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Mapping External Reference Pricing Practices for Medicines

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Abbreviations

EAHC	European Commission Executive Agency for Health and Consumers
EASP	Andalusian School of Public Health
EC	European Commission
ERP	External reference pricing
GDPpc	Gross Domestic Product per capita
HAI	Health Action International
GFATM	The Global Fund to fight AIDS, Malaria and Tuberculosis
IGFAM	UK Intergovernmental Forum on Access to Medicines
LMIC	Low- and middle-income countries
MSH	Management Sciences for Health
OTC	Over-the-counter
PMPRB	Patented Medicine Prices Review Board, Canada
PPI	Pharmaceutical Price Information
PPRI	Pharmaceutical Pricing and Reimbursement Information
R&D	Research and development
UK	United Kingdom
WHO	World Health Organization

Executive summary

Objectives

One option to manage or regulate medicine prices is External Reference Pricing (ERP) which is increasingly being used worldwide, particularly in higher- income countries, or being considered to be used, mainly in low- and middle-income countries. ERP is the practice of using the price(s) of a pharmaceutical product in one or several countries in order to derive a benchmark or reference price for the purposes of setting or negotiating the price of the product in a given country. There is little evidence on the effects of ERP either for the country that applies it, or for the countries being referenced to.

The UK's Intergovernmental Forum on Access to Medicines (IGFAM) has debated whether ERP is an impediment to differential pricing, especially in lower-income countries that may be referenced to by more wealthy and lucrative countries. Therefore, this study was undertaken to map and better understand the use of ERP, in particular which countries do not use ERP, which countries use ERP, the structure and processes used, and which low- and lower-middle income countries are being referenced to. This information would be used to test the hypothesis that a very limited number, if any, of low-income and lower-middle income countries are used as price reference countries by higher-income countries, therefore pharmaceutical companies would be able to offer lower prices to lower-income countries without affecting their business model in higher-income countries.

Methodology

Data collection was undertaken in two stages from October 2013 to August 2014. In Stage 1, a brief initial questionnaire was disseminated to 367 key national informants and contacts known to the World Health Organization (WHO) and Health Action International (HAI), and identified via various mailing list servers and other mechanisms. Questions were asked to ascertain which countries had medicine pricing and/or reimbursement regulations, were or were not using ERP, were planning to use ERP, and whether any countries were referencing to their prices. Data from 73 countries were collected and collated using LimeSurvey. In Stage 2, a detailed questionnaire was sent via email to countries using ERP according to the responses to the Stage 1 questionnaire, plus those in the Pharmaceutical Pricing and Reimbursement Information (PPRI) network, that covers mainly European countries, in order to characterise the use of ERP. Data was also collected from recently published research and other sources. Data from 27 countries which reported using ERP were analysed. A questionnaire was also sent to the countries who were planning to use ERP (5 responded).

Results

We identified 55 countries that were using ERP, 45 countries that were not, and 14 countries that were planning to use ERP. Most countries using ERP are in the European region, and classified by the World Bank (2014) as high-income countries. Only five low-income countries were using ERP. The majority of countries (9 of 14) planning to use ERP were middle-income countries.

Countries using ERP are referencing mainly to countries in their geographical area, although there were exceptions. Three criteria are mainly being used to select the countries to reference to (1) in the same region (2) similar/comparable income levels (3) similar socioeconomics conditions. ERP-using countries tend to reference to countries with a higher GDP per capita.

Fifteen of 27 countries knew they were being referenced to but some information was contradictory with information from other sources, mainly publications. Ten countries recalled being asked for price information.

Some countries use price databases, such as the Management Sciences for Health's (MSH) International Drug Price Indicator Guide or the EURIPID database.

Most countries have a formal, explicit document regulating the application of ERP. While the majority of countries simultaneously use several criteria for pricing and reimbursement, it was not clear how these criteria are combined or weighted, or whether they are used according to a certain order or conditions. Almost all countries use ERP for on-patent prescription medicines, and many also use it for generic prescription medicines. The number of products where the price has been set using ERP varied substantially among the countries, from only a few to the several hundred.

The most frequent prices sought are the manufacturer's/ex-factory price, followed by the wholesale price. A key requirement for applying ERP is the accessibility of price information. Most countries stated that they use freely-accessible websites to access prices which is likely biasing the selection of the countries and databases they reference to. Most countries use official price lists, which is problematic as they rarely provide actual transaction prices. In some countries, companies are required to provide prices in other countries. Eleven of the 27 countries said that they do not validate or cross-check the price data with other sources. Eight countries reported that they use the lowest price in the basket of countries, five countries use the median price, and six countries use the mean price. Most countries do not revise the price following price changes in the reference countries.

Conclusion

Based on information from 100 countries, we found no examples of high-income countries referencing low-income countries as defined by the World Bank. On the basis of this finding, low prices offered by pharmaceutical companies to low-income countries would not result in reduced prices in high-income countries as a consequence of current, formal ERP practices. Moreover, the practical difficulties of identifying prices in low-income countries, especially actual prices (net of discounts, rebates, etc.) as opposed to official prices, makes the possibility of high-income countries referencing prices in low-income countries very unlikely. A key secondary finding of this study is that ERP is not a "simple" system to operate and requires substantial human and institutional resources, and accurate information, to implement effectively. Low-income countries which do not at present use ERP should consider these substantial resource requirements before they decide to attempt to implement such a system.

1. Introduction and objectives

A number of pharmaceutical policy options exist to manage medicine prices and volumes (supply and demand side measures). Many factors influence the choice of policies including who is paying for the medicine (government, insurance system, patient), the type of product (single-source or multi-source), the value and volume of the medicine, etc.

One option to manage and regulate medicine prices is External Reference Pricing (ERP), which is increasingly being used worldwide, particularly in higher income countries, or being considered to be used, mainly in low- and middle-income countries. ERP, sometimes known as international reference pricing, is the practice of using the price(s) of a pharmaceutical product in one or several countries in order to derive a benchmark or reference price for the purposes of setting or negotiating the price of the product in a given country¹.

ERP differs from internal reference pricing (IRP), which is the practice of using the price(s) of identical medicines (ATC 5 level) or similar products (ATC 4 level) or even with therapeutically equivalent treatment (not necessarily a medicine) in a country in order to derive a benchmark or reference price for the purposes of setting or negotiating the price of the product in a given country.

Despite its increasing use, there is little empirical research and not much evidence on the effects of ERP either for the country that applies it, or for the countries being referenced to. But, as with all medicine pricing policies, ERP is thought to pose problems, as identified in the WHO/HAI review on ERP which was written by Jaime Espin and Joan Rovira from the Andalusian School of Public Health (1), and concerns are growing about its appropriateness in Europe and outside it (2). Of particular concern to lower-income countries is that ERP might be an obstacle for a pharmaceutical company offering lower prices to lower-income countries.

For a number of years, the UK's Intergovernmental Forum on Access to Medicines (IGFAM) has discussed practices that impede the offering of lower prices to lower-income countries. IGFAM has identified ERP as a perceived impediment to offering lower prices to lower-income countries, especially in lower-income countries that may be referenced to by more wealthy and lucrative countries. Therefore, this study was undertaken with the objective of mapping and better understanding the use of ERP, in particular:

- which countries do not use ERP
- which countries use ERP, the structure and processes used, and which low- and lower-middle income countries are being referenced to.

The study included:

1. Reviewing the literature published since the WHO/HAI review, particularly on the use of ERP in low- and middle-income countries;

¹ WHO/HAI Review Series on Pharmaceutical Pricing Policies and Interventions. Working Paper 1: External Reference Pricing. Accessible on <http://www.haiweb.org/medicineprices/policy/index.html>

2. Identifying key informants and ascertaining which countries do not use ERP and which countries do use ERP; and
3. Characterising the use of ERP in those countries using ERP.

This information would be used to test the hypothesis that a very limited number, if any, of low-income and lower-middle income countries are used as price reference countries by higher-income countries, therefore pharmaceutical companies would be able to offer lower prices to lower-income countries without affecting their business model in higher-income countries.

Not for distribution or citation

2. Background

The 2011 WHO/HAI review on ERP by the authors stated:

In recent years, many countries have introduced the practice of External Reference Pricing (ERP), where the national regulated price is derived from or somehow related to those in a 'basket' of reference countries. ERP is defined in this paper as "The practice of using the price(s) of a pharmaceutical product in one or several countries in order to derive a benchmark or reference price for the purposes of setting or negotiating the price of the product in a given country". There are many modalities of ERP with varying combinations of methods for choosing or calculating external reference prices and also many ways to apply ERP in practice. Therefore, assessing the impact or merit of ERP, in relation to other pricing approaches, can be difficult.

Countries need to consider the appropriateness of ERP along with all other options for attaining efficient medicine prices, including promoting price competition through the introduction of competitive policies – especially in the case of off-patent medicines – as well as other price regulation options. The application of ERP should be objective and transparent, in order to provide opportunities for assessing its effects, make decision-makers accountable, reduce uncertainty for the pharmaceutical industry, and diminish the risk of discrimination and corruption.

A non-systematic literature review identified two recent and relevant studies on ERP that had not been included in the 2011 WHO/HAI review i.e. a 2013 RAND Corporation study and a 2014 report by the European Commission's Executive Agency for Health and Consumers.

The RAND study (3) focussed on the role of reference pricing as a means to determining pharmaceutical prices in high-income countries (Canada, France, Germany, Italy, The Netherlands and Spain) and on the potential effects on the prices of medicines in the UK. The study found that:

- ERP, or international price comparison, is a common strategy to control prices of pharmaceuticals that are protected by intellectual property rights and benefit from a legal monopoly (on-patent medicines).
- The pharmaceutical market in the UK only accounts for a small proportion of global sales, however, UK prices are important as many countries reference their prices against those in the UK.
- High variability of ERP across different settings and in the relative importance of this approach in comparison with other pricing strategies.
- There was considerable variation in the terminology and practices used, and understanding the complexities of countries included in reference baskets requires considerable semantic clarification.
- There was considerable overlap between countries that cross-reference, and it remains challenging to estimate the direct, immediate impact on external reference baskets.

- The international impact of pricing changes in the UK is likely to be minimal or indirect, largely because of the diverse ways in which reference pricing is implemented in the countries examined.

The most recent publication on ERP is a 2014 report of a project commissioned by the European Commission Executive Agency for Health and Consumers (EAHC) to further identify and assess “Unwanted effects at EU Member States level of ERP schemes that are the result of medicinal product price setting decisions taken in one EU MS that set off dynamic effects in other EU MS and/or in the decision initiating MS itself” such as price instability and suboptimal patient access to medicines (4).

The assessment was based on a simulation model. This is a legitimate and potentially useful approach, especially in areas where controlled experiments are not feasible (pricing policy certainly is one such area). However, it must be acknowledged that simulation models can be biased and misleading and their results should be considered with care, unless the predictive capacity of the model has been appropriately validated with empirical data.

The project covered all the 28 European Union Member States and some other OECD member countries i.e. Australia, Canada, Iceland, Japan, South Korea, Mexico, New Zealand, Norway, Switzerland, Turkey, and United States. The results indicate that in Europe, by 2013, 23 countries out of 31 use ERP as the main criterion when setting the price of a new medicine i.e. Iceland, Ireland, Norway, Portugal, France, The Netherlands, Switzerland, Estonia, Latvia, Lithuania, Czech Republic, Denmark, Austria, Slovenia, Croatia, Hungary, Slovakia, Romania, Bulgaria, Greece, Cyprus, Malta and Luxembourg. Six countries (Spain, Belgium, Germany, Finland, Poland and Italy) use ERP as supportive information. Two countries (UK and Sweden) do not apply ERP. According to this study, outside Europe ERP is also used by Australia, Canada, Japan, South Korea, Mexico, New Zealand and Turkey.

The simulation exercises, using scenarios to assess the price dynamics through ERP-based systems and the impact of changes in ERP policies, suggests some effects of ERP. For example, ERP, used as the only criterion, led to lower price erosions than would be observed in real-life, suggesting that other pricing policies, potentially amplified by ERP, are involved in driving prices down.

Frequent price revisions, iterative price cuts, large country baskets, price calculation methods, genericisation impact, and sources of prices were among the most influential parameters on the evolution of medicine price over time through ERP-based systems.

The simulations suggest that ERP incentivises launch sequence strategies by pharmaceutical companies, but does not result in substantial price convergence over time.

The report concludes that ERP seems an appropriate tool to set prices, at least for some countries.

A study (Espin and Rovira, forthcoming) tried to assess the impact of ERP on the availability and prices of medicines in the EU. The study applied an observational design, consisting of an analysis of historical annual average prices of products accepted by the EMA centralized market authorization system in the initial and final periods of the 2000-2009 decade. Two sets

of new medicines approved by the EMA centralised procedure were selected from the EMA website: products approved between 2000 and 2003 (27 products), and those approved in 2007 (33 products). The samples were restricted to solid oral presentations of prescription medicines used mainly in ambulatory care.

The results show that launch prices of new products tend to converge in Europe. A second finding is that a shorter delay to marketing is associated with countries with higher gross domestic product, increased public spending on health, a higher percentage of GDP on health expenditure and a higher price, all results being statistically significant.

Comparing the two sets of medicines - at the beginning and at the end of the period - the analysis highlights an increase in the proportion of countries where a certain number of new medicines never reach the market. However, in the countries where the new products are marketed, the delays to market availability tend to decline and converge across countries.

The analysis found a large variability even after controlling for the factors that were expected to explain the variations in launch prices of the products. These results suggest that factors other than those considered in the analysis play an important role in determining the structure of international prices at a given time and in explaining its evolution over time. These factors might include some characteristics of the medicines such as therapeutic value and the existence of competitors. The authors acknowledged that the design of the study does not allow one to unambiguously assign the variations in prices and launch delays to the effects of ERP as other factors, mainly parallel trade, might be partly responsible for the trends and variability observed.

Two of the main effects and problems of ERP identified in the literature, which are assumed to decrease availability², are:

- The convergence of prices, which usually implies that lower-income countries that formerly might have had relatively lower prices, have seen their prices rise towards an international or EU average, making medicines more unaffordable.
- Lower-income countries are assumed to experience longer delays in new medicines reaching their markets. An increasing proportion of new medicines might never reach these markets.

As has been shown, there is limited and inconclusive empirical evidence to support these claims, which are mainly based on theoretical reasoning and modelling. One of the likely reasons why there is little evidence on the effects of ERP is that the term includes a large number of modalities, which vary substantially in key aspects. It is probably difficult to identify where and when ERP is actually implemented, and to what extent it is implemented.

National regulators have probably looked for a long time at the prices of medicines in other countries in order to find some benchmarks to justify and support their positions when negotiating prices with suppliers. In the past, most countries used a cost-plus (or cost of

² Availability is also affected by marketing authorisation, pricing and reimbursement procedures. It is, therefore, not easy to assess and quantify the relative importance of each potential cause on the observed delays.

production) criterion to regulate the price of medicines. This approach has been progressively discredited and abandoned in many countries for a number of reasons, including not incentivising production efficiency and not being feasible for pricing on-patent products (where price is assumed to allow the originator company to recover all R&D expenditure, not only that of the successful product whose price is being regulated). Therefore, pricing/reimbursement departments, or regulators, may have always had an eye on international prices and used the information, if convenient, as part of their argument to justify a price that the company decries as “too low”. This practice might not be ERP in a strict sense, but it is likely to have similar effects than a more formal ERP system that is supported by explicit regulatory provisions. Some countries use ERP together with other pricing criteria, but it is not always clear which criterion is used at a given time and for a given pricing decision.

