‘Average Wholesale Price’ (AWP) has for many decades been the standard for determining pharmaceutical reimbursement to pharmacies in public and private health care programmes. The AWP has been controversial (Curtiss et al. 2010).

In contrast to these methods for referencing prices for regulatory purposes, it appears that referencing medicines prices as a means of evaluating public sector procurement with regard to other countries is not well represented (Tayler 2004; OECD 2006; WHO and UNICEF 2008; Waning et al. 2008; GFATM 2009). Most publications are very general and do not propose specific benchmarks to evaluate procurement
For ARVs, other documents propose the use of the Clinton Foundation HIV/AIDS Initiative prices (e.g. Clinton Foundation 2008) or the ARV prices reported by Médecins sans Frontières (MSF) as benchmarks (WHO and UNICEF 2008). Clinton Foundation ARV prices are available to countries participating in the Clinton Foundation Procurement Consortium and represent price ceilings at or below which the particular suppliers must price their products when selling or communicating price quotes for specified products to Consortium members. MSF prices for ARVs are those provided by the manufacturers themselves; and actual prices paid by procurement authorities might be different. Others have used global median medicine price as the ‘reference’ (Waning et al. 2008), which can be calculated using the reported procurement prices of HIV treatment programmes funded or supported by international aid organizations such as the Global Fund to fight AIDS, Tuberculosis and Malaria. It is worth noting that the proposed ‘procurement’ benchmarks reported in the literature mentioned above are global reference points and that regional benchmarks are generally missing.

Given the relative paucity of studies that develop specific benchmarks for measuring this aspect of procurement efficiency, we chose to illustrate the use of price benchmarking for public procurement for countries from the Latin America and Caribbean (LAC) region. The LAC region is clearly relevant for the global response to HIV: it is the third most affected region in the world after sub-Saharan Africa and South and South-East Asia, with over 2.2 million people living with HIV (Cohen 2006; UNAIDS 2007a; UNAIDS 2007b). In addition, ARV medicines represent one of the highest expenditures on HIV and AIDS in most LAC countries, with 30-60% of their total budgets for HIV and AIDS spent on ARV drugs (UNGASS 2008). About 240 000 people need anti-retroviral therapy (ART) in the LAC region but are not receiving it (WHO/UNAIDS/UNICEF 2008).

In this paper, we have developed several methods for benchmarking the procurement price of some ARV combinations in order to illustrate what procurement agencies could do to compare themselves with such references and to evaluate their efficiency.

### Methods

#### Data source and cleaning

For this study, the Global Price Reporting Mechanism (GPRM) was used, which is a publicly available database containing public sector price information on procurement of ARV medicines reported by the Global Fund, various international aid organizations (e.g. United Nations Children’s Fund, Clinton HIV/AIDS initiative) and countries’ procurement offices (WHO 2009). We chose 2008 data because it was the most recent year when a large number of LAC countries reported to the GPRM.

We included procurements of the following adult, solid-dosage ARV medicines (e.g. tablets, capsules and caplets) procured by the majority of countries in the region: abacavir 300 mg; didanosine 100 mg, 200 mg and 400 mg; efavirenz 200 mg and 600 mg; lamivudine 150 mg; lopinavir/ritonavir 200/50 mg; nevirapine 200 mg; stavudine 30 mg and 40 mg; zidovudine 100 mg and 300 mg; zidovudine300+lamivudine150mg (fixed dose combination); and zidovudine500mg+lamivudine150mg+nevirapine200mg (fixed dose combination). We excluded procurement records for liquids and pediatric solid dosages as well as procurements of ARVs with a purchase price of zero (US$0) and procurements with unit prices >US$10, because we did not find any manufacturer reporting unit price above this value for the selected ARV (MSF 2009). From the ARVs, we created seven ARV combinations, chosen based on the most frequently used first- and second-line combinations which can be assembled from the individual ARV procurement reports: four first-line and three second-line ARV combinations (see Box 1).

