

# International drug price comparisons: quality assessment

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## ABSTRACT

**Objective.** To quantitatively summarize results (i.e., prices and affordability) reported from international drug price comparison studies and assess their methodological quality.

**Methods.** A systematic search of the most relevant databases—Medline, Embase, International Pharmaceutical Abstracts (IPA), and Scopus, from their inception to May 2009—was conducted to identify original research comparing international drug prices. International drug price information was extracted and recorded from accepted papers. Affordability was reported as drug prices adjusted for income. Study quality was assessed using six criteria: use of similar countries, use of a representative sample of drugs, selection of specific types of prices, identification of drug packaging, different weights on price indices, and the type of currency conversion used.

**Results.** Of the 1 828 studies identified, 21 were included. Only one study adequately addressed all quality issues. A large variation in study quality was observed due to the many methods used to conduct the drug price comparisons, such as different indices, economic parameters, price types, basket of drugs, and more. Thus, the quality of published studies was considered poor. Results varied across studies, but generally, higher income countries had higher drug prices. However, after adjusting drug prices for affordability, higher income countries had more affordable prices than lower income countries.

**Conclusions.** Differences between drug prices and affordability in different countries were found. Low income countries reported less affordability of drugs, leaving room for potential problems with drug access, and consequently, a negative impact on health. The quality of the literature on this topic needs improvement.

## Key words

Prescription drugs; drug price; pharmaceutical trade; review.

Health care costs are a major concern for decisionmakers and individuals worldwide. The economic burden of pharmaceutical drugs contributes substantially to these costs (1). National authorities have attempted to retain low drug prices in order to keep medicine affordable (2).

Thus, drug policymakers are obligated to find a balance that will maximize health benefits and facilitate, maintain, or improve access to drugs. International drug price comparisons can help nations establish and tailor a proper pricing system to their unique socioeconomic characteristics.

Drug prices can be compared using various sources. Since 1986, Management Sciences for Health, which is affiliated with the World Health Organization, has annually published the *International Drug Price Indicator Guide*. That initiative provides valuable information that is user friendly and available to the public. It al-

lows manufacturers and policymakers to set prices that will be acceptable and relative to those in other similar countries (3). Additionally, the website of the Organisation for Economic Co-operation and Development (Paris, France) provides information on aggregate pharmaceutical expenditures for various drugs in all of its participating nations (4).

International drug price comparisons can be used to evaluate the affordability of drugs in the domestic market. Comparisons measuring affordability can help explain the relationship between different costs that are incurred by both the manu-

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facturers and society and how the burden of the drug costs is distributed. In addition, affordability adjustments can potentially provide valuable information to policy makers regarding which drug policies succeed in lowering prices as well as what price level should be considered acceptable compared to other nations. Adjusting drug prices by average income-per-person (Gross Domestic Product [GDP] per capita) is one way of measuring affordability. GDP is the primary measurement for income within a nation. Adjusting prices for GDP per capita allows the reader to understand the value of the drug with respect to the amount of income the average person has available to spend on pharmaceuticals.

The literature on international drug-price comparisons displays marked variations in reported results. Therefore, it is important to examine the quality of these studies and identify methodological characteristics that lend themselves to accurate comparisons of drug prices across different countries. There are several methodological challenges related to comparing prices on a multinational level that have been previously discussed in the literature. One paper cites six criteria necessary to conduct an international price comparison (1). The pros and cons of these criteria have been described elsewhere (5).

Different indices, economic parameters, price types, baskets of drugs, and manufacturing weights are some examples of the methodological issues that challenge the ability to draw comparisons. The application of these different methodologies can result in a marked variability in study results. Consequently, each international drug price study must have some components in order to fulfill their purpose of comparing international drug prices. Because a comprehensive review of the literature failed to locate research that has definitively summarized papers on this topic, the objective of this review was to quantitatively summarize results (i.e., prices and affordability) reported from international drug price comparison studies and assess their methodological quality.

## MATERIALS AND METHODS

Acceptable articles were those describing original research that compared drug prices between two or more countries. No restrictions were placed on location of the research, year of publication, data

sources for price comparisons, or type of prices used in the studies. Prices could be compared at any level, such as the pharmacy, distribution, or manufacturers' price lists, as long as the same types of prices were used in each country of interest. In addition, languages accepted were those of major Western countries (i.e., English, Spanish, French, Portuguese, Italian, and German).

The most relevant, electronic databases—Medline, Embase, International Pharmaceutical Abstracts, and Scopus—were searched from the first year available for each (i.e., inception) to May 2009. In an attempt to identify as much of the targeted literature as possible, key search words were used and combined in three word blocks: “drug prices,” “cross-national,” and “comparison.” Within each block, similar key words and heading terms were used and combined. For example, within the “cross-national” block, we applied the following sequence of terms: cross-national OR cross border OR cross jurisdiction OR cross-regional OR international OR multi-national OR foreign OR global OR worldwide. The search result was then combined with the other search blocks using AND as separators. This was applied to all electronic databases used in the literature search. Additionally, a manual search was conducted of the bibliographies of the retrieved studies. Furthermore, an effort was made to identify papers from the grey literature (i.e., relevant publications not captured by the electronic database search) by systematically combining search words in Google™/Google Scholar™ (Mountain View, California, United States). Irrelevant articles were discarded using the inclusion/exclusion criteria established *a priori*. The citations were retrieved by one reviewer, and a second one confirmed selection results. Titles and abstracts were read first and full-text reading followed after the inclusion of relevant studies.