Conversely, many countries with a more formally-defined ERP mechanism do not strictly apply it, but rather use the reference price computed as a benchmark for price negotiations. This may result in a substantially higher regulated price, especially when the medicine concerned has a high therapeutic value and/or is under some form of market exclusivity that gives the supplier a strong negotiating power.

Moreover, there are different ways of enforcing a formal ERP system. At one end of the continuum, there are the countries that apply ERP in a strict way, i.e. they compute a reference price and force suppliers to a “take it or leave it” decision. At the other end, there are countries that use ERP in a very informal way, such as a reference for a negotiation process perhaps combined with other criteria, and are prepared to accept a higher price in order to ensure the availability of the medicine.

The problem for the empirical analysis of the effects of ERP is that, depending on where a country lies in this continuum, the effects are likely to differ substantially. In addition, it is usually impossible to assess at what point in the continuum each country lies.

Other difficulties for assessing the effects of ERP include:

- To identify the precise times when ERP became operational in a country, when it experienced significant formal changes (e.g. the basket of reference countries changed), and the way in which it is implemented in practice.
- To separate the effects of the various factors that might impact on the same variables (e.g. ERP and parallel trade are both likely to lead to price convergence, especially in the EU).
- The limitations in the accessibility, validity and comparability of information on actual transaction prices.

The generalisation of ERP is probably one of the main factors that incentivise companies to hide transaction prices, for instance, by granting discounts, rebates and other advantages on the condition of confidentiality or non-disclosure of the actual price. As a result, available information on prices is usually restricted to official list prices which are systematically and substantially higher than real transaction prices.

Despite the challenges in analysing the extent and use of ERP in reality, we undertook this study in the hope of shedding further light on which countries do and do not use ERP, and whether our hypothesis (that a very limited number, if any, of low-income and lower-middle income countries are used as price reference countries by higher-income countries) is valid or not.

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3. Methodology

Data collection was undertaken in two stages from October 2013 to August 2014. In Stage 1, an initial questionnaire was widely disseminated to ascertain which countries were or were not using ERP, or where thinking of using ERP. In Stage 2, a detailed questionnaire was sent to those countries using ERP in order to characterise its use, and a questionnaire was sent to countries planning to use ERP. Following compilation of the findings, a request was made to IGFAM for the pharmaceutical industry to review and validate the findings. No response was received. An interactive map showing which countries do and do not use ERP and who they reference to, is available on HAI's website (<http://www.haiweb.org/medicineprices/>).

Stage 1: Initial questionnaire

In Stage 1 (October 2013 to March 2014), LimeSurvey (<https://www.limesurvey.org/en/>) was used to collect and collate data. National key informants and contacts known to HAI through its medicine pricing work, and to WHO's Department of Essential Medicines and Health Products through its country pharmaceutical profile work, were added to the LimeSurvey database. Countries in the Pharmaceutical Pricing and Reimbursement Information (PPRI) network, predominantly European, were not included in stage 1 as the EC report (4) identified which used ERP.

The initial questionnaire consisted of 9 questions (see Annex I). The questions were designed to identify if the contact was a key informant, whether or not ERP was being used in their country or was planned to be used, and whether any countries were referencing to their prices (where known). To help identify key informants, they were asked to provide details of officials working on medicine pricing and/or financing/reimbursement, or others who they feel should be contacted.

Invitations to complete the questionnaire (as well as the questionnaire itself) were disseminated via LimeSurvey to 367 contacts, in 129 countries, in English, Spanish, French or Russian. An automated reminder email was sent to non-respondents. HAI then sent personal emails to those who did not respond to the automated reminder. Where required, formal letters were sent to countries requesting the information.

HAI and WHO HQ were unable to identify contacts in all countries. So the initial questionnaire was posted on various mailing list servers including E-DRUG, E-LEK (Russian), E-MED (French), E-FARMACOS (Spanish) and Drug-info (Southern Africa). It was also sent to the Ecumenical Pharmaceutical Network for distribution to its members. In addition, WHO regional offices were asked to provide contact details, plus alternative contacts for non-responding countries.

A total of 367 survey invitations were sent via LimeSurvey (most countries had multiple contacts). Of these, completed questionnaires were received from 73 countries (the majority were filled by key informants).

Stage 2 Detailed questionnaire

A longer and more detailed questionnaire was developed to characterize the use of ERP. It was sent to key informants in four countries to pilot test but only one (Iran) responded by the deadline. One question was added, making a total of 31 questions (see Annex II). The questionnaire was sent via personal email (not LimeSurvey) to the PPRI countries (the Andalusian School of Public Health is a member of this network) and to the key informants who said that ERP was being used in their country in the initial questionnaire (in English, Spanish or French). In parallel, a questionnaire was developed for the countries that were thinking of using ERP (see Annex III). It consisted of 18 questions and was available in English and Spanish.

Multiple reminder emails were sent, and numerous phone and face-to-face interviews were held to generate responses. In total, detailed questionnaires from 28 countries were received, although the analysis was made with 27 countries due to the fact that one response was incomplete. The deadline for the detailed questionnaire was end of April, but several questionnaires were received after this deadline (the last one was received on August 20th). Of the 15 questionnaires sent to countries thinking of using ERP, five countries responded.

HAI emailed individuals in countries who said they knew they were being referenced to, but were not using ERP so were not sent the detailed questionnaire, asking for the name of the countries. Of the eight countries that were contacted, responses were received from three.

During phone consultations or email exchanges, it was found that a few countries who said they used ERP were in fact not using it (some countries were confused about the definition of ERP). If a contact stated that ERP was being used/not used, and a key informant from the same country stated otherwise, the response of the better informed key informant was used in the analysis.

Table 1 summarises the number of countries contacted, by World Bank 2014 income levels, to collect information on the use of ERP. In addition, various mailing list servers and other sources were used to obtain data.

Table 1. Countries contacted directly, by World Bank income level

	High-income countries (n=75)	Upper-middle income countries (n=55)	Lower-middle income countries (n=50)	Low-income countries (n=34)
No. of countries contacted in Stage 1 (via Limesurvey, emails, letters)	23	38	40	28
No. of countries in PPRI network contacted	32	9	4	0

4. Results

Initial questionnaire

Responses to the initial questionnaire, responses from PPRI network members, and information from other sources (contacts, literature review and previous studies from the authors) resulted in the identification of 55 countries that were using ERP, 45 countries that were not using ERP, and key informants from 14 countries declared they were planning to use ERP in the future. Tables 2, 3 and 4 summarise the results, categorised by 2014 World Bank income levels.

Table 2. Use of ERP by countries, by World Bank income group

	<i>High-income</i>	<i>Upper-middle income</i>	<i>Lower-middle income</i>	<i>Low-income</i>	
USING ERP	Austria	Albania	Bolivia	Guinea	
	Belgium	Brazil	Côte d'Ivoire	Madagascar	
	Canada	Bulgaria	Egypt	The Gambia	
	Czech Republic	Colombia	El Salvador	Togo	
	Estonia	Hungary	Ghana	Vietnam	
	Finland	Iran	Lao PDR		
	France	Jordan	Moldova		
	Greece	Lebanon	Morocco		
	Iceland	Malaysia	Pakistan		
	Ireland	Mexico	Sudan		
	Israel	Romania	Timor-Leste		
	Japan	Turkey	Ukraine		
	Latvia	Tuvalu	West Bank and Gaza		
	Lithuania				
	Malta				
	Netherlands				
	Norway				
	Poland				
	Portugal				
	Saudi Arabia				
	Slovakia				
	Slovenia				
	Spain				
	Switzerland				
	NOT USING ERP	Australia	Argentina	Cameroon	Afghanistan
		Chile	China	Djibouti	Bangladesh
New Zealand		Ecuador	Fed.States Micronesia	Burkina Faso	
Qatar		Fiji	India	Burundi	
South Korea		Grenada	Kosovo	Comoros	
Sweden		Kazakhstan	Kyrgyzstan	Dem. Rep. Congo	
UK		Mauritius	Mongolia	Ethiopia	
USA		Nigeria	Philippines	Guinea-Bissau	
		Palau	Solomon Islands	Haiti	
		South Africa	Sri Lanka	Malawi	
		Suriname	Syria	Nepal	
		Tunisia	Vanuatu	Somalia	
				Zimbabwe	

Note: The Cook Islands answered yes to the use of ERP and Somaliland answered no to the use of ERP, but they are not listed by the World Bank.

Table 3. Countries planning to use ERP by World Bank income group

	<i>High-income</i>	<i>Upper-middle income</i>	<i>Lower-middle income</i>	<i>Low-income</i>
PLANNING ERP	Chile Qatar	China Ecuador Kazakhstan South Africa Suriname	Kosovo Kyrgyzstan Mongolia Solomon Islands	Burundi Comoros Haiti

Table 4. Number of countries and percentage distribution by income group and ERP status

Number of countries	High-income countries	Upper-middle income countries	Lower-middle income countries	Low-income countries	Total
Using ERP	24 (75%)	13 (52%)	13 (52%)	5 (28%)	55
Not using ERP	8 (25%)	12 (48%)	12 (48%)	13 (72%)	45
Planning on using ERP	2 (25% of non-users)	5 (42% of non-users)	4 (33% of non-users)	3 (23% of non-users)	14
Number of countries in analysis	32	25	25	18	100

The largest number of countries using ERP were high-income countries (24), with equal numbers in the upper-middle income and in the lower-middle income categories (13 countries in each). Only 5 low-income countries declared they use ERP. A clear association emerges when comparing these figures with the number of countries not using ERP by income group. High-income countries are most likely to use ERP. Among upper-middle income and lower-middle income countries, the number not using ERP was identical to that of ERP users. Among low-income countries, those not using ERP are dominant (13 vs. 5). It is worth noting that most countries stating they are planning to use ERP were in the three lower-income groups. These figures should be taken with caution, as they have been derived from multiple and heterogeneous sources.

In the initial questionnaire, countries were also asked if they were aware of any countries, formally or informally, taking the price of medicines in their country as a reference for setting their own prices. The following countries stated they were aware they were being referenced to:

High-income countries: Australia, New Zealand

Upper-middle income countries: Argentina, Colombia, Iran, Jordan, Lebanon

Lower-middle income countries: Bolivia, Cameroon, Kosovo, Morocco, Pakistan, Sudan,

Vietnam

Low-income countries: Madagascar

Countries using ERP

According to the different sources used in this study, 55 countries use ERP. Most of them are in the European region and classified as high-income countries. Only five low-income countries declared they use ERP. Twenty-six (26) middle-income countries (upper and lower) stated they use ERP, including some European countries (Bulgaria and Hungary, for example), some Latin American countries (Colombia and Brazil, for example), and some African countries (Ghana and Côte d'Ivoire).

Countries not using ERP

There are two categories of countries that are not using ERP: those that have official price or reimbursement regulations but do not use ERP (according to our survey they were Bangladesh, Burkina Faso, Burundi, Djibouti, Federated States of Micronesia, Fiji, India, Kazakhstan, Kyrgyzstan, Mauritius, Mongolia, New Zealand, Nigeria, China, Philippines, South Korea, Suriname, Syria and Tunisia) and countries who do not have official price or reimbursement regulations so are not using ERP (United Kingdom, United States of America, Afghanistan, Chile, Comoros, D. R. Congo, Ethiopia, Grenada, Guinea Bissau, Haiti, Kosovo, Malawi, Nepal, Palau, Qatar, Solomon Islands, Sri Lanka, Vanuatu and Zimbabwe).

Countries planning to use ERP

Key informants in 14 countries indicated in the first questionnaire that they were planning to implement ERP i.e. Burundi, Chile, Comoros, Haiti, Kazakhstan, Kosovo, Kyrgyzstan, Solomon Islands, Mongolia, China, Qatar, Suriname, Ecuador and South Africa. Responses to the second questionnaire were received from Burundi, China, Kosovo, Kyrgyzstan and Qatar.

The justifications provided by the respondents for introducing ERP were rather general e.g. because ERP is used by most countries. Many countries only stated as a justification the need to control medicine prices because they seem to be too high, but they did not provide a specific justification for planning to use ERP.

The criteria currently used for regulating prices in these countries were:

- China: Cost-plus calculations (cost of production of the medicine plus a certain profit or margin) and prices of similar medicines on the market to treat the same condition or disease (internal reference pricing). In the future, in addition to ERP they plan to use economic evaluation (pharmacoeconomic) studies and Health Technology Assessment.
- Burundi: Cost-plus calculations
- Kyrgyzstan: Wholesale prices of similar medicines (including one generic) are grouped for calculating rated price. Then certain margins and regional coefficients are added to

get a basic price. Depending on the type of state drug beneficiary packet, the reimbursement price can be 50% or 100% of the basic price.

When asked about the countries and/or price databases they are likely to reference, three said neighbouring countries. Two international databases (MSH's International Drug Price Indicator Guide and the Global Price Reporting Mechanism of The Global Fund to fight AIDS, Malaria and Tuberculosis) were also mentioned.

Of the countries planning to use ERP, all stated that they were not aware of being referenced by other countries using ERP. They also stated that they had no definite plans for introducing ERP, nor did they provide even a tentative date for implementing ERP.

Although it was not identified in the initial questionnaire, the study team learned that Ecuador had recently passed a new regulation that has ERP as one of the potential criteria, and South Africa has approved new legislation on the use of ERP which they plan to implement when the regulations are finalized. We have summarised the information obtained as case studies.

Ecuador moving from cost-plus to ERP

Medicine prices in Ecuador appear to be relatively low in relation to other countries in the region. However, prices of a given medicine can vary enormously – sometimes more than tenfold – between manufacturers.

Ecuador recently passed a Presidential Decree (N° 400, 14 July 2014, Reglamento para la Fijación de Precios de Medicamentos de Uso y Consumo Humano) that foresees the use of ERP. In the past, Ecuador used a cost-plus approach to setting medicines prices. The system was said to favour foreign companies and imported goods, as the cost calculation for these products was based on the declared import price, which was difficult to scrutinise and verify. Local manufacturers were requested to certify their cost statements by presenting evidence (invoices) of all cost components, a more restrictive criterion according to local manufacturers. Ecuador intends to use ERP for new medicines that have a therapeutic advantage over existing competitors, while products showing no advantage will be assigned a maximum price i.e the lowest price of similar existing products.

Ecuador regulates the price of all medicines defined as “strategic”, which includes all those in the Cuadro Nacional de Medicamentos Básicos (CNMB), a positive list of publicly financed medicines (mainly, essential medicines plus competitors of the strategic medicines that are not in the positive list). Controlling medicines prices is the responsibility of the Consejo Nacional de Fijación y Revisión de Precios (National Board for the Establishment and Revisions of Prices). This body is composed of delegates from four ministries: Ministry of Public Health (that will act as the president of the Board), Ministry of Industry and Productivity, Ministry for the Coordination of Social Development and the Ministry of the Coordination of Production, Employment and Competitiveness. The Board is assisted by a Technical Secretariat composed by a full-time staff of about 12 people.

The basket of reference countries will include members of MERCOSUR, ALBA, UNASUR, plus the USA, the European Union, and elsewhere. The Board will set the maximum consumer price, in national currency, at the average of the three lowest prices in the basket of countries, adjusted by purchasing power parity. Note: in Ecuador the regulated price is the final patient price (not the manufacturer's price or the wholesaler's price).