We created these combinations from the individual ARV, although lopinavir/ritonavir is always a fixed-dose combination. Nevertheless, some countries purchased different dose presentations of the same ARV (for instance, zidovudine 100 mg and zidovudine 400 mg) and some purchased fixed-dose combinations of two ARVs (in addition to lopinavir/ritonavir) instead of single ARVs. In those cases where there were two or three different prices for the same ARV combination therapy, we chose the combination which was bought by most countries since our aim was to compare prices between countries. In the case of two second-line combinations, lamivudine+didanosine+lopinavir/ritonavir and zidovudine+didanosine+lopinavir/ritonavir, an equal number of countries purchased didanosine 100 mg and 400 mg. We decided in both cases to use whichever combination price was lower. This turned out to be a combination employing didanosine 100 mg rather than didanosine 400 mg. We did not calculate annual ARV combination costs based on fewest number of tablets or capsules.

Individual component ARV prices obtained from the GPRM were not adjusted for the impact of add-on costs due to shipping, insurance, taxes and other charges (so called ‘INCO’ terms or International Commercial Terms), which have been estimated to add 15% to the total cost (US Government Accountability Office 2005). About 30% of the LAC purchases of ARVs in the GPRM lacked information about shipping terms. There is no clear and obvious relationship between such shipping terms and individual ARV price points (data available from the authors). This uncertainty is not unique to our analysis and has been mentioned by others (Vasan et al. 2006; Chien 2007; Waning et al. 2009). It means, however, that the present analysis is precise only to a magnitude of at least plus or minus 15%. We took this into consideration by conducting a sensitivity analysis and calculated a lower (-15%) and an upper (+15%) price.

<table>
<thead>
<tr>
<th>Box 1 Antiretroviral medicine combinations studied</th>
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<tr>
<td><strong>First-line ARVs</strong></td>
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<tr>
<td>stavudine (40 mg) + lamivudine (150 mg) + nevirapine (200 mg)</td>
</tr>
<tr>
<td>zidovudine (300 mg) + lamivudine (150 mg) + efavirenz (300 mg)</td>
</tr>
<tr>
<td>stavudine (40 mg) + lamivudine (150 mg) + efavirenz (300 mg)</td>
</tr>
<tr>
<td><strong>Second-line ARVs</strong></td>
</tr>
<tr>
<td>abacavir (300 mg) + didanosine (100 mg) + lopinavir/ritonavir (200/50 mg)</td>
</tr>
<tr>
<td>lamivudine (150 mg) + didanosine (100 mg) + lopinavir/ritonavir (200/50 mg)</td>
</tr>
<tr>
<td>zidovudine (300 mg) + didanosine (100 mg) + lopinavir/ritonavir (200/50 mg)</td>
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We converted unit pricing information to price per adult patient per year (US dollars) using the information on dosing recommended by WHO (2008) for each of the ARVs. A flowchart of the extraction and cleaning process can be found in Figure 1.

The price of each combination was calculated as follows. We calculated the weighted average price per patient per year of each component ARV in each country. We did this by summing the pooled expenditures (in US dollars) for innovator and generic versions for that particular ARV in 2008 for that specific country, and dividing it by the number of pooled innovator and generic units (e.g. tablets, capsules) purchased in 2008 for that ARV in that country. Then we calculated the price of each combination in that country in 2008 by adding the average prices of each of the component ARVs that make up the combination. We define this as the 'average annual ARV patient price per combination'. Prices were calculated by taking into account the dose that each patient requires per day based on WHO recommendations for a 60 kg adult (WHO 2008).

All statistical analyses for the study were done with the software STATA, version 11.0.

**Data analysis**

We identified price variations of our ARV combinations in 13 countries in the LAC region that reported to the GPRM in 2008.
‘Benchmarking’ of prices for combination therapies

For various ARV combinations in 2008, we calculated the average annual patient price (as described above), which we called the ‘GPRM reported price scenario’, as well as an upper and lower 15% price range to take INCO uncertainties into account.