The Decree establishes that the Ministry of Public Health might use special mechanisms for price setting in exceptional cases. The bylaw of the Decree – still being formulated in September 2014 – will define in more detail the future mechanisms for implementing ERP in Ecuador.

New legislation on ERP in South Africa

The Republic of South Africa issued legislation in May 2014 (Medicines and Related Substances Act (101/1965): Regulations relating to a transparent pricing system for medicines and scheduled substances: Benchmark Methodology) detailing how ERP will be used in the country.

The proposed methodology covers originator brand medicines and scheduled substances but does not apply, so far at least, to generics. The proposal endorses the principle of differential pricing as a reasonable approach to a fair contribution to research and development (R&D) costs by all countries using an innovative medicine. The proposal also endorses the criterion of therapeutic performance and cost-effectiveness as drivers of the pricing of new medicines. The proposal plans to use the lowest price in a selected basket of countries as the ultimate price for benchmarking. However, in order to minimise negative unintended effects, the new method will be implemented in a phased (pilot) approach over two years. Exemptions are foreseen for individual products in certain circumstances.

The proposed basket of reference countries includes Australia, Canada, New Zealand, and Spain. The data search will focus on ex-manufacturers prices. There are clearly defined procedures for identifying comparator products and their prices. The proposed method requires the applicant to identify and supply the relevant information to the pricing authorities.

Second Detailed Questionnaire

As explained in the methodology section, a detailed questionnaire with 31 questions was developed to assess the current use of ERP in the countries that were identified as using this criterion. Twenty-seven (27) completed³ questionnaires were received, mostly from European countries (see Table 5).

Table 5. Distribution of countries responding to the detailed questionnaire, by continent

Africa
Ghana - Republic of Guinea - Sudan
Americas
Canada - Colombia
Asia & Australasia
Iran - Japan - Jordan- Lebanon - Malaysia - Pakistan - Tuvalu
Europe
Albania - Austria - Belgium - Czech Republic - Hungary – Iceland - Latvia - Moldova - Poland - Slovakia - Spain - Switzerland - The Netherlands – Turkey - Ukraine

Table 6. Distribution of countries responding to the detailed questionnaire, by World Bank income levels

High-income
Austria - Belgium -Canada -Czech Republic - Iceland - Japan - Latvia -Poland -Slovakia -Spain - Switzerland- The Netherlands
Upper-middle income
Albania - Colombia - Hungary - Iran -Jordan - Lebanon -Malaysia -Turkey - Tuvalu
Lower-middle income
Ghana - Moldova - Pakistan - Sudan - Ukraine
Low-income
Republic of Guinea

³Bolivia answered the questionnaire but it was incomplete

Figure 2. Use of ERP globally showing countries referenced to

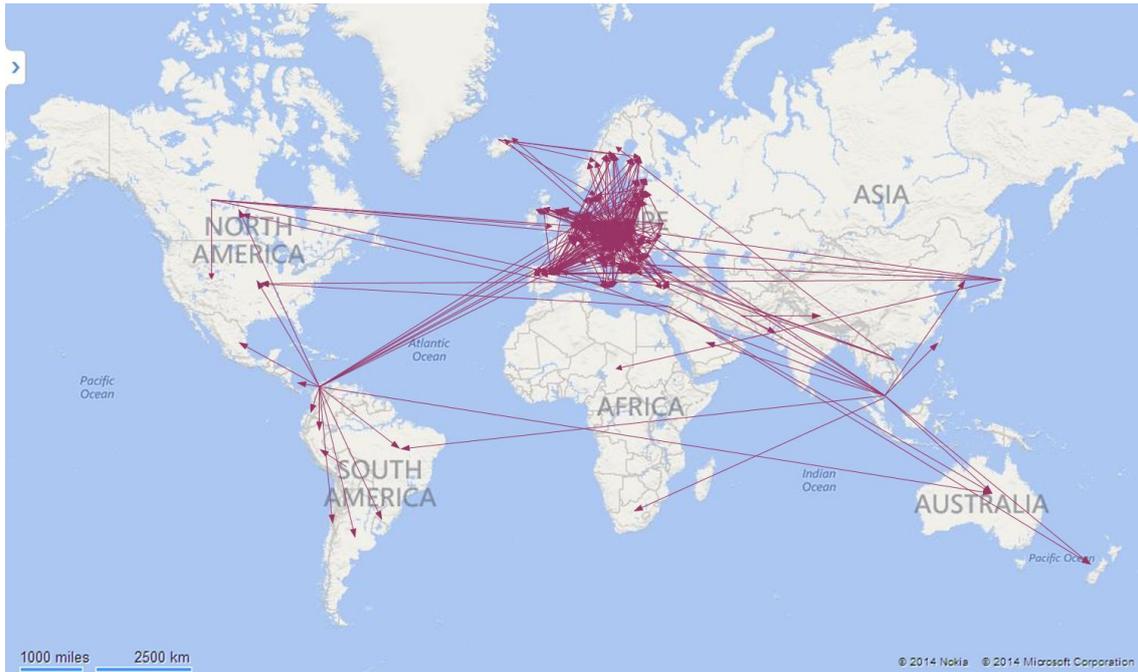
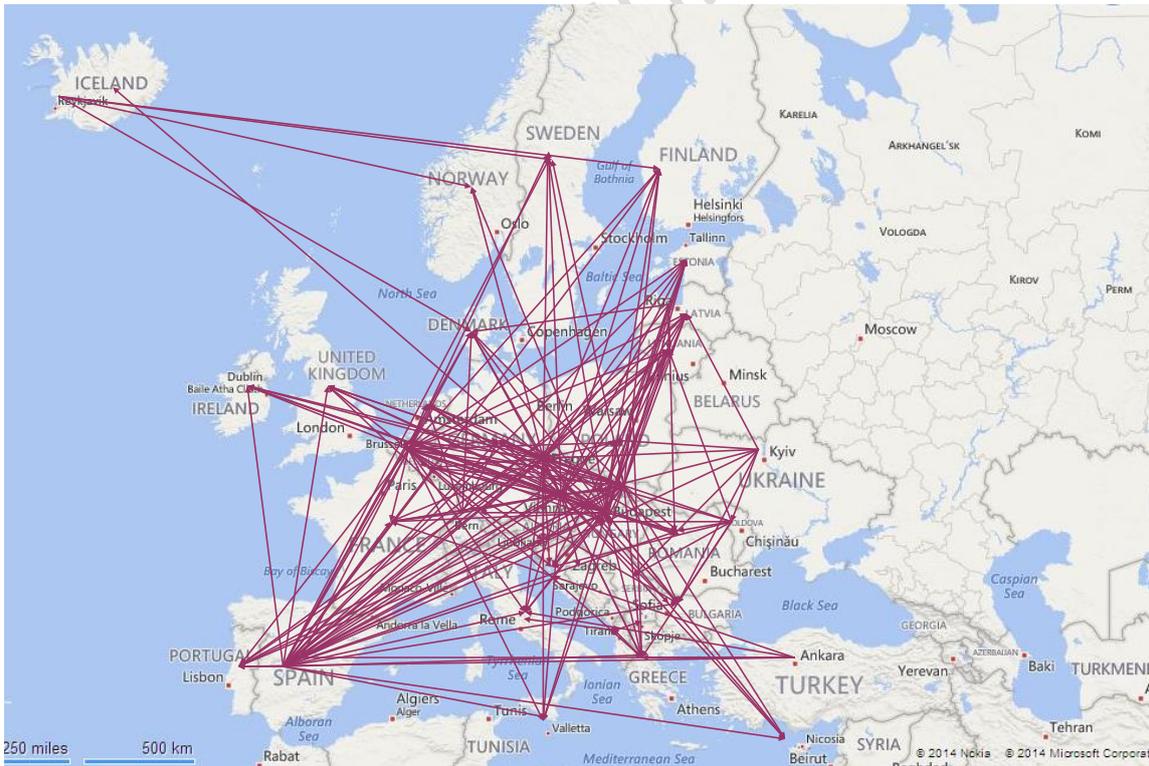


Figure 3. Use of ERP in Europe showing countries referenced to



Analysis of the answers to the detailed questionnaire

This section summarises the answers of the countries to the detailed questionnaire and some specific comments by the authors of this report. The questionnaire included two initial questions aimed at "setting the scene" on the use of ERP.

1. When using ERP, to which countries and/or price databases does your country reference?

Four countries (all the African countries plus Tuvalu) stated they use of the MSH International Drug Price Indicator Guide. Some countries are using IDA Foundation's electronic price catalogue and MSF's Untangling the Web (Republic of Guinea), the British National Formulary (Sudan), IHS data (Malaysia) or the EURIPID database (several European countries).

Countries are referencing mainly countries in their geographical area, with some exceptions such as Jordan (that uses as the reference the median of prices in the UK, France, Spain, Italy, Belgium, Greece, Netherlands, Australia, Cyprus, Hungary, Ireland, New Zealand, Portugal, Czech Republic, Croatia and Austria). Colombia references countries from both within the region (Argentina, Brazil, Chile, Ecuador, Mexico, Panama, Peru, Uruguay) and outside it (Spain, Australia, Canada, France, Norway, Germany and Portugal), and Iran references to Turkey, Greece and Spain. Most of the European countries only use other European countries as references.

In Canada the federal government price references on-patent products to the USA, Germany, Switzerland, Sweden, the UK, Italy and France. Provincial governments are using ERP in negotiating reductions in the price of generics, which are ultimately pegged against domestic brand name prices. In a later section the characteristics of the countries referenced to are analysed in more detail.

The second key question was related to the awareness of being referenced.

2. Are you aware of any other countries referencing your country prices (i.e. using your prices as a reference for setting or negotiating their prices)?

This question was intended to cross-validate the answers of the ERP-countries on the respective country baskets. However, the answers showed some contradictions. For example, Ghana reported that Nigeria is using Ghana's medicines prices as a reference, but according to the answers of Nigeria, this country is not using ERP.

Fourteen countries do not appear to know if other countries are using their prices as a reference. In total 12 out of the 27 countries that answered the detailed questionnaire were not aware of the use of their prices as a reference by other countries. In the European context most countries know which countries are using their prices as reference (mainly European countries but also some non-European). For instance, Hungary stated that it is referenced by Israel and Iceland, and suggested that it might also be referenced by South Korea (although the informant in South Korea said ERP was not being used in his country). In most of the cases, the referencing is mainly regional-based; for instance, Jordan stated that it is (informally) referenced by Lebanon, United Arab Emirates, Saudi Arabia and Iraq; Ghana stated that it is

referenced by Kenya, Nigeria and Togo; and the Czech Republic is referenced to by Austria, Belgium, Bulgaria, Greece, Hungary, Malta, Poland, Romania and Slovakia.

We assume that the information provided by an ERP country on the countries it references to is more reliable than the responses given by a country on which countries are referencing it. For instance, it is very likely that if a country official was once informally asked by someone from another country about medicines prices in the former, the official might assume that his country is being referenced by the country from where the request came from. This hardly constitutes ERP.

The second group of questions were general in nature, aimed at gaining a better understanding of pricing and reimbursement policies in the countries that reported using ERP.

3) Is there a unit/department responsible for setting/negotiating the price of medicines in your country? If YES please explain what units or departments are responsible.

The answers can be divided into three categories:

1. Countries that do not have a unit for medicine price regulation (Latvia, Hungary and Poland)
2. Countries with a unit dealing with medicine price regulation, sometimes within the Ministry of Health (Malaysia) or a Medicines Agency (Iran)
3. Countries where medicine pricing is a function of organisations involved in the procurement and supply of medicines (Ghana).

4) Is there a unit/department responsible for setting /negotiating the price of medicines for reimbursement or payment by a health system or insurer in your country?

In several countries this kind of unit does not exist (Guinea, Ghana, Pakistan, Tuvalu and Albania); in other countries it is the same unit that is responsible for pricing (for example, in Switzerland the Section Pharmaceuticals within the Directorate of Health and Accident Insurance; in Spain the General Directorate for National Health System Basic Portfolio and Pharmacy; in Slovakia the Ministry of Health's Section of Pharmacy and Drug Policy, Department of Categorisation, Pricing and Drug Policy, etc.) In some countries this unit is independent, for example, in Sudan where pricing is dealt with by the National Medicines and Poisons Board and reimbursement by the National Health Insurance Fund, or in Turkey where pricing is dealt with by the Medicines and Medical Devices Agency, Ministry of Health and reimbursement by the Social Security Institute. This split of roles and responsibilities is the norm in countries with a health insurance system. In Iran two different ministries share these functions: the Ministry of Health deals with pricing, and the Ministry of Welfare deals with reimbursement. In Spain and some other countries pricing is carried out by an Inter-ministerial Committee for Pricing, where three ministries (Health, Industry and Finance) are represented.

The next set of questions asked about the way regulated prices are set.

5) What criteria do these units or departments use to determine the price of medicines?

Only four countries used ERP as a single criterion i.e. Colombia, Albania, Slovakia and The Netherlands. In most countries, additional criteria to ERP are used for setting the price of the medicines. Pakistan, Japan, Lebanon, Belgium, Spain (according to the legislation, but not in practice) use cost-plus (cost of production of the medicine plus a certain profit or margin), mainly in combination with internal reference pricing (prices of similar medicines on the market to treat the same condition or disease). In Europe, many countries stated that they use economic evaluation and health technology assessment (Austria, Belgium, Spain, Hungary, Poland, Latvia and Turkey). Malaysia stated this as well. At the federal level in Canada, the Patented Medicine Prices Review Board (PMPRB) sets a price ceiling for patented products and payers (public and private to a lesser degree) conduct economic assessments and negotiate reimbursement levels. These levels are generally below the ceilings established by the PMPRB and not transparent to the PMPRB if prices are agreed to as part of the confidential product listing agreements.

The answers and studies reinforce the widespread perception that cost-plus pricing, although often mentioned in official regulatory texts, is seldom used in practice for pricing medicines. Some regulators may maintain it as a way to have access to the economic and accounting information of the companies.

6) If additional criteria are used besides ERP (e.g. price of similar medicines for the same indication, cost-plus calculations etc.), in what way are the criteria combined? (Please describe)

When countries are simultaneously using several criteria for pricing and reimbursement, as was found in the previous question, it is important to know how these criteria are combined or weighted, or whether they are used according to a certain order or conditions. Unfortunately, the responses do not clarify how important ERP is in relation to the other criteria, as most countries did not provide an answer or gave a general statement such as "All the criteria are considered to gain best value for money" (Malaysia), "All the criteria have the same weight" (Poland) or "ERP is necessary but not sufficient criterion" (Hungary). A few countries provided a clearer explanation and justification of the main criteria for reimbursement. For instance, Latvia stated that "The main economic criteria for a pharmaceutical to be reimbursed are a justified price - based on comparison with other available treatments and prices in other Baltic States and EU Member States - cost-effectiveness data, relevance of pharmaceutical expenditure with expected therapeutic effectiveness, and budget impact".

The answers to this question highlight one of the traits of the regulation of medicine prices that makes it intrinsically difficult to assess the impact of single specific or "pure" criteria. Countries are not able - or willing - to precisely describe the various criteria they claim to be using. Therefore, it is impossible for the analyst to associate observed impacts to concrete pricing criteria.

The next two questions inquired about the starting year of using ERP and the existence of a legal framework that legitimates the use of ERP.

7) What year did your country start using ERP?

Some countries stated that they started using ERP in the 90's, but did not provide a more precise date e.g. Spain answered "1990?" and Iceland "at least since 1996". Other countries gave a more detailed account, e.g. "In 1996 Switzerland started using ERP for all medicines. Before 1996 it was only used for foreign medicines." Most countries stated that they started to use ERP in the 2000's, in some cases with a very concrete date (e.g. Jordan - 29th January 2004). A few countries declared very recent implementation (Malaysia, Ukraine and Albania were all since 2012).

As in the previous questions the answers confirm a second difficulty when trying to assess impacts using time-series analysis. If it is not feasible to identify the timing of a policy, i.e. precisely defining when a certain pricing criterion started to be used, there is no way to associate to this policy any changes in variables that might have happened as a causal effect of the former.

8) Is there a national legal framework for the use of ERP (i.e. an official document describing the procedures for price regulation)? If YES please name it and send us a copy or link

Not all the countries have a legal framework to support their use of ERP (6 of the 27 countries said they had no such framework). The legal framework is in some cases internal (Spain, for example, stated that there is an "internal protocol for the Pricing Committee"), but in most cases there is a formal/legal document that regulates ERP (most countries provided a link to the website where the legislation is available). In some cases, the regulation is specific for ERP as is the case in Austria where the Regulation on Procedural Rules for Calculation of the EU average price [Regelung für die Vorgehensweise der Preiskommission bei der Ermittlung des EU-Durchschnittspreises according to Art. 351c.6 ASVG] was published in 2005 then updated in 2008. However, in most cases, the regulation of ERP is part of the pricing of medicines regulation.

The fact that most countries have a formal, explicit document regulating the application of ERP is positive for two reasons. On one hand, it allows a better understanding of how the system works, and of its similarity to the modalities of ERP applied in other countries. From the point of view of the actual effects of regulation, making it explicit also makes it more predictable, thereby reducing the uncertainties associated with discretionary or ill-defined regulation.

The next set of questions specifically related to the current use of ERP.

9) Which type of medicines is ERP applied to?

This question addresses the scope of medicines regulated by ERP i.e. whether ERP is used for all medicines, or only for some specific types such as on-patent prescription medicines, generic prescription medicines, imported medicines, locally manufactured medicines, medicines reimbursed by a national insurer or the health system, over-the-counter (OTC) medicines (non-prescription medicines), certain therapeutic groups of medicines (e.g. cancer medicines, diabetes medicines).

In some countries (Latvia and Poland) there is single criterion for the use of ERP i.e. only for medicines reimbursed by a national insurer or the health system. Austria has a similar approach i.e. ERP is applied to all new medicines applying for inclusion in the positive list in the

outpatient sector; if OTC medicines are reimbursed, an uncommon but possible situation, ERP also applies. In other countries the criterion is broad, but well defined, as in Hungary ("ERP is used in Hungary in case of applications for new active substances, new indications, new route of administration, price increase, reimbursement rate increase; in general the applications are for innovative medicines, but not necessarily").

Almost all countries use ERP for on-patent prescription medicines. Most reporting African countries (Guinea and Sudan) use it for imported medicines, as do Pakistan, Tuvalu, Lebanon, Ukraine, Albania, Turkey, Belgium, The Netherlands and Switzerland. ERP is used for generic prescription medicines in almost all of the responding countries, with the exception of Spain and Switzerland.

Underlying the variety of product types for which ERP is used is likely to be different objectives, priorities and values of the national authorities and regulators.

10) What criteria are used to select the countries you reference to? (Please describe)

The survey showed that three main criteria are used for selecting the countries to reference to:

1. In the same region
2. Have similar/comparable income levels, and
3. Have similar socioeconomics conditions

Pakistan mentioned all three criteria. Being in the same region or a neighbouring country was a reason stated by Colombia, Iran ("Turkey as a neighbour country with similar culture, population, other indices and with a very tight price for OB (Original Brand) medicines, not for generics"), Ukraine, Austria, Spain, etc.

Poland was very specific in how the criteria used relates to countries with similar (socio) economic conditions to themselves i.e. they reference to "Countries with the GDP per capita similar to Poland (+/- 15%)".

A different approach is taken by those who select the reference countries because they have low prices (such as Latvia and Iran). For example, Iran mentioned that it selected Greece because it has "low price for OB (Original Brand) in the EU" and Spain "for branded generics in the EU". Some countries, such as Japan, stated there was no official information on the selection criteria.

This is a topic where practices might be the most questionable. As the pharmaceutical market and industry are becoming increasingly globalised, the geographic criterion makes less sense than it might have made in the past. Choosing countries that have a similar income level is also a questionable criterion, as the reference price in any country can be adjusted by means of the purchasing power parity or GDP per capita related indicators.

11) What types of prices sources do you use? Optional, Please list the sources / websites

A key requirement for applying ERP is the accessibility of price information. The answer from Sudan justified the country selection criteria along this line ("The Board decided to use the

latest edition of the British National Formulary as a benchmark for medicines pricing because it is easily accessible"). The availability of data was also mentioned by Colombia and Malaysia. Moldova uses a different criterion, by selecting countries with a population of less than 25 million (Revised legislation in 01/04/2011).

Most countries stated that they use freely-accessible websites to access prices. Although they were invited to list the sources/websites, few provided a link. Turkey, Belgium and The Netherlands reported that they also request information from national authorities through personal communications. Some European countries made reference to EURIPID (a European price database, funded by the European Commission that is only accessible to authorities in Member States) as one of the sources of information.

This is one of the weaknesses of ERP. The widespread growth of ERP use leads to a progressive reduction in the accessibility and transparency of actual transaction prices. In order to avoid the potential spillover effects of ERP, suppliers try to hide actual transaction prices. Official websites mostly give catalogue prices or official maximum prices, hence the relationship with transaction prices is not easy to assess.

As has been mentioned previously, the basket of reference countries is a key component in the design of an ERP system. It is not only important which countries are selected, but also the reasons for this selection and the accessibility to real price data in the selected reference countries. The next question was related to this issue.

12) In your list of reference countries, what proportion usually has price information publicly?

Eleven of the 27 countries that answered the questionnaire said that all their reference countries have price information that is publicly available. Five countries said that only half of the countries have price information that is publicly available, and two countries said very few countries have publicly available price information.

Countries where all or most of their reference countries have price information that is publicly available probably reflects a selection bias. Where reference countries do not have publicly available price information other criteria (other than data availability) are used for selecting the basket of countries.

13) Of your list of reference countries, please name the countries most frequently used in practice

This question was intended to explore whether a subset of the countries included in the basket was more frequently used because of greater data availability or other reasons. However, most countries stated that nearly all countries included in their basket are frequently used.

14) What is the procedure if prices are not publicly available in some of the reference countries?

Taking into account that reference countries might not have the price information requested at all times, we were interested in knowing the options taken if prices are not available in some of the reference countries. Some countries (namely Sudan, Colombia, Lebanon,

Malaysia, Albania, Hungary, Belgium, Slovakia and Iceland) only select a country as a reference country if they can access its medicines prices information.

Other countries reported using alternatives means to obtain prices e.g. in Ghana they ask "colleagues in Nigeria, Kenya and Togo what their (procurement) prices are"), look for prices in other countries (Pakistan and Malaysia), or request the manufacturer to submit information about the price (Jordan, Turkey, Poland). In Japan if they cannot find the required price in at least two countries, they does not use ERP.

In Canada, the Patented Medicine Prices Review Board (PMPRB) requests the manufacturer to submit documentary information for international prices. Where the international price sets the price ceiling, the PMPRB will verify the price submitted by the manufacturer. The prices sources that are used and the back out formulas to get to the ex-factory gate level are available on the PMPRB website and are updated annually. Should a price not be found in the Usual and Customary (U&C) price sources used by PMPRB, they assess other price sources submitted by patentees on a case-by-case basis. The PMPRB does not look for prices outside its basket of seven reference countries. When a new patented product is sold in fewer than 5 countries at the time it is first sold in Canada, the EPR will be calculated on an interim basis. At the end of three years there is a re-determination.

15) What type of price is searched in the reference countries?

The most frequent single price sought is the manufacturer's/ex-factory price (Jordan, Lebanon, Turkey, Hungary, Poland, Spain, Belgium and Switzerland), followed by the wholesale price (Sudan, Iran, Malaysia and Iceland). Other single price answers were the retail price (Pakistan), the procurement price (Ghana), and the drug price list (Japan). Tuvalu refers to MSH supplier prices which includes non-profit supplier prices and tender prices.

Eight countries sought two or more prices, which usually were the manufacturer's price and the wholesale price (Colombia, Ukraine, Albania, Latvia, Slovakia, The Netherlands, Austria and the Czech Republic). Austria stated that they use the prices provided by the PPRI, while the Czech Republic state that they use any price available, which is then recalculated. The Netherlands stated that *In England and Belgium the given ex-factory price and pharmacy sale prices are converted to pharmacy purchase price.*

It is worthwhile to state the complex procedure used by the Patented Medicine Prices Review Board (PMPRB) in Canada:

The PMPRB solely regulates ex-factory prices. For ERP purposes, they have a list of Usual and Customary sources for ex-factory prices which is published on-line. When, for whatever reason, ex-factory prices are unavailable, the PMPRB will use pharmacy retail prices from the reference countries if, and only if, distribution margins in the reference countries are statutorily regulated.

PMPRB staff routinely uses price information obtained from national formularies to validate the foreign prices patentees submit, in a process called Foreign Price Verification (FPV). This process typically involves a series of calculations needed to remove mark-ups and embedded taxes from formulary prices. Beginning with the manufacturer, the drug product may be sold to

a wholesaler or directly to a pharmacy or hospital. As the drug travels through the distribution chain, the price may be marked up several times. In some countries, formulary prices also include a value-added-tax (VAT).

In the six European comparator countries that the PMPRB considers in its price reviews (i.e., France, Germany, Italy, Sweden, Switzerland and the United Kingdom), retail and wholesale mark-ups (as well as any sales taxes) are determined by means of publicly available formulas. With these formulas in hand, PMPRB staff can derive ex-factory prices from formulary prices. Staff then uses these derived ex-factory prices to perform FPV. (Similar calculations are not possible in the case of the United States, where wholesale and retail mark-ups are not regulated.)

Because the policies of foreign reimbursement plans can change from one year to the next, PMPRB staff, in consultation with appropriate officials in the comparator countries, update the FPV “backing-out” formulas in the second quarter of each year (that is, before patentees submit foreign prices for the first six months of that year).

The detailed and explicit procedure reported by Canada compared with the vague and simplistic criteria reported by other countries, highlighting the variety of practices which are labelled as ERP, but in fact represent very different pricing practices that cannot be legitimately analysed as an homogeneous category.

16) When do you collect prices in the reference countries?

This question resulted in a variety of answers, which were often difficult to categorise.

The most frequent answer can be considered to be “When the national price is set” as stated by Pakistan, Latvia, Hungary, Poland, Czech Republic, Spain, Belgium, Iceland and Tuvalu. A variety of timings were described across the countries:

- Pakistan: Prices are fixed before the registration letter is issued and price prevailing at that time in the reference countries is used.
- Latvia: When the product is evaluated for reimbursement, but there are price reviews for the pharmaceuticals which are included in the Positive list.
- Czech Republic: Prices are collected in one of 21 days after the beginning of the pricing procedure.
- Spain: price either at this moment or at the previous month if there is any exchange rate change
- Belgium: When ERP is used as supportive to the pricing decision. Applicants are compelled to list the prices applicable in the EU countries in their price claim. For the 2013 exercise: 1st of January
- Iceland: When an application for maximum wholesale price is processed
- Tuvalu: Annually, when medicines are procured

Four countries (Iran, Malaysia, Japan and Turkey) stated that the timing of data collection is not systematic. Japan explained that they collect the data when each reference countries' price list is updated.

Four countries take the prices at defined times of the year: Jordan (1st January), Slovakia (twice a year, October and April), Albania (November) and Ukraine (quarterly).

Special single country approaches included:

Sudan: Price published in the latest edition of the British National Formulary

Lebanon: Price at the time of product registration in the reference country, but there is re-pricing every five years after the first registration

Canada: The PMPRB collects international prices for regulatory purposes when:

- the product is launched in Canada,
- on a semi-annual basis for existing drug products (January and June), and
- for investigations and complaints

Colombia: From reference countries where prices are generated on a monthly basis, they compute the average price in the months of the year immediately before the price in Colombia is set. Where monthly data are not available, as well as in the case of institutional procurement, they take the price of the most recent transaction.

The Netherlands: The price lists (of the reference countries) of April are used for the reference pricing of October. The price lists of October are used for the reference prices of the following April.

Switzerland: In order to apply for the national price, applicants need to provide the official prices in the reference countries at the time of submission of the reimbursement application. If new prices become available during the assessment period by the federal office of public health, the new prices are used. Generally said, all prices available at the time of issuing the reimbursement license are considered.

Austria has a specific service, the Pharmaceutical Price Information (PPI), for gathering the price of medicines. This service includes most updated price information in line with the national sources (e.g. if price data in a country are published monthly, PPI will also provide the data on a monthly basis)".

Iran does not have a defined time for the reference prices.

Tuvalu does it "annually when medicines are procured"

Sudan stated when the price is "published in the latest edition of the British National Formulary"

Slovakia collects the prices twice a year (October and April)

17) Do you use the official list /catalogue price in the reference countries or do you try to find out the actual transaction price i.e. after the application of any of discounts or rebates?

One of the most controversial issues on the reference prices collected and used in ERP, and in price comparisons in general, is whether the data reflect actual transaction prices (after the application of any discount or rebates) or just official/list/catalogue prices. Most countries use

official lists, probably because the discounts and rebates are "confidential information and can thus not be assessed" (as stated by Austria). In some countries, manufacturers are requested to provide the actual transaction price, as in Turkey, Jordan, and Czech Republic ("mainly in case our findings in a particular country are not correct").

18) Do your regulations require under some form of penalty a manufacturer/importer to report the product price in the reference countries? If NO, do you ask the manufacturer/importer to report the product price in the reference countries?

Ten countries (Jordan, Lebanon, Turkey, Latvia, Poland, Slovakia, Sudan, Pakistan, Czech Republic and apparently Canada) indicated that the prices are requested under some form of penalty.

In Canada, patentees are required to report the ex-factory prices at which they sell their products in any of the seven comparator countries specified in the Regulations. It is critical that patentees accurately report foreign prices because of the role they play in the price tests that the Patented Medicine Prices Review Board -PMPRB- applies when conducting its price reviews, as well as in the PMPRB's reporting on pharmaceutical price trends. If patentees were to overstate foreign prices, this could lead the PMPRB to accept Canadian prices that are excessive in light of actual market conditions, to the detriment of Canadian consumers.

Three other countries (Belgium, Austria and Switzerland) request the information, but do not impose any penalty for non-compliance.

Iran, Hungary and Iceland do not require companies to report prices, but they are asked to voluntarily provide them.

Colombia, Malaysia, Ukraine, Albania, Japan, Spain and The Netherlands neither require the information be provided, nor voluntarily ask for it.

It is interesting to see that a large number of countries do not use – among others – that simple and cheap procedure to obtain reference prices, i.e. asking the applicant to provide this information under some form of sanction for not reporting or for reporting incorrectly.

19) Is the price information obtained (from lists, manufacturers etc.) validated or crossed check with information from other sources? If YES please describe how this is completed

The process of price validation is an important issue related to the use of ERP due to several factors that have been previously mentioned i.e. not all prices are publicly accessible, different prices are used in the comparisons (ex-factory, wholesale price etc.), official prices are often reduced through discounts and/or rebates etc.