These GPRM-based procurement prices for various ARV combinations were used to estimate how many patients could be treated by a given ARV combination, assuming a country’s total expenditure (in US dollars) for a given ARV combination would be used to purchase ARVs at a ‘benchmark’ price for the ARVs, rather than the ‘GPRM reported price scenario’, as described above. The total expenditure (in US dollars) for a given ARV combination was calculated by multiplying the number of units purchased per year with the average price per patient per year of each component ARV, and taking the sum of the expenditure for each individual ARV necessary to assemble the combination.

We created four different benchmarks which complement each other in monitoring the procurement process: (1) ARV combinations, each of whose individual components are priced close to manufacturing cost; (2) ARV combinations, each of whose individual components are priced at the lowest generic ARV price in the region, regardless of country; (3) ARV combinations, each of whose individual components are priced at the lowest innovator ARV price in the region, regardless of country; (4) ARV combinations, each of whose individual components are priced at the median global transaction price for lower-middle-income countries (LMICs) according to the definition of the World Bank (World Bank 2011).

**Benchmark 1: Cost of production**

We used individual ARV manufacturing costs provided by Pinheiro et al. (2006) to calculate the lowest direct manufacturing cost (LDMC) and highest direct manufacturing cost (HDMC) of that ARV for 2008. Pinheiro et al. (2006) determined the LDMC and the HDMC for a series of ARVs based on the lowest and highest active pharmaceutical ingredient (API) prices reported by the WHO and the direct and indirect production costs from Brazil’s public production facilities. In addition, they determined the percentage that the API represents of the LDMC and the HDMC. It was necessary to project the API costs for 2008 using 2006 and 2007 API costs reported by the WHO (Pinheiro et al. 2006; WHO 2007) using linear regression. Then we calculated the LDMC and HDMC using the percentage that APIs represent of the total direct manufacturing cost according to Pinheiro et al. (2006). The LDMC and HDMC for each individual ARV of the seven ARV combinations under study (see above) was used to calculate the LDMC- and HDMC-based annual cost per patient of the combination. Next, we calculated how many patients could be treated with the amount spent in that country for the given ARV combination. This was done by dividing the country’s total GPRM-based expenditure on the ARV combination for 2008 by the respective LDMC and HDMC benchmark-based annual cost per patient of the same ARV combination.

**Benchmark 2: Lowest regional generic price**

For the prices for each of the seven ARV combinations, we identified the lowest generic ARV annual price per patient in the region for each component of the combination. As for Benchmark 1, we calculated how many people could be treated for each combination by dividing the amount of that country’s GPRM-based expenditure for each ARV combination by the benchmark (i.e. the lowest generic annual cost per patient of the same ARV combination).

**Benchmark 3: Lowest regional innovator price**

The prices for each of the seven ARV combinations were calculated by using the lowest innovator ARV annual price per patient in the region for each component of the combination. Similar to the first scenario, we calculated how many people could be treated for each combination by dividing the amount of that country’s GPRM-based expenditure for each ARV combination by this benchmark (i.e. the lowest innovator annual cost per patient of the same ARV combination).

**Benchmark 4: Global median transaction price (MLMTP) for lower-middle-income countries**

For each component ARV in a combination, we calculated the median procurement price from all LMICs as of 2008 using a published GPRM report (WHO 2010b) to obtain the annual ARV price per combination reported. Similar to the other scenarios, we calculated how many people could be treated for each combination by dividing the amount of that country’s GPRM-based expenditure for each ARV combination by this benchmark (i.e. the median LMIC annual cost per patient of the same ARV combination).

**Creating a comparator metric: the patient ratio**

We created a comparator metric (the ‘patient ratio’) for various countries for 2008 and for each benchmark. The numerator of this ratio varies, as this depends on the number of patients that could be treated using the various ‘benchmark’ prices for the ARV combinations, as described above. The denominator of this metric remains constant and is the number of patients that could be treated with the GPRM-based annual expenditure for this combination in 2008. A patient ratio greater than 1 for a given benchmark means that the particular country could be treating more patients than it currently is (based on the present annual GPRM-based expenditure) if it had procured the ARV combination at the benchmark price. Put more bluntly, a ratio >1 means that the procurement authority is paying more for the ARV combination than the benchmark. A patient ratio less than 1 means that purchasing the ARV combination at the benchmark price offers no advantages over the present annual expenditure.

**Results**

In total, 16 countries in the LAC region reported to the GPRM in 2008 from which 13 were included in the analysis as they bought sufficient volume to assemble the seven ARV combinations studied. The profiles of those countries used in the analyses [in terms of people affected by HIV/AIDS, the Gross National Income (GNI) and health spending] are summarized.
in Table 1. Haiti is the only low-income country of the region, and of all the countries, it has the highest number of people living with HIV/AIDS and the second highest prevalence (among the 15–45 year age group) after Guyana. Three upper-middle-income countries were included, of which the Dominican Republic has the highest total number of patients affected by HIV.

Cross-country comparison of ARV combination prices
The annual ARV first-line combination procurement prices per patient per year for 2008 ranged between US$97 and US$915. For a detailed description of individual ARV prices see Supplementary Data Appendix 1.

In brief, public-sector procurement prices for second-line ARV combinations varied more between countries than did first-line ARV combinations. For Guatemala, El Salvador and Antigua and Barbuda, all second-line combinations were above US$2000 per patient per year (see Supplementary Data Appendix 1 for all prices). The prices for first- and second-line combinations cannot be explained by GNI or by number of people affected in each country (data available upon request).

Benchmarking
First-line ARVs
The ‘patient ratios’ for all four benchmarks for stavudine+lamivudine+nevirapine are in Figure 2, and the ratios for zidovudine+lamivudine+efavirenz are in Figure 3, including ±15% error bars to take the uncertainty in INCO terms into account. We chose these two combinations because stavudine+lamivudine+nevirapine is consistently the lowest priced and zidovudine+lamivudine+efavirenz is consistently the highest priced procured combination in all countries (except Nicaragua). Supplementary Data Appendix 2 presents a table with the patient ratios for all ARV combinations and benchmarks.

All countries except El Salvador and Peru are procuring these particular first-line combinations at less than the global median procurement price benchmark (patient ratio <1). Further, because the particular benchmark is based on the global median price, this indicates that, except for El Salvador and Peru, the countries Haiti, Nicaragua, Bolivia, Honduras, Guatemala, Guyana, Ecuador, Dominican Republic, Jamaica, and Antigua and Barbuda are procuring these ARV combinations at a price that is in the lower 50% of the global price range for this combination in all LMICs.

Comparing countries’ public-sector procurement prices against the lowest regional innovator price for the particular ARV combination reveals that for stavudine+lamivudine+nevirapine, countries are already procuring at lower than this benchmark (i.e., patient ratio <1). Hence, the patient ratio suggests that procuring these ARVs at the least expensive regional innovator price would not result in any ‘opportunity costs’ in terms of additional patients that could be treated.

Importantly, all of the LAC countries we have analysed are procuring these two combinations at more than the lowest regional generic price for the combination, all countries could be treating between 1.17 and 3.80 times more patients (Figures 2 and 3). For stavudine+lamivudine+nevirapine, most countries pay more than or close to the ‘lower end’ of the marginal cost of manufacturing (LDMC), except for the Dominican Republic which pays less (Figure 2). All countries are paying less than the ‘upper end’ of the marginal cost of manufacturing (HDMC). In short, for this combination, most countries are procuring this

<table>
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<th>Table 1 Total number of countries included in the data extracted from Global Price Reporting Mechanism and their profiles</th>
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<tr>
<td><strong>Country</strong></td>
</tr>
<tr>
<td><strong>Low income</strong></td>
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<tr>
<td>Haiti</td>
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<td><strong>Lower-middle income</strong></td>
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<td>Bolivia</td>
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<td>Honduras</td>
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<td>Guatemala</td>
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<td>Guyana</td>
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<td>Nicaragua</td>
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<td>El Salvador</td>
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<td>Belize</td>
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<tr>
<td><strong>Upper-middle income</strong></td>
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<tr>
<td>Dominican Republic</td>
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<tr>
<td>Jamaica</td>
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<tr>
<td>Antigua and Barbuda</td>
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n.a. = data not available.
Figure 2 Patient ratios for first-line ARV therapy stavudine+lamivudine+nevirapine at various benchmark prices. A patient ratio of 1 means that the procurement price is the same as the benchmark price. A ratio of <1 means that the procurement price is below the benchmark and >1 means that the procurement price is above the benchmark price.