Eleven countries said that they do not validate or cross-check the information with other sources. Among the countries that do validate the data, Canada described their process very clearly: *For new drugs, PMPRB staff routinely uses price information obtained from national formularies to validate the foreign prices that patentees submit, in a process called Foreign Price Verification (FPV). This process typically involves a series of calculations needed to remove mark-ups and certain taxes embedded in formulary prices. Beginning with the manufacturer,*

the drug product may be sold to a wholesaler or directly to a pharmacy or hospital. As the drug travels through the distribution chain, the price may be marked up several times. In some countries, formulary prices also include a value added tax (VAT). In the six European comparator countries that the PMPRB considers in its price reviews (i.e., France, Germany, Italy, Sweden, Switzerland and the United Kingdom), retail and wholesale mark-ups (as well as any sales taxes) are determined by means of publicly available formulas. The PMPRB staff derives ex-factory prices from formulary prices. Staff then uses these derived ex-factory prices to perform FPV. (Similar calculations are not possible in the case of the United States, where wholesale and retail mark-ups are not regulated.) Because the policies of foreign reimbursement plans can change from one year to the next, PMPRB staff, in consultation with appropriate officials in the comparator countries, updates the FPV backing-out formulas in December of each year. These formulas are then published on the PMPRB website in January of each year and apply to that entire calendar year. The above procedure is only used for existing drugs in the context of an investigation or Board Hearing.

Some European countries stated they use EURIPID as a tool to validate prices (Poland, Spain and Belgium). Spain also mentioned the PPRI network, and informal contacts via e-mail or phone, as ways to cross-check prices.

20) How are product differences – such as variations in medicine strength, pack size, minor formulation differences etc. – in the reference countries managed if they do not match the product in your country? (Please explain)

Another important issue is how variations in medicine strength, pack size, minor formulation differences, etc. are addressed when the product in the reference country does not quite match the product being priced.

Some countries (Switzerland and Pakistan) use a "linear calculation" or the price is "calculated on the basis of pro-rata". In Malaysia they "select another country which has the available data of the same product, strength and size". In Ukraine, similarly to Poland, they take "the closest amount of the pack and calculate the DDD price". In the Czech Republic and Iceland the difference may vary up to 10%.

21) Which source, date and type of exchange rate are used to translate the prices in reference countries into your currency? (Please describe)

Usually regulators use the official exchange rate set by the national bank of the respective country (e.g. Swiss National Bank, Czech National Bank, Republic of Guinea Central Bank) and the European Central Bank in the case of countries in the Euro-zone.

Regarding the date of the exchange rate, in some countries the methodology is precisely described as in Canada: "The exchange rates used are the simple average of the thirty-six monthly average noon spot exchange rates for each country (taken to eight decimal places), as published by the Bank of Canada for the thirty-six months ending with the last month of the pricing period under review". In Japan it is defined as "the average rate of exchange over the last year" and in Moldova "over the previous month". In Albania it is defined as "the official exchange rate of the average for the last six months (as reported by the Bank of Albania)".

This part of the pricing procedure does not seem to pose major challenges or difficulties to regulators. Of course, it is important for a country regulator to decide whether, and how often, temporary changes in the exchange rate require a revision of the prices previously calculated with a different exchange rate. This is part of a set of broader questions, such as how often should prices initially set by ERP be updated and whether they should be updated using the same formula or algorithm. Price updates might be based on criteria such as inflation in costs of production.

22) What procedure or criteria are used to combine/aggregate the reference countries prices into a single reference price? Does the method used vary for different types of medicines (e.g. generics and on-patent medicines)?

The largest number of countries (8) answered that they applied the lowest price in the basket of countries (Iran, Albania, Turkey, Hungary, Poland, Czech Republic and Spain). That said, Spain also said that there is no general formula but is decided on a case-by-case basis.

The Czech Republic mentioned a second option i.e. *The average of the three lowest prices identified in the countries of the reference basket (two in case of highly innovative medicine; in case of price extreme – i.e. the lowest price of medicine is more than 20% lower than average of second and third lowest price, is the price set in amount of mentioned average).*

Five countries use the median price (Sudan, Jordan, Lebanon, Ukraine and Malaysia) across the basket of countries. In Malaysia, the method varies for different types of medicines i.e. on-patent medicines are priced using the median, while generic medicines are based on the median price among the local manufacturers and the lowest price from other countries.

The simple average/mean is the option used by six countries - Pakistan, Japan, Belgium, Iceland, Austria and Switzerland.

Japan applies a slightly more complex method. If the highest price is 3 times higher than the lowest price, they use the average of all prices. Also, if the highest price is more than 2 times higher than the arithmetic mean of other prices, the highest price is considered as double of the arithmetic mean of other prices, and then they compute the average of all prices.

Austria does not use ERP for generics, but rather internal price referencing.

The Netherlands applies the weighted average/mean of the prices found in the reference countries.

Iceland applies the average price of the pack in each country for on-patent medicines. For generics, the average price of all packs of all equivalent generics in the same country is determined, then the average of the average price in each country is used.

Two countries apply the average of the three lowest prices in the basket. Moldova uses the average of the three lowest manufacturer prices for the compared medicine. The price of generic medicines is compared using ERP, but should not exceed 75% of the ex-works price of the originator medicine, approved by the MoH. Slovakia applies the average of the three

lowest prices within the EU countries; if there are only two, the average of those two is used, and if there is only one, that is the price.

In Latvia the price must not be higher than the third lowest price in the Czech Republic, Romania, Slovakia, Hungary and Denmark, and not higher than the price in Estonia and Lithuania. If the price submitted for reimbursement is higher, the manufacturer has to decrease it to obtain reimbursement.

Colombia uses the percentile 25 criterion. Prices per unit of the product with the lowest concentration are converted to the national currency. The resulting prices are ordered and the percentile 25 price is selected. This means that 25% of the prices collected are under the said price.

Canada uses the formula HIPC:

The simple average of the monthly average noon spot exchange rates for each country for the 36-month period ending June or December of any given year are used in the review of prices for existing medicines in the first and the second half of the year, respectively. The exchange rates used are as published by the Bank of Canada (taken to eight decimal places).

The PMPRB uses price tests based on the “Levels of Therapeutic Improvement” of a drug product (schedule 8 of the Guidelines). The following are the price tests used for the 4 Levels of Therapeutic Improvement:

Breakthrough Drug products	Median International Price Comparison (MIPC) Test
Substantial Improvement	Higher of: 1) Top of the Therapeutic Class Comparison (TCC) test 2) MIPC test
Moderate Improvement	Higher of: 1) Midpoint of: i) Top of the TCC test and ii) MIPC test; and 2) Top of the TCC test If it is impossible to conduct a TCC test then use the MIPC test.
Slight or No Improvement	1) Top of the TCC test If no comparable drug products, use the lower of i) the bottom of the TCC test of superior drug products and ii) the MIPC test. If it is impossible to conduct a TCC test then use the MIPC test. 2) Reasonable Relationship (RR) test
All Levels	Highest International Price Comparison (HIPC) test

The TCC test is described in Schedule 3 of the Guidelines. This test compares a new patented drug product’s National Average Transaction Price and the Market-Specific Average Transaction Prices in each class of customer – hospital, pharmacy, wholesaler and province/territory with the price of drug products identified for comparison purposes that are sold at prices that the PMPRB considers not to be excessive.

The HIPC test is described in Schedule 6 of the PMPRB Guidelines. The MIPC test is described in Schedule 5 of the Guidelines, and is used at introduction only. As noted in the table above, the use of the MIPC test varies depending on the level of therapeutic improvement.

If we have multiple price customers for a drug product within a comparator country, the Board Staff practice is to take the simple average of the prices across these customers.

This is also a key issue for the main research question of this study, i.e. the potential negative effect for a country being referenced to by another country. If a specific ERP regulation states that it will select as its reference price the lowest price found in any of the countries in the basket, the negative effects for the country selected are likely to be worse for the lowest price country, as the company may insist on increasing the price or may choose not to market their product in that country, than if the reference price was computed as the mean of all prices in the basket.

23) Is the reference price revised when prices change in the reference countries?

Most countries do not revise the price following price changes in the reference countries (Colombia, Iran, Japan, Albania, Pakistan, Sudan and Austria).

In the case of Pakistan, changes might occur when a manufacturer requests a price increase.

Regulations in Sudan state that prices will be changed if prices change in the reference countries (but this rule is not enforced) and if the exchange rate changes.

Several countries carry out different forms of ERP-based, periodic price revisions:

Canada: The PMPRB reviews prices annually. At no time can the Canadian price exceed the HIPC (Highest International Price Comparison) based on an annual price review process.

The Netherlands: Every 6 months the reference price is revised to account for changes in reference prices and the exchange rate.

Turkey: Prices are revised if prices change in the reference countries.

Moldova: Since the manufacturer's price should be registered on an annual basis, changes of the ERP might be noted within the comparison period.

Spain: There are periodic revisions if prices change in the reference countries, or if the product is launched in additional reference countries.

Slovakia: The ERP application is made twice per year.

Iceland: A committee revises the price catalogue every other year to lower the price. Usually only for packs whose annual turnover is more than 3.5 million ISK without VAT= 22,500 Euro. The medicine catalogue is updated every month. The company can request that the pack price is updated according to the import currency. The committee calculates the medicine exchange rate each month. See the answer to Q21.

Other countries use criteria other than ERP for price revisions:

Ukraine: There are periodic revisions, yearly on the 01 June, taking into account the consumer price index of medicines. Prices in reference countries are not considered.

Malaysia: Prices will be revised yearly or on a case-by- case basis, based on current available prices.

Poland: There are no revisions of the reference price. The administrative decision of the reimbursement is issued for two years (first and second decision). After the expiry of the first administrative decision, the process of price negotiation starts. During that process, prices in EU/EFTA countries are checked and the Polish prices are verified.

Hungary: When a manufacturer requests a price increase.

However, in some cases the answers do not clearly state if the revisions are based on the application of ERP:

Jordan: There are price revisions after two years of registration for a new medicine, and every 5 years, which is the period of re-registration.

Lebanon: There are periodic revisions every five years for re-pricing purposes.

Latvia: There are price reviews for the pharmaceuticals which are included in the Positive List and when a manufacturer requests a price increase.

Czech Republic: According to the Act No. 48/1997 Coll, there are periodic revisions once every three years.

Switzerland: There are periodic revisions every time a new indication or a new pack gets listed.

Again, national practices vary substantially giving rise to a broad heterogeneous set of modalities of ERP with likely different impacts.

24) Do you foresee any changes in ERP regulation or use in your country in the next two years?

Most countries (19) declared that they do not foresee any changes in the ERP regulation (Republic of Guinea, Sudan, Colombia, Canada, Pakistan, Lebanon, Japan, Ukraine, Turkey, Latvia, Hungary, Poland, Slovakia, Czech Republic, Spain, Belgium, Iceland, The Netherlands and Austria).

Japan, however, reported that *there is movement to have a price revision every year and it might affect ERP, but pharmaceutical industries objected to it.*

Five countries reported possible changes in the future:

Iran: *Yes, unfortunately the pricing regulation had some changes towards deregulation in the past 3 years and the system has just restarted 6 month ago.*

Jordan: *Through the MeTA [Medicines Transparency Alliance] Program there is a call to change the ERP regulation to include countries which have a similar GDP.*

Moldova: *Changes to the regulation are expected to consider the list of countries; criteria for selection of countries; and maintaining the procedure of price registration only for Rx products.*

Albania: *It is previewed to make a new draft of the external reference price methodology in the coming year by experts from different ministries.*

Switzerland: *Yes, but the changes under discussion cannot be disclosed yet.*

To summarise, ERP systems are not expected to experience major changes. Jordan and Moldova foresee only minor changes in the basket of countries and in the latter case, in the scope of medicines. Iran, Albania and Switzerland might undergo more modifications, but no concrete details were disclosed.

It is interesting that many countries do not expect to introduce changes in their ERP systems, when price systems are constantly evolving and being adjusted, often as a reaction to new strategies of the industry.

25) How many staff (in terms of fulltime-equivalents, FTE) work in your country to manage the ERP process?

Colombia	8 people
Canada	4 people (FTE) at the Patented Medicine Price Review Board
Pakistan	Two people manage the ERP process along with other work. No-one works full-time on the ERP process.
Iran	3 people
Jordan	6 pharmacists
Lebanon	4 people
Malaysia	2- 3 people
Japan	9 people
Moldova	4 specialists. However, the evaluation and determination of the manufacturer's price for registration is not the single responsibility of the Department.
Ukraine	6 people at the State Expert Centre (monitoring prices in reference countries)
Latvia	Unknown ⁴
Hungary	0.05 FTE
Poland	5 people
Slovakia	2 people

⁴ ERP is part of information which is checked during therapeutic and economic evaluation to make a decision on reimbursement and it can't be separated from all the evaluation and decision making process.

Czech Rep.	6 people working full-time where ERP takes about 65% of their time, and 21 people working part-time (0.5 FTE) where ERP takes about 90% of their time.
Spain	About 10 people, but not full-time, but as part of the whole process
Belgium	0.5 FTE
Iceland	3.7 FTE. The ERP work is less than one full staff member ⁵ .
Netherlands	2 people (approximately)
Austria	FTE are not known ⁶
Switzerland	14 people (4 lawyers and 10 pharmacists) working in the Section of Pharmaceuticals, responsible for every aspect of getting and maintaining drugs on the reimbursement list.

Leaving aside a few outliers such as Hungary and Belgium, most countries seem to manage the ERP system with a staff of between 2 and 10 people. Often these units have additional responsibilities, such as overall price regulation or even financing/reimbursement issues.

26) Do agencies from other countries ask you for your prices? If YES, How many requests do you get annually? Please give the approximate number. What countries have asked you for prices? Please list the countries. What medicine prices have been requested? Please list the medicines:

Twelve countries stated that they do not get requests for prices from other countries i.e. Colombia, Canada, Pakistan, Iran, Lebanon, Malaysia, Japan, Ukraine, Albania, Latvia⁷, Iceland⁸ and Switzerland.

Ten countries give an affirmative answer:

- Jordan. It had two requests this year, from Lebanon and from Saudi Arabia. Additional countries that have asked for prices include the United Arab Emirates, Iraq and Egypt. Medicines which prices have been requested are Zyprexa (olanzapine) and Revolade (eltrombopag).

⁵ The work regarding ERP is a part of daily operations of the Committee. They carry out two tasks: A. Processing maximum wholesale price applications and B. Performing the price revision process every second year, when the whole price catalogue is under revision. Other functions of the committee include processing max wholesale applications, applications for general reimbursement and application for individual reimbursement if there is no precedent and reimbursement applications for special care high cost medicine. The committee also decides the pharmacy retail margin and updates and publishes the medicine price catalogue every month. The English version can be accessed at: <http://www.lgn.is/?pageid=83>

⁶ the ERP process involves a department in the Ministry of Health which runs the Secretariat of the Pricing Committee; members of the Pricing Committee who attend the meetings; and the PPI team of several experts at GÖG to keep the PPI service always up-to-date.

⁷ Japan and Latvia assume that because prices are publicly available, they have not received such questions.