LDMC = Lowest direct manufacturing cost; HDMC = highest direct manufacturing cost; LRGP = lowest regional generic price; LRIP = lowest regional innovator price; MLMTP = Median lower-middle-income country transaction price.

Figure 3 Patient ratios of first-line ARV therapy zidovudine+lamivudine+efavirenz at various benchmark prices. A patient ratio of 1 means that the procurement price is the same as the benchmark price. A ratio of <1 means that the procurement price is below the benchmark and >1 means that the procurement price is above the benchmark price.

LDMC = Lowest direct manufacturing cost; HDMC = highest direct manufacturing cost; LRGP = lowest regional generic price; LRIP = lowest regional innovator price; MLMTP = Median lower-middle-income country transaction price.
combination at a price that is between the lower and upper limits (as we have calculated them) of the marginal manufacturing cost.

For the combination zidovudine-lamivudine-efavirenz, it would appear that all countries except El Salvador are procuring this combination at less than both the lower limit and upper limits of manufacturing cost (Figure 3). Certainly paying less than the LDMC would appear to be an irrational result, and points to one limitation of this particular benchmark (see Discussion section).

Second-line ARVs

Figures 4 and 5 show the patient ratios for all four benchmarks for the lowest price second-line ARV combination (lamivudine-didanosine-lopinavir/ritonavir) and the highest price second-line ARV combination (abacavir-didanosine-lopinavir/ritonavir). Supplementary Data Appendix 2 shows the patient ratios for all three combinations and benchmarks. For these two particular second-line combinations, procurement prices were all at or above the global median price benchmark (patient ratio >1) except for Guyana. This means that only Guyana, of all the LAC countries analysed, paid a price that is in the lower 50% of the price range in LMIC globally. Significantly more patients could be treated if the LAC countries would procure these two combinations using the global median price (between 1.09 and 3.90 times more patients, depending on the country).

Procuring these second-line ARVs at the lowest regional innovator price as well as the lowest regional generic price would also result in being able to treat many more patients (patient ratios ranging from 1.55 to 4.96, depending on the country and ARV combination).

For both of these second-line combinations, all countries are consistently paying more than the LDMC and less than the HDMC. Indeed, all countries would be able to treat between about 1.2 and 6 times as many patients if they procured either of these second-line combinations at the LDMC.

Discussion

This is not the first analysis of the GPRM (Vasan et al. 2006; Chien 2007; Waning et al. 2008; Waning et al. 2009; Wirtz et al. 2009), although, aside from Waning et al. (2008), this is one of the rare attempts to develop a series of benchmarks that can help procurement agencies identify opportunities to evaluate their procurement efficiencies.

We use data from Latin America to illustrate the use of the developed benchmarks. The LAC region is less often the focus of attention by the international donor community than countries of sub-Saharan Africa, but benchmarking is nevertheless very relevant for HIV-affected countries and can provide relevant policy lessons—not only for those in the region relying on donor funding but also for those countries which domestically finance their HIV programmes. Previous work on ARV pricing in the LAC region has tended to concentrate on Brazil (Pinheiro et al. 2006; Nunn et al. 2007; Nunn et al. 2009).

There is no general agreement how to set benchmark prices for different countries. A previous study on benchmarking (Waning et al. 2008) has suggested global median procurement prices, the Clinton Health Access Initiative price lists (e.g. Clinton Foundation 2008) or the MSF prices. The results show that whereas for first-line combinations, prices were lower than the global median price for lower-middle-income countries, for second-line ARVs most countries pay more than the global median price. As aggregating prices over the entire globe may simply be inappropriate in some situations, the global median procurement price should be used in combination with a regional benchmark, if possible. MSF prices are manufacturer-quoted prices and might not reflect actual procurement prices. Another difficulty in using MSF and Clinton Foundation prices is that many Latin American countries do not qualify for the reduced pricing regimes by manufacturers or do not form part of countries of the Clinton Foundation consortia.