⁸ The official price catalogue is available to everyone on our website. You can subscribe to e-mail notifications when they appears on our website. An English version of the price catalogue is accessible at <http://www.lgn.is/?pageid=83>

- Hungary. Approximate number of requests is 2-5 annually; countries that have made requests are Israel, Czech Republic, Slovakia and Poland.
- Poland. Approximate number of requests is 4 annually⁹ mainly made by Spain, the Czech Republic and Estonia. The received a request for the price of apixaban.
- Slovakia. Their price list is publicly available every month on their website listing the ex-factory price, the wholesale price, the retail price, and the retail price with VAT. Sometimes they receive questions of clarification from agencies.
- Czech Republic. They receive approximately 10 requests annually, from Poland, Malta, Portugal and elsewhere, usually seeking prices of new molecules
- Spain. They receive approximately 12 requests annually, mainly from Austria, Italy, Sweden, Greece, Luxemburg, Malta, Lithuania, Slovenia, Slovakia, etc. Requests have been made for new oral anticoagulants, vemurafenib, anti-hepatitis C medicines etc.
- Belgium. Their data source of reimbursed pharmaceuticals is shared (database transmission on a monthly basis) by individual direct mail with the following countries: Israel, The Netherlands, Slovakia, Spain and EURIPID. Ex-factory prices and retail prices (incl. VAT) are shared. They also provide information requested via the PPRI network.
- The Netherlands. They receive approximately 2 requests annually. Israel has asked for prices of all reimbursed medicines and many hospital-only medicines.
- Austria. They stated that in order not to discriminate any third party, the PPI service can be used by any person or entity, against a compensation for the working time.

This is an area where there probably is a lot of scope for improvement based on inter-country collaboration. Setting up price information systems, price databases and efficient price exchange mechanisms would save countries money (in terms of time spent collecting data) and allow them access to more valid and reliable international price information.

27) In the last five years, how often has a product not been marketed or withdrawn from the market or from public reimbursement, because the price you set in your country using ERP was considered too low by the manufacturer? Please state the number of times this has happened.

Five countries stated that this has never happened i.e. Canada, Colombia, Iran, Ukraine and Iceland.

Jordan stated this has happened once, Pakistan said four times, and Latvia said up to ten times (approximately).

Several other countries stated that this situation happens seldom:

- Japan. There are few cases where a product has not been marketed or withdrawn from public reimbursement. Even in such rare cases, Japan uses many methods including ERP to set price, so it cannot be said that it was because of ERP.
- Spain. Rarely
- The Netherlands. None or only a few

⁹ All reimbursement prices of medicines in Poland are available in the EURIPID database.

- Switzerland. Single cases each year, mainly withdrawals

Most countries did not answer this question. Others stated that they did not know:

- Hungary. We cannot judge it as the companies do not have to report the reason for withdrawing a product from reimbursement
- Moldova. There is no strong evidence on refusals to import medicine due to too low prices proposed for approval by the Government.
- Austria. Not aware of any case.

This question highlights the heterogeneity of ERP systems in the way the computed price is used at the price fixing stage. Two ERP systems might produce the same “initial” reference price, but the effect on the actual price might vary enormously depending on the way the price is used for instance if it is presented to the applicant as a “take it or leave” price, or if it used as a starting point for a price negotiation that considers the possibility of setting a final price above the initially computed reference price.

28) In the last five years, how often has the ERP become the price in your country i.e. was not revised in price negotiations or other pricing criteria?

Never: Japan, Ukraine, and The Netherlands.

Seldom (up to 10% of the time): Pakistan, Malaysia, Latvia, Hungary, and Belgium.

Often (up to 40% of the time): Iran, Jordan, and Switzerland.

Frequently (More than 40% of the time): Lebanon, Czech Republic, Spain, and Colombia (this however happened only during the last year, when regulations have been enforced).

Always: Slovakia and Iceland (for new medicines)¹⁰

The responses to question 27 also apply to question 28.

29) In 2013 how many medicines/molecules had their price set using ERP? Please give the estimated number. Please give the percentage (%) compared to all the medicines that are price controlled in your country. Please provide a list of medicines (by INN) priced using ERP (optional)

Pakistan	The prices of 21 brands/formulations were fixed on the basis of ERP
Iran	50 medicines; about 60% of medicines that are eligible for ERP such as anti-cancer medicines, interferon, MABs, medicines for metabolic disorders, iron chelators etc.
Jordan	12 out of 61. 20% of all the medicines that are price controlled
Japan	6 out of 58. 10.3% of all the medicines that are price controlled

¹⁰ Every other year, at least, there is an official price revision. The ERP price is nearly always used. In a few instances, the committee has either postponed, by a few months, the publication of the new price or accepted up to 15% higher price for packs whose turnover will be lower than 3.5 million IKR under the new lower price.

Ukraine	None
Hungary	50 (approx.), around 10%, NA
Slovakia.	400 medicines approximately. All medicines in Slovakia are priced through ERP.
Czech Rep.	In 2013 the price was set (revised) for about 900 medicinal products (about 100 molecules); it is about 16.0 % of all price controlled medicinal products in the country
Belgium.	These data cannot be provided without a detailed analysis; maximum 10%
Iceland ¹¹	718 products had their price revised. Total number of products in the price catalogue is 2,966 =24.2% 364 new products were published in the 2013 catalogue. All had their price set by ERP. The medicine price catalogue has 810 INN, how many of these have been revised with lower price is not available.
Austria	All new reimbursable medicines in the out-patient sector
Switzerland	Around 15 of all New Chemical Entities (NCEs) for which the price is equal to the average price in our basket countries (very rough estimate)

The number of products where the price has been set using ERP varied substantially among the countries, from the 1 or 2 digit order to the several hundred. This variability probably reflects both differences in definitions and terminology, and the fact that some countries use ERP routinely, while other countries use it only in specific circumstances.

30) Please provide detailed examples for one or two medicines that you have priced using ERP i.e. prices for the products found in each reference country, the initial reference price you computed, and the actual price you set or negotiated in your country? You may blind the name of the products (e.g. product A, product B) (optional)

Iran	Herceptin (trastuzumab): Turkey: 384€, Greece: 515€, Spain: 678€, Iran 384€ CPT price; it means the user price will be about 550€ due to importer, distributor and pharmacy mark-ups .
Jordan	Xarelto (rivaroxaban) 15 mg; Diamicron (gliclazide) MR 60 mg
Hungary	ERP is not the main criterion for inclusion into the reimbursement system. As we use the minimum price of the reference basket for ERP, companies do not lower the official price below this threshold.
Canada	See the following link for a list of medicines that have been reviewed by the PMPRB: http://www.pmprb-cepmb.gc.ca/english/view.asp?x=572

¹¹ In 2013 the committee published its biannual price revision for products with a turnover more than 3.5 million IKR.

Czech Rep.	Product A – Price set at 778.81 CZK (average of three lowest prices).
Iceland	<p>Prices quoted here are the wholesale price without VAT. Iceland’s price can be different from comparison because of fluctuations of the Icelandic krona against the Euro, SEK, NOK or DKK, since the decision of maximum wholesale price. All prices are according to April price catalogue and April exchange rate.</p> <p>Advate (recombinant antihemophilic factor) is a hospital medicine and priced according to lowest price in ERP countries. Modigraf (tacrolimus) and Relvar Ellipta (fluticasone furoate/vilanterol) are pharmacy medicines and priced according to the average price in ERP countries. All these products have had their price accepted or revised within last six months.</p>
Switzerland	<p>Daily therapy costs of comparator product 1: CHF 164.20</p> <p>Daily therapy costs of comparator product 2: CHF 186.89</p> <p>Average Daily therapy costs (therapeutic price comparison): CHF 175.55</p> <p>ERP: Average daily therapy costs in country basket (6 countries): CHF 176.60</p> <p>Agreed price per pack of 28: CHF 4930.10 (corresponding to daily therapy costs of CHF 176.08)</p>

This question was intended to validate the stated use of ERP as a formal, rigorous pricing method i.e. using well defined procedures and algorithms as opposed as the more informal practice of looking at price information from other countries as an informal benchmark to support more open price setting procedures. The answers provide some evidence that at least a few countries apply the more formal modalities of ERP.

31) Is there anything else you would like to tell us about the use of ERP in your country?

Guinea	The use of ERP is not generalized in the pricing of medicines in Guinea. At the Ministry of Health level there is a price structure that determines the mark-ups for wholesalers and retailers. This structure does not consider ERP.
Canada	Links are provided to their Guidelines, Regulations, and the Patent Act ¹²
Pakistan	Pharmaceutical companies, particularly multinationals (MNC), prefer to market new chemical entities (NCEs) in countries where prices are not regulated and then quote these prices to authorities in countries which regulate prices of NCEs. MNCs are also marketing NCEs with different brand names and even in different strengths, different dosage forms etc. in different countries to avoid comparison.

¹² <http://www.pmprb-cepmb.gc.ca/english/View.asp?x=73>; <http://laws-lois.justice.gc.ca/eng/acts/P-4/index.html>; <http://laws-lois.justice.gc.ca/eng/regulations/SOR-94-688/index.html>; <http://www.pmprb-cepmb.gc.ca/english/View.asp?x=1733>

Malaysia	Malaysia is still in the process of setting price control mechanisms. ERP is one of the criteria to be considered for price setting. Currently, ERP is used to benchmark procurement prices. A legal framework is crucial in order to implement ERP successfully.
Ukraine	In Ukraine, ERP is experimental and is used only within a pilot project of state regulation of prices for antihypertensive medicines. The pilot began on 1 June 2012. Patients get up to 90% reimbursement of antihypertensive medicines (10 INNs). This rate depends on the price of the medicine. For other policies or programmes, EPR is not yet used but the Ministry of Health has prepared a Decree of the Cabinet of Ministers of Ukraine on the reference countries which is now being assessed in the PPRI. If this Decree is approved, EPR will be used by the Ministry of Health. ¹³
Iceland	ERP in Iceland is simple and understood by all participants.
Austria	We believe that the procedure in Austria (that price information, submitted by the manufacturer, can be checked by an independent body) is a valuable approach to perform ERP.
Switzerland	We face several issues using ERP: ex-factory prices are not always available, discounts/rebates in reference countries are not published i.e. actual reimbursement price is not available

By way of summary, Table 7 (a and b) lists countries using ERP (termed 'referrers') and the countries they reference to (grouped into four regions i.e. Europe, Africa, the Americas, and Asia / Oceania) based on the information provided in the detailed questionnaires. For example, the first data column shows that Albania (ALB) references to Macedonia (MKD), Greece (GRC) and Italy (ITA). Note: other sources of data (such as the EU report and the RAND report) were not used in compiling this table.

¹³ At the time of publishing this report, Ukraine had finished the pilot and implemented ERP widely.

Table 7a. Use of ERP- Referrer and referenced countries

REFERENCED	REFERRER																						#	
	ALB	AUT	BEL	CZE	HUN	ISL	LVA	MDA	POL	NLD	SVK	ESP	CHE	TUR	UKR	CAN	COL	IRN	JPN	JOR	LBN	MYS		SDN
Austria AUT			AUT	AUT	AUT						AUT	AUT	AUT							AUT				7
Belgium BEL		BEL		BEL	BEL					BEL	BEL	BEL								BEL	BEL			8
Bulgaria BGR		BGR	BGR	BGR	BGR			BGR			BGR	BGR			BGR							BGR		8
Croatia HRV			HRV	HRV	HRV			HRV	HRV		HRV	HRV								HRV				9
Cyprus CYP		CYP	CYP	CYP	CYP						CYP	CYP								CYP		CYP		8
Czech Rep. CZE		CZE	CZE		CZE		CZE	CZE			CZE	CZE			CZE					CZE				9
Denmark DNK		DNK	DNK	DNK	DNK	DNK	DNK				DNK	DNK	DNK											9
Estonia EST		EST	EST	EST	EST		EST		EST		EST	EST												8
Finland FIN		FIN	FIN	FIN	FIN	FIN					FIN	FIN												7
Macedonia MKD	MKD																							1
France FRA		FRA	FRA	FRA	FRA					FRA	FRA	FRA	FRA	FRA		FRA	FRA		FRA	FRA	FRA			14
Germany DEU		DEU	DEU	DEU	DEU					DEU	DEU	DEU	DEU			DEU	DEU		DEU					11
UK		UK	UK	UK	UK					UK	UK	UK	UK			UK	UK		UK	UK	UK		UK	14
Greece GRC	GRC	GRC	GRC	GRC	GRC			GRC	GRC		GRC	GRC		GRC				GRC		GRC				12
Hungary HUN		HUN	HUN	HUN			HUN	HUN	HUN		HUN	HUN			HUN					HUN				10
Iceland ISL					ISL																			1
Ireland IRL		IRL	IRL	IRL	IRL						IRL	IRL								IRL				7
Italy ITA	ITA	ITA	ITA	ITA	ITA						ITA	ITA		ITA		ITA				ITA	ITA			11
Latvia LVA		LVA	LVA	LVA	LVA				LVA		LVA	LVA			LVA									8
Liechtenstein LIE					LIE																			1
Lithuania LTU		LTU	LTU	LTU	LTU		LTU	LTU	LTU		LTU	LTU												9
Luxembourg LUX		LUX	LUX	LUX	LUX						LUX	LUX												6
Malta MLT		MLT	MLT	MLT	MLT						MLT	MLT												6
Netherlands NLD		NLD	NLD	NLD	NLD						NLD	NLD	NLD							NLD				8
Norway NOR					NOR	NOR												NOR						3
Poland POL		POL	POL	POL	POL						POL	POL			POL									7
Portugal POR		POR	POR	POR	POR				POR		POR	POR		POR			POR			POR	POR			11
Moldova MDA															MDA									1
Romania ROM		ROM	ROM	ROM	ROM		ROM	ROM			ROM	ROM											ROM	9
Serbia SRB								SRB							SRB									2
Slovakia SVK		SVK	SVK	SVK	SVK		SVK	SVK	SVK			SVK			SVK									9
Slovenia SVN		SVN	SVN	SVN	SVN						SVN	SVN												6
Spain ESP		ESP	ESP	ESP	ESP						ESP			ESP			ESP	ESP		ESP	ESP			10
Sweden SWE		SWE	SWE	SWE	SWE	SWE					SWE	SWE				SWE								8
Turkey TUR																		TUR					TUR	2
Switzerland CHE																CHE					CHE			2

Table 7b. Use of ERP - Referrer and referenced countries

REFERENCED	REFERRER									#
	BOL	CAN	COL	IRN	JPN	JOR	LBN	MYS	PAK	
AFRICA										
South Africa ZAF								ZAF		1
AMERICAS										
Peru PER	PER		PER							2
USA		USA	USA		USA		USA			4
Uruguay URY			URY							1
Mexico MEX			MEX							1
Panama PAN			PAN							1
Canada CAN			CAN				CAN			2
Chile CHL			CHL							1
Ecuador ECU			ECU							1
Argentina ARG			ARG							1
Brazil BRA			BRA					BRA		2
ASIA/MID EAST										
Taiwan TWN								TWN		1
Bangladesh BGD									BGD	1
Saudi Arabia KSA								KSA		1
India IND									IND	1
South Korea KOR								KOR		1
OCEANIA										
Australia AUS			AUS			AUS		AUS		3
New Zealand NZL						NZL		NZL		2

Based on the data in Tables 7a and 7b, Table 8 shows the referencing practices of countries by World Bank economic levels. Across the 12 high-income countries in the analysis, there were a total of 156 cases of referencing to other high-income countries. There were 18 cases of referencing (by seven high-income countries) to upper-middle income countries. Across the eight upper-middle income countries in the analysis, there were a total of 77 cases of referencing to high-income countries. There were 17 cases of referencing (by six upper-middle income countries) to other upper-middle income countries. Data was available for five lower-middle income countries and no low-income countries. Across three of the lower-middle income countries, there were 10 cases of referencing to high-income countries and 8 cases of referencing to upper-middle-income countries. Two lower-middle income countries were referencing two other lower-middle income countries, and one low-income country was referencing to one other low-income country.