Curtiss et al. (2010) provide criteria to judge different benchmarks, all of which can be evaluated and prioritized, itself not a trivial exercise. Some of the considerations which should be taken into account to judge alternative benchmarks are whether the pricing data are accessible, whether they are timely, accurate and easily understood as well as relevant to the products under consideration (Curtiss et al. 2010). Provider organizations such as social security institutions or Ministries of Health should review these criteria and decide which are locally relevant benchmarks and which of the benchmarks are complementary in the planning of the procurement negotiation process.

Our study proposes four benchmarks: the lowest generic regional price, the lowest regional innovator price, as well as introducing the procurement price of other countries at the same income level (MLMTP) and the lowest (LMDC) and highest manufacturing cost (HMDC). For stavudine-lamivudine-nevirapine, most countries are apparently procuring ARVs for their public sectors at more than the lowest and less than the highest direct manufacturing cost, an impressive achievement if true. We have found that for zidovudine-lamivudine-efavirenz, all countries are apparently procuring ARVs for their public sectors at less than our lowest and highest direct manufacturing cost (LDMC/HDMC) benchmarks. This points out some limitations to these particular benchmarks. First, we have extrapolated data from ARV producers in one country (Brazil) from 2006 and have applied it to a range of other countries, although none of which is capable of producing ARVs de novo (i.e. starting from raw materials). Second, although creating a benchmark associated with actual costs of manufacturing would be a great advance as this benchmark price offers a way to identify major potential cost savings, such information on real costs of manufacturing is unfortunately very difficult to obtain. More transparency in data about manufacturing costs would enable procurement agencies to identify potential inefficiencies.

Indeed, the lowest regional generic price benchmark might actually be more feasible as a reference for off-patent ARVs. The regional lowest innovator price as a procurement benchmark might be more appropriate for newer first- and second-line ARV combinations in which there are no generic forms currently on the market to create a benchmark, even in LMICs. The ‘best’ benchmark does not exist and should be chosen by its purpose and accuracy in defining some common value at a given point in the chain of medicine procurement and distribution.
Figure 4 Patient ratios of second-line therapy abacavir-didanosine-lopinavir/ritonavir at various benchmark prices. A patient ratio of 1 means that the procurement price is the same as the benchmark price. A ratio of <1 means that the procurement price is below the benchmark and >1 means that the procurement price is above the benchmark price.

LDMC = Lowest direct manufacturing cost; HDMC = highest direct manufacturing cost; LRGP = lowest regional generic price; LRIP = lowest regional innovator price; MLMTP = Median lower-middle-income country transaction price.

Figure 5 Patient ratios of second-line therapy didanosine-lamivudine-lopinavir/ritonavir at various benchmark prices. A patient ratio of 1 means that the procurement price is the same as the benchmark price. A ratio of <1 means that the procurement price is below the benchmark and >1 means that the procurement price is above the benchmark price.

LDMC = Lowest direct manufacturing cost; HDMC = highest direct manufacturing cost; LRGP = lowest regional generic price; LRIP = lowest regional innovator price; MLMTP = Median lower-middle-income country transaction price.
The number of additional patients that could be treated is an illustrative way to express the ‘risk’ of procuring ARV at a higher price. Not surprisingly, we found that most countries in the LAC could be treating a larger number of patients than they do at present (e.g. using 2008 prices) if procurement prices were closer to the lowest regional generic price. For all second-line combinations, a price closer to the global median price for LMICs, and indeed, closer to the lowest regional innovator price, would also result in treating more patients. Consequently, patent status of the ARV in a particular country would not necessarily be a barrier to procurement of cheaper ARVs if the minimum innovator price would apply to the entire region.

For financial policy and health planning, the present comparative analysis can help identify those countries which were paying many times more than others in the region. Two countries, El Salvador as well as Guatemala in the case of second-line combinations, stand out as the countries which paid more than others in the region. It is relevant, particularly for El Salvador and Guatemala, to examine underlying causes of their high ARV prices and create strategies to lower prices, if possible. Findings from previous research in El Salvador indicate that in 2007, prices in the private sector were extremely high for both originator brands and generics (about 58 and 28 times the international reference prices used, respectively), possibly related to high mark-ups of importers/distributors and pharmacies (Cameron et al. 2011).

There are several limitations to this study. One major limitation is that we did not independently verify the information reported to the GPRM, for instance by contacting procurement agencies of various countries to verify prices. Since there is no general agreement on the data analysis and cleaning method of the GPRM, we performed a calibration with the method of Waning et al. (2009) using the GPRM (Supplementary Data Appendix 3), which does provide sufficient assurance that our method is externally valid with regard to inferences about relative differences between LAC countries and relative differences among benchmarking protocols in the LAC.

One difference between the Waning et al. (2009) method and ours is the way we treated price ‘outliers’. Briefly, using the Waning et al. (2009) method for dealing with outliers would have eliminated El Salvador from consideration and as the present analysis is restricted to the LAC, their method would unnecessarily bias the results. We had to pool procurements for both innovator and generic ARVs as the number of procurements for some individual ARVs was often quite small in some countries. Also we did not take ‘pill burden’ into account when estimating prices of ARV combinations, which might introduce a small bias, as physicians and patients both may prefer regimens requiring fewer pills taken per day, but we do not know its magnitude. We calculated a weighted average instead of a median ARV price for the individual ARVs. Estimating the median is useful if there is a large number of procurements with a wide variation in prices. However, we were dealing with small procurement sample sizes for individual countries. Weighted averages would best reflect the price paid per year.

We did not perform an analysis of paediatric formulations—this is difficult to do as assumptions have to be made about weight and dosage. There are too few procurements of newer paediatric fixed-dose combinations in the LAC region to perform a reasonable analysis.

The actual cost to a country of treating any ‘extra’ number of patients is more than just the cost of ARVs as there are other variables and fixed costs involved. Although we may be able to quantify ‘how many additional patients could be treated if country X bought ARVs at a certain price’, the question of ‘which patients’ and how many additional patients to actually enrol remains unresolved (Rosen et al. 2005).

Also, the method is much easier if we were benchmarking fixed dose combinations (FDCs) as we would not need to add the price of individual components. Although triple FDCs are rapidly becoming the standard of care for adults and children (WHO 2010c), the methods described in this paper will still be useful until all those in need receive FDCs.

Finally, we note that subsequent years have seen very few LAC countries reporting to the GPRM (Supplementary Data Appendix 4), possibly because many LAC countries are no longer receiving financial aid from the Global Fund. Only in the years before 2009 is there a sufficient variety of countries to be included to perform cross-sectional studies on prices between countries. We think this is not reflective of any limitation on the benchmarking methodology itself.

**Conclusion**

The critical point coming out of this study is the need for greater transparency in the prices of medicines. Given the apparent trend towards fewer LAC countries reporting to the GPRM, LAC countries could, in principle, use GRPM prices from other regions (e.g. Europe or Asia) to develop procurement benchmarks. Most preferably, procurement authorities in LAC countries should be creating their own publicly-available databases for use within the LAC. We further point out that using benchmarking on a routine basis could be a useful instrument for policy makers when analysing costs as it promotes medicines procurement that reasonably allocates scarce resources. The ‘best’ benchmark does not exist and should be chosen based on its purpose, its accuracy, the accessibility of information and type of product (generic or innovator). Some rational allocation of financial resources due, in part, to price benchmarking and careful planning by policy makers and programme managers can assist a country in negotiating lower ARV procurement prices and should form part of a sustainable procurement policy. A lack of market intelligence on regional prices is no longer an excuse for poor performance from a procurement authority.

**Supplementary Data**

Supplementary Data are available at Health Policy and Planning online.

**Acknowledgement**

We would like to thank Richard O. Laing for his valuable comments on an earlier version of the manuscript.

**Funding**

We would like to thank the Ford Foundation and the National Institute of Public Health in Mexico for providing the funding for the study.
Conflict of interest
None declared.

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