Based on the countries in this analysis, there were no examples of high-income and upper-middle income countries referencing to lower-middle income and low-income countries. The majority of countries were found to be referencing to more wealthy countries or countries of similar wealth to themselves.

Table 8. Referrer and referenced countries by World Bank economic levels

REFERENCED	REFERRER COUNTRIES BY WORLD BANK ECONOMIC LEVEL 2013			
	High-income (n=12)	Upper-middle income (n=8)	Lower-middle income (n=5)	Low-income (n=0)
High-income countries	156 (n=12)	77 (n=8)	10 (n=3)	-
Upper-middle income countries	18 (n=7)	17 (n=6)	8 (n=3)	-
Lower-middle income countries	0	0	2 (n=2)	-
Low-income countries	0	0	1 (n=1)	-

n= number of referrer countries

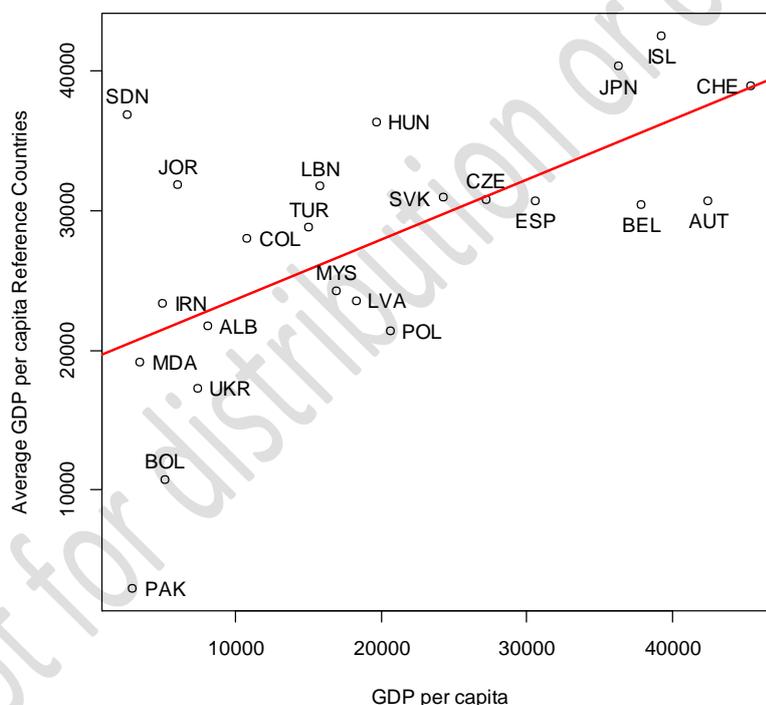
Do countries using ERP reference countries with lower GDP per capita?

One of the assumed negative effects of the widespread use of ERP is that if relatively affluent countries use as a reference the prices in low-income countries, manufacturers might not be willing to offer those countries relatively lower prices, because manufacturers claim and fear the spillover effects, i.e. the risk that affluent countries start requesting the same low prices. The assumed result is that manufacturers might either stop offering (or never start offering) lower prices to low-income countries or that they will simply not market some medicines in low income countries in order to avoid that risk or the political costs of not lowering the price of a medicine in a country unable to finance the product at the price of higher-income countries. In fact, manufacturers often claim that they cannot offer lower differential prices to low-income countries because they are referenced to by higher-income countries and spillover effects would take place. This assumption means that the loss of revenue derived from lowering the price in a country below those applied in higher-income countries would not be restricted to the country concerned but to the loss of revenue produced by the price-lowering effect of ERP on other more affluent countries (the spillover effect).

The main objective of this research was to find out whether countries using ERP reference either low-income countries, or countries with a lower GDPpc. This situation would not necessarily imply that the assumed negative effects would occur, but rather the possibility or risk that it might occur. On the other hand, if no referencing to lower-income countries is observed, we could conclude that no spillover effects can take place. Therefore, the claim of some manufacturers that they cannot sell at lower, differential prices to lower-income countries is in principle unfounded.

This question can be addressed in different ways. Figure 4 graphically displays the association found between the GDPpc of the referencing countries and the average GDPpc of the countries on the reference basket of the former, i.e. the regression line between the two variables. Table 9 shows the data on which Figure 4 is based.

Figure 4. Association between GDP per capita and the average GDP per capita of the reference countries



The value of the slope is 0.43; this means that any additional Euro of GDPpc is associated with a difference (increase) of 0.43 Euro. A correlation analysis was carried out using Kendall's tau, which resulted in an estimate of 0.41, with a statistical significance of $P=0.006$. The practical implication of this finding is that ERP-using countries tend to reference on average countries with a higher GDPpc. However, this does not exclude the possibility of some low-income countries being referenced and being at risk of experiencing the potential negative effects.

Table 9. GDP per capita data on countries in the analysis

Country		GDP per capita (2012 US\$)	Average GDP per capita US\$ – Reference Countries
TUR	Turkey	15001,406	28826,4056
HUN	Hungary	19637,585	36379,145
ISL	Iceland	39223,958	42563,1135
LVA	Latvia	18254,656	23553,06457
POL	Poland	20591,752	21396,28225
SVK	Slovakia	24249,107	30954,55915
UKR	Ukraine	7373,99	17256,93338
CHE	Switzerland	45417,809	38962,81233
CZE	Czech Republic	27190,922	30845,60304
AUT	Austria	42408,575	30761,67258
ALB	Albania	8052,178	21740,14933
BEL	Belgium	37883,057	30449,59804
LBN	Lebanon	15756,935	36947,266
MDA	Moldova	3415,028	19158,63189
SDN	Sudan	2544,629	36941,063
IRN	Iran	4977,093	23354,63933
MYS	Malaysia	16922,374	24284,10691
PAK	Pakistan	2880,667	2934,5885
JOR	Jordan	6042,293	31848,39681
COL	Colombia	10791,73	28043,05388
ESP	Spain	30557,473	30720,91596
JPN	Japan	36265,746	40359,88075
BOL	Bolivia	5099,273	10719,482

Table 10 shows the countries more frequently referenced by countries with a higher GDPpc. This figure (the number of countries referencing a given country) can be considered as an indicator for the latter being at risk of experiencing a negative effect from being referenced, because the spillover of ERP affects more countries and hence a larger market.

Table 10. Countries more frequently referenced by countries with a higher GDPpc

Number of countries referencing	Countries referenced
7	Latvia, Romania
5	Bulgaria, Croatia, Hungary
5	Estonia, Lithuania, Poland, Portugal
4	Cyprus, Greece, Malta, Slovakia
3	Czech Republic, Italy

There are, however, other factors that might increase the risk of adverse effects of being referenced to by higher income countries, such as the economic relevance of the referring country or the difference in GDP per capita.

Table 11 shows countries referencing to countries with a lower GDPpc. The second column shows the GDPpc in 2012 of the referring country (in US\$). The third and fourth columns show the total number of countries referred and the number of those countries with a lower GDPpc than the referring country. Column 5 shows the average difference in GDP of the countries that have a lower GDP than the referring country. The last column shows the referred country that has a smaller GDPpc and the difference expressed as a percentage in relation to the corresponding value of the referring country.

ERP is used by countries with quite different GDPpc, from Pakistan (US\$2,880) to Austria (US\$42,409) as shown in Table 10. The total number of referenced countries also varies substantially, from 2 countries (Pakistan) to 30 (Hungary). A number of EU Member States reference all EU and no other countries.

Austria is the country in our sample that references the greatest number of countries with a lower GDPpc, both in absolute numbers and as a percentage of all countries in its basket.

Among non-European countries it is noteworthy to mention the case of Malaysia where more than half (6) of the eleven countries they reference have a lower GDPpc than itself.

Table 11. Countries that reference to countries with a lower GDPpc

Referrer country	GDPpc in US\$	Total number of referenced countries	Number of referenced countries with a lower GDPpc	Average difference in GDPpc as a %	Referenced country with the largest GDPpc difference as a % in relation to the referrer country
Hungary	19,637	30	4	-19.6	Romania: -34.8
Latvia	18,254	7	1	-29.8	Romania: -29.8
Poland	20,591	8	3	-9.8	Croatia: -13.5
Slovakia	24,249	27	9	-22,0	Romania: -47.2
Czech Republic	27,191	27	13	-22,8	Romania: -52.9
Austria	42,409	27	26	-32,1	Romania: -69.8
Belgium	37,883	27	21	-32,7	Romania: - 66.2
Spain	30,557	27	16	-26,7	Romania: -58.1
Ukraine	7,374	8	1	-53.7	Moldova: -53.7
Malaysia	16,992	11	6	-22,7	South Africa: - 32.8
Pakistan	2,880	2	1	-29,9	Bangladesh: -29.9
Colombia	10,792	17	2	-3,7	Ecuador: -6.8

The relatively small number of countries that answered the questionnaire makes it difficult to apply statistical tools to ascertain any associations between the variables collected by the survey. No general traits emerge either, except the apparent trend of EU countries referencing all other EU countries.

According to the last column of Tables 10 and 11, Romania seems to be the country more likely to suffer the negative effects of ERP. Not only is it the country more frequently referenced to by countries with a higher GDPpc, it is often the referenced country with a relatively lower GDPpc in relation to the referencing country. In various cases the GDPpc of Romania is less than half that of the referencing country.

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5. Discussion

This study was undertaken to try to resolve the question as to how widely ERP was used in low- and lower-middle income countries and whether higher-income countries included low- or lower-income countries in their reference basket. This was important to address the concern expressed by pharmaceutical companies that if they offered lower differential prices to poorer countries these prices would be used in ERP systems to drive down prices in high-income countries adversely affecting the bottom line of these companies. Despite the limitations noted in the next section of the report, all of the information gathered has tended to indicate that ERP is hardly used in low- or lower-income countries and that most countries refer to other countries with similar or higher national income levels.

While the first questionnaire was only able to gather data from 73 countries, we had data from at least 14 other PPRI countries on practices in high-income European countries. In addition, data on ERP practices in any one country would come from other countries that would include that country in their basket of countries they would refer to. Thus if no high-income countries referred to any low- or lower-income country in their basket there should not be a concern about whether those poorer countries used ERP or believed that they were being referred to.

Our analysis showed that only 13 out of 50 lower-middle income countries, and five out of 34 low-income countries, reported that they are using ERP. While there were many countries for which no data was available it is likely that if these countries were using ERP, data would be available. Based on the experiences of PPRI network members, individuals tasked with implementing ERP often struggle with it. They struggle with issues such as choosing the basket of countries to refer to, which prices to refer to, how to deal with missing data, and how to update their data on a regular basis. If there were people in low- or lower-middle income countries who were attempting to implement ERP it is likely they would have responded to calls on E-Drug and other media that was used. So in this case the absence of data can be taken to mean that there is unlikely to be any other low- or lower-middle income countries which use ERP that have been identified. The finding that none of the high-income countries reported using low- or lower-middle income countries in their national baskets should be a reassurance to pharmaceutical companies considering whether to offer differential (lower) prices to countries that have less ability to pay for their products.

African countries and Tuvalu stated that they use MSH's International Drug Price Indicator Guide as the basis for ERP. The International Drug Price Indicator Guide reports prices (supplier and buyer) of generic products that are widely available in international trade. These are not the type of products that pharmaceutical companies have expressed concern about providing differential prices to lower-income countries. The international generic tender market is completely different to the patent protected originator brand market, which is the prime focus of high-income countries which use ERP.

The answers to the detailed questionnaire highlight some findings and conclusions, but they also raise questions on the use and potential effects of ERP.

The procedures reported show large differences across countries in the way the national ERP systems are designed and run. At one extreme, Canada has a sophisticated, clearly defined and explicit set of rules for applying ERP. In other countries, the traits of the system are vaguely defined, probably leaving a lot of discretion to national regulators in their application to the pricing procedure for individual products.

Most countries reference countries of a similar or higher GDP per capita. We found, however, examples of the inverse relationship. For instance, Belgium and Austria (with a 2012 GDP per capita of US\$37,883 and US\$ 42,408, respectively) reference Romania (US\$12,802) and Bulgaria (US\$14,301). This situation is relatively frequent in Europe, as many countries include all or most EU Member States in their baskets. The previous examples, selected for the purpose of illustration, reflect the largest differences found in the available data for Europe. Theoretically, the risk of a country suffering unintended adverse effects of ERP increases, *ceteris paribus*, as the difference in wealth between the referrer and the referenced country increases. The risk increases if the ERP rule or algorithm gives more weight to low prices, for instance, if the reference price is defined as the lowest price in the basket. In fact, the Spanish regulator claims the right of Spain to the lowest price found in any EU Member State.

Outside Europe we found examples of this problematic relationship among lower-income countries, e.g. Ukraine (US\$7,374) referencing Moldova (US\$3,415), and Pakistan (US\$2,880) referencing Bangladesh (US\$2,093).

This is certainly an issue that deserves further analysis and monitoring, because it could lead either to upward pressures in the medicines prices in lower-income countries that are being referred to, or to lack of availability of certain important medicines in those lower-income countries.

The study found that few countries, only four in our set, exclusively use ERP to determine prices for particular medicines (usually patent-protected originator brands). Those using several criteria or approaches were not able to clearly explain whether and how the various criteria are weighted, combined or complement each other. This situation produces undesirable regulatory uncertainty for potential manufacturers, which might ultimately lead to less innovation and higher prices.

Countries were often not able to provide a precise date for the establishment of ERP, which gives support to the assumption that ERP might have started as an informal common-sense practice of the regulators.

The types of medicines most likely to be subject to ERP are on-patent prescription medicines, imported medicines and medicines reimbursed by the national health system. These are probably the targets of all or most other price regulation systems, not just ERP.

There are three main criteria for selecting the countries in the basket: belonging to the same region, having similar/comparable income, and having similar socioeconomics conditions. Some more pragmatic reasons are low prices and the availability of price information.

Most countries seem to rely on free public websites as the main source of price information in reference countries. As previously stated, the choice of reference countries might be because information is available.

The ex-factory price is the most frequent price sought in the reference countries, followed by the wholesale price. This choice makes sense as the ex-factory price is the one that reflects the price variations attributable to manufacturers' strategies and decisions. Consumer prices are highly influenced by internal factors, such as mark-ups for wholesalers and retailers, and taxes.

Regulators seem to (have to) basically rely on official/list prices, rather than on actual transaction prices. This situation may in the long run render ERP ineffective and irrelevant as discounting and rebating are widely applied especially for hospital medicines (5).

When submitting applications, less than half of the countries require companies to provide prices in the reference countries, and not all of the countries impose penalties for not complying with this obligation (when it exists). Moreover, many regulators do not cross-check the information found in websites or provided by applicants. This seems quite unfortunate, as requiring companies to disclose this information is not a very costly option, either for the company or for the regulator, and could therefore be a key source of information to begin the search for valid reference prices. Companies may be unwilling to supply such information especially if they are required to report discounted prices. Selecting a valid and convenient source of exchange rate does not seem to pose any major problem to regulators.

Most countries select either the lowest price in the basket of countries, the median price or a simple average, or the average of the three lowest prices. Most countries apply price revisions to the initial price set. But few determine the new price using ERP.

The number of staff involved in ERP is difficult to assess, because officials usually are not devoted to ERP on a full-time basis. The figures provided by the survey, after removing the outliers, suggest staffing levels between 2 and 10 people.

Price setting agencies do not seem to systematically rely on direct communication with other agencies in order to collect the required price information.

Regarding the degree of strictness in setting prices according to the ERP algorithm, most countries seem to adopt a rather flexible approach and products are not often withdrawn from the pricing and reimbursement process as a result of the ERP regulation. The fact that the estimated reference price seldom becomes the effective selling price reinforces the perception of a flexible approach to implementing ERP. This can be partly attributable to the decision by potential applicants not to apply in a given country where they expect to be assigned a lower price.

The number of medicine prices set by ERP varies widely across countries, from less than a dozen to 500-900 per year.

Unlike in previous studies, respondents were able and willing to provide some simple illustrations of how ERP is applied in practice.

The present study did not shed much light on the effectiveness of ERP in regulating the prices of medicines. However, by comparing the procedures applied by different countries, regulators might learn from each other. They might not be able to identify and implement best practices, but they might be able to identify and skip bad practices.

Assessing the impact of ERP can be tentatively addressed by modelling and scenario-building approaches. The model developed and applied by the EC for Europe could probably be used to assess the impacts on lower-income countries at a worldwide level. But a valid evidence-based assessment of the effects of ERP should start with the development of appropriate price databases that record transaction prices and volumes of transactions for each relevant medicine or market segment.

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6. Limitations

It was anticipated that the dataset would be limited by the key informant identification, and the response rate to the questionnaires. Complete responses to the initial questionnaire were received from 73 countries. Most responses, but not all, were from key informants. When a contact provided the name and contact details of a key informant, all efforts were made to contact that person. In a number of cases, no responses were received to these requests.

It was hoped that postings on the various mailing list servers (such as E-Drug) would boost the number of responses to the initial questionnaire. This was not the case, although data was received from a few countries where we had no contacts or key informants.

The response rate to the longer and detailed questionnaire was far lower than hoped, especially for countries outside of Europe. This was a key limitation in identifying which countries were being referenced to and to characterising the use of ERP.

Another difficulty was that in some cases conflicting answers were given e.g. one country would say they knew a particular country was referencing to them, but that country responded that they do not use ERP. This may have been due to responders misunderstanding the terminology as some countries said they use ERP but upon receiving the detailed questionnaire, or in telephone discussions, they realized that they did not use ERP.

7. Conclusions

Based on information from 100 countries, we found no examples of high-income countries referencing low-income countries as defined by the World Bank. On the basis of this finding, low prices offered by pharmaceutical companies to low-income countries would not result in reduced prices in high-income countries as a consequence of current, formal ERP practices. Moreover, the practical difficulties of identifying prices in low-income countries, especially actual prices (net of discounts, rebates, etc.) as opposed to official prices, makes the possibility of high-income countries referencing prices in low-income countries very unlikely.

A key secondary finding of this study is that ERP is not a “simple” system to operate and requires experienced human, information and IT resources in order to address the complexities of the method and implement it effectively. Low-income countries which do not at present use ERP should consider these requirements before they decide to attempt to implement such a system.

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Annex I: Initial questionnaire

1. Contact details
 - a. Name
 - b. Email address
 - c. Phone number
 - d. Institution/organisation
 - e. Position
2. Country
3. Are you in some way (for example: officer of the Ministry of Health or similar authority, procurement officer, academic) involved medicines pricing and/or the reimbursement of medicines in your country?
Yes/No
4. Do you know how medicines are priced and reimbursed in your country?
Yes/No
5. Do you have official price regulations and/or reimbursement regulations for medicines in your country? (regulations may differ across categories of medicines, patient groups etc.).
Yes/No/Do not know
6. Is External Reference Pricing used in your country?
ERP is the practice of using the price(s) of a pharmaceutical product in one or several countries in order to derive a benchmark or reference price for the purposes of setting or negotiating the price of the product in a given country. In this project, we are including other external price sources such as the International Drug Price Indicator Guide and WHO WPRO's Price Information Exchange etc.
Yes/No/Do not know
7. Are you actively planning to use ERP in your country?
Yes/No/Do not know
8. Are you aware of any countries, formally or informally, taking the price of medicines in your country as a reference for setting their own prices?
Yes/No/Do not know
9. Please provide the names and contact details of officials working on medicine pricing and/or financing/reimbursement, or others who you feel we should contact, in your country.
 - a. Name
 - b. Institution
 - c. Email address
 - d. Phone number

Annex II: Detailed questionnaire for countries using ERP

Country:
Name:
Organisation / Ministry:
Unit:
Function:
Phone:
Email:

Date:

ERP is the practice of using the price(s) of a pharmaceutical product in one or several countries in order to derive a benchmark or reference price for the purposes of setting or negotiating the price of the product in a given country

TWO KEY QUESTIONS

1. When using ERP, to which countries and/or price databases¹⁴ does your country reference?
Please name the countries and/or price databases:
2. Are you aware of any other countries referencing your country prices (i.e. using your prices as a reference for setting or negotiating their prices)? YES /NO
If the answer to this question is YES, please name the countries referencing your country prices:

GENERAL QUESTIONS ABOUT PRICE REGULATIONS (in order to understand the context)

3. Is there a unit/department responsible for setting/negotiating the price of medicines in your country? YES/NO
If YES please explain what units or departments are responsible:
4. Is there a unit/department responsible for setting /negotiating the price of medicines for reimbursement or payment by a health system or insurer in your country? YES/NO
If YES please explain what units or departments are responsible:
5. What criteria do these units or departments use to determine the price of medicines?
 - a. Only External Reference Pricing (ERP)
 - b. ERP plus additional criteria (*more than one can be selected*):
 - i. Cost-plus calculations (cost of production of the medicine plus a certain profit or margin)
 - ii. Prices of similar medicines on the market to treat the same condition or disease (internal reference pricing)
 - iii. Economic evaluation (pharmacoeconomic) studies
 - iv. Health Technology Assessment
 - v. Other (*please describe*):
6. If additional criteria are used besides ERP (e.g. price of similar medicines for the same indication, cost-plus calculations etc.), in what way are the criteria combined? (*please describe*):

USE OF ERP and LEGAL FRAMEWORK

7. What year did your country start using ERP?
8. Is there a national legal framework for the use of ERP (i.e. an official document describing the procedures for price regulation)? YES/NO
If YES please name it and send us a copy or link:
If NO please explain how you apply ERP:

ERP SETTINGS

¹⁴ For example, Global Price Reporting Mechanism or MSH International Drug Price Indicator Guide

9. Which type of medicine is ERP applied to? (*you can select more than one option*):
- On-patent prescription medicines YES/NO
 - Generic prescription medicines YES/NO
 - Imported medicines YES/NO
 - Locally manufactured medicines YES/NO
 - Medicines reimbursed by a national insurer or the health system YES/NO
 - Over-the-counter (OTC) medicines (non-prescription medicines) YES/NO
 - Certain therapeutic groups of medicines (e.g. cancer medicines, diabetes medicines) YES/NO
If YES, please list the therapeutic groups:
 - Other types of medicines (*please describe*):

10. What criteria are used to select the countries you reference to? (*please describe*):

11. What types of prices sources do you use?
- Free public website
 - Free public website that requires access authorization
 - Website that requires payment
 - Publications (e.g. paper catalogue)
 - Personal communications with national authorities

Optional, Please list the sources / websites

12. In your list of reference countries, what proportion usually have price information publicly?
- All of them
 - About half of them
 - Very few
 - Other proportion (*please describe*):

13. Of your list of reference countries, please name the countries most frequently used in practice:

14. What is the procedure if prices are not publicly available in some of the reference countries?
- Only use reference countries where you can access prices
 - Search for prices in other countries
 - Use alternative pricing criteria (*please explain*):

15. What type of price is searched in the reference countries? (*more than one can be selected*)
- Ex-factory (manufacturer) price
 - Import price
 - Wholesale selling price
 - Price paid by consumers (retail price) with or without value added tax (VAT) and other sales taxes (*please clarify*)
 - Other (*please explain*):

16. When do you collect prices in the reference countries?
- No systematic time
 - Price at the time of product registration in the reference country
 - Price at the time of product launch in the reference country
 - When you set your national price (*please explain*):
 - Average price over a certain period (*please explain*):
 - Price at a defined time e.g. 1 January of the year (*please explain*):
 - Other (*please explain*):

17. Do you use the official list /catalogue price in the reference countries or do you try to find out the actual transaction price i.e. after the application of any of discounts or rebates? *Please explain*:

18. Do your regulations *require* under some form of penalty a manufacturer/importer to report the product price in the reference countries? YES/NO

If NO, do you *ask* the manufacturer/importer to report the product price in the reference countries? YES/NO

19. Is the price information obtained (from lists, manufacturers etc.) validated or crossed check with information from other sources? YES/NO
If YES please describe how this is completed:
20. How are product differences – such as variations in medicine strength, pack size, minor formulation differences etc. – in the reference countries managed if they do not match the product in your country? *(please explain)*:
21. Which source, date and type¹⁵ of exchange rate is used to translate the prices in reference countries into your currency? *(please describe)*:
22. What procedure or criteria are used to combine/aggregate the reference countries prices into a single reference price?
- Simple average/mean of the prices found in the reference countries
 - Weighted average/mean of the prices found in the reference countries (if so, please explain how you weight them):
 - Lowest price of the reference countries
 - Median price of the reference countries
 - No general formula but decided on a case-by-case basis
 - Other formula/criteria *(please explain)*:

Does the method used vary for different types of medicines (e.g. generics and on-patent medicines)? YES/NO

If YES, please explain:

23. Is the reference price revised when prices change in the reference countries?
- There are no revisions of the reference price
 - There are periodic revisions *(please explain)*
 - Only if prices change in the reference countries
 - If the exchange rate changes
 - If the product is launched in additional reference countries
 - When a manufacturer requests a price increase in your country
 - Other reasons *(please explain)*:
24. Do you foresee any changes in ERP regulation or use in your country in the next two years?
YES/NO
If YES please describe:
25. How many staff (in terms of fulltime-equivalents, FTE) work in your country to manage the ERP process?

CONSEQUENCES of using ERP

26. Do agencies from other countries ask you for your prices? YES/NO
If YES,
How many requests do you get annually? *please give the approximate number*:
What countries have asked you for prices? *please list the countries*:
What medicine prices have been requested? *please list the medicines*:
27. In the last five years, how often has a product not been marketed, or withdrawn from the market or from public reimbursement, because the price you set in your country using ERP was considered too low by the manufacturer? *Please state the number of times this has happened*:
28. In the last five years, how often has the ERP become the price in your country i.e. was not revised in price negotiations or other pricing criteria?
- Never
 - Seldom (up to 10% of the time)
 - Often (up to 40% of the time)
 - Frequently (more than 40% of the time)

¹⁵ e.g. buy rate, selling rate, mid-point, something else

e. Always

29. In 2013 how many medicines/molecules had their price set using ERP?
please give the estimated number:
please give the percentage (%) compared to all the medicines that are price controlled in your country:
Please provide a list of medicines (by INN) priced using ERP (optional)
30. Please provide detailed examples for one or two medicines that you have priced using ERP i.e. prices for the products found in each reference country, the initial reference price you computed, and the actual price you set or negotiated in your country? You may blind the name of the products (e.g. product A, product B) (optional)
31. Is there anything else you would like to tell us about the use of ERP in your country?

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Annex III: Questionnaire for countries thinking of using ERP

Country:
Name:
Organisation / Ministry:
Unit:
Function:
Phone:
Email:

Date:

ERP is the practice of using the price(s) of a pharmaceutical product in one or several countries in order to derive a benchmark or reference price for the purposes of setting or negotiating the price of the product in a given country

1. Why are you planning on using ERP? Please explain.
2. If you start using ERP, to which countries and/or price databases¹⁶ will you likely reference? Please name the countries and/or price databases:
3. Are you aware of any other countries referencing your country prices (i.e. using your prices as a reference for setting or negotiating their prices)? YES /NO
If YES, Do they send you an official request asking you for your prices? YES/NO
If YES, How many requests do you get annually? *please give the approximate number:*
What countries have asked you for prices? *please list the countries:*
What medicine prices have been requested? *please list the medicines:*
4. Is there a unit/department responsible for setting/negotiating the price of medicines in your country? YES/NO
If YES please explain what units or departments are responsible:
5. Is there a unit/department responsible for setting /negotiating the price of medicines for reimbursement or payment by a health system or insurer in your country? YES/NO
If YES please explain what units or departments are responsible:
6. What criteria do these units or departments currently use to determine the price of medicines?
 - a. Cost-plus calculations (cost of production of the medicine plus a certain profit or margin)
 - b. Prices of similar medicines on the market to treat the same condition or disease (internal reference pricing)
 - c. Economic evaluation (pharmacoeconomic) studies
 - d. Health Technology Assessment
 - e. Other (*please describe*):
7. If you plan to use ERP as well as additional criteria (e.g. price of similar medicines for the same indication, cost-plus calculations etc.), in what way will the criteria be combined? (*please describe*):

If you have definite plans to use ERP please proceed with the next question and complete the questionnaire.

If you are thinking of using ERP, but have no definite plans, please go to question 18

USE OF ERP and LEGAL FRAMEWORK

8. What year will your country start using ERP?

¹⁶ For example, Global Price Reporting Mechanism or MSH International Drug Price Indicator Guide

9. Have you already developed a national legal framework for the use of ERP (i.e. an official document describing the procedures for price regulation)? YES/In preparation/To be developed
If YES please send us a copy on (erp@haiglobal.org)

ERP SETTINGS

10. Which type(s) of medicine(s) will ERP be applied to? (*you can select more than one option*):
- On-patent prescription medicines YES/NO
 - Generic prescription medicines YES/NO
 - Imported medicines YES/NO
 - Locally manufactured medicines YES/NO
 - Medicines reimbursed by a national insurer or the health system YES/NO
 - Over-the-counter (OTC) medicines (non-prescription medicines) YES/NO
 - Certain therapeutic groups of medicines (e.g. cancer medicines, diabetes medicines) YES/NO
If YES, please list the therapeutic groups:
 - Other types of medicines (*please describe*):
11. How will you collect prices in your reference countries?
- Internet
 - Personal contacts
 - Other (*please explain*):
12. What will you do if you can't obtain prices in some of the reference countries?
- Only use reference countries where you can access prices
 - Search for prices in other countries
 - Use alternative pricing criteria (*please explain*):
13. What type of price(s) do you plan to look for in the reference countries? (*more than one can be selected*)
- Ex-factory (manufacturer) price
 - Import price
 - Wholesale selling price
 - Price paid by consumers (retail price) with or without value added tax (VAT) and other sales taxes (*please clarify*)
 - Other (*please explain*):
14. Will your regulations *require* under some form of penalty a manufacturer/importer to report the product price in the reference countries? YES/NO
If NO, will you be asking the manufacturer/importer to report the product price in the reference countries? YES/NO
15. How do you plan to validate the price information obtained (from lists, manufacturers etc.)?
16. How will you manage product differences – such as variations in medicine strength, pack size, minor formulation differences etc. – in the reference countries if they did not match the product in your country? (*please explain*):
17. What procedure or criteria will be used to combine/aggregate the reference countries prices into a single reference price?
- Simple average/mean of the prices found in the reference countries
 - Weighted average/mean of the prices found in the reference countries (if so, please explain how you weight them):
 - Lowest price of the reference countries
 - Median price of the reference countries
 - No general formula but will be decided on a case-by-case basis
 - Other formula/criteria (*please explain*):
18. Is there anything else you would like to tell us about the future use of ERP in your country?