Data extracted from the selected studies were tabulated, along with a summary of the methods used and results reported by each. Again, one reviewer summarized study results, and a second, confirmed data extraction. The following data were collected from each acceptable study: authors, year of publication, study objectives, countries examined, drugs compared, economic parameters used for converting currencies and adjusting prices, and results reported.

The quality of the articles was assessed using the methodology criteria suggested by Andersson (1). Although other articles mentioned similar criteria, Andersson's paper was selected due to its comprehensiveness and clearly defined objectives. However, because the purpose of this paper was not to create a quality ranking, scale, or checklist, a validation was not conducted. Nonetheless, the six criteria stated by Andersson were widely discussed in the literature, and four other authors considered the criteria's scientific rigor to be sufficient for conducting international drug price comparisons (5–8). The six criteria called for studies that: (i) selected countries with similar health parameters (e.g., disease patterns, therapeutic tradition, level of drug consumption, etc.); (ii) focused on a non-biased representative sample of drugs (e.g., high volume drugs selected systematically); (iii) identified a specific type of price (i.e., manufacturer's price, retail price, wholesale acquisition cost, etc.); (iv) considered the differences in drug production and packaging (i.e., package size, strength, dosage, etc.); (v) had a type of price index (i.e., Laspeyer's, Paasche's, and Fisher's indices, discussed below); and (vi) had selected a type of currency conversion(s) used to compare the prices (e.g., exchange rates [US dollars], Purchasing Power Parities [PPPs], etc.) (1). Drug prices were reported for the year in which the relevant study analysis was conducted. These criteria were used in order to assess whether or not the selected studies were appropriate for price comparisons. Credits were assigned to all criteria that were met, with all points considered equal; that is, there was no weighting associated with the quality criteria.

## RESULTS

### Literature search

The literature search found 1 828 published papers. Figure 1 depicts the search strategy and results. After reading titles and abstracts, 130 papers were selected for full-text review. After applying the exclusion criteria, 27 of the papers found within the research databases were selected for analysis, of which 13 met all of the criteria and provided usable, original data (1, 2, 5, 7, 9–17). The 14 other papers were excluded due to lack of original data (i.e., reviews, comments, letter

to the editors, etc.) (18–31). Through the grey literature search, an additional eight relevant studies were found that also fulfilled the inclusion criteria (6, 8, 32–37). In all, the entire literature search yielded 21 articles that were accepted for the review (1, 2, 5–17, 32–37).

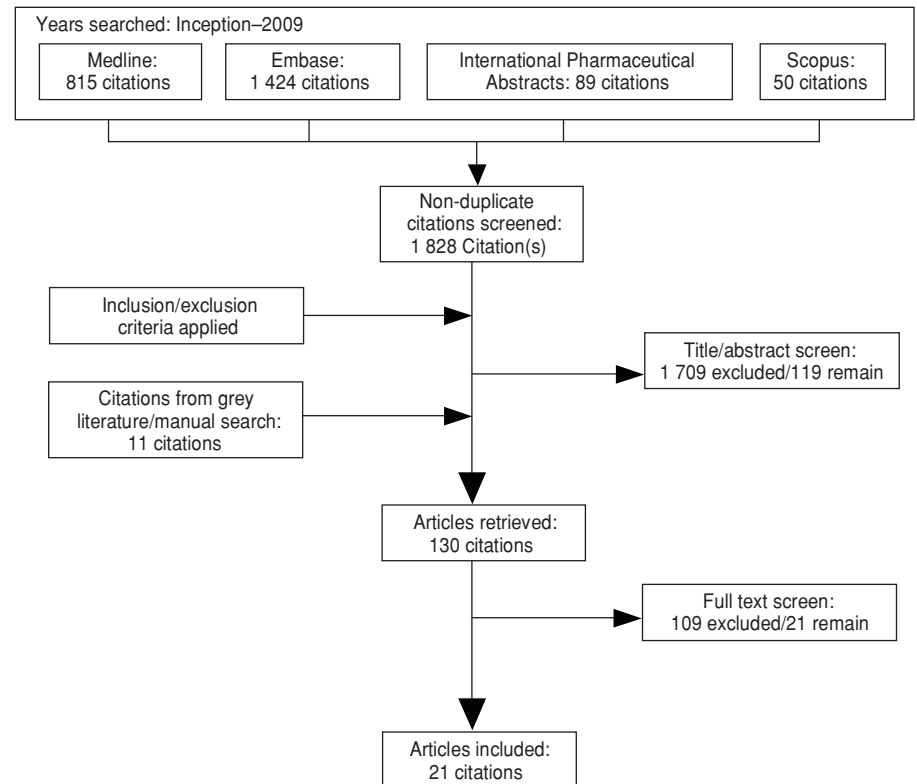
### Overall characteristics of studies

The total number of countries compared by the 21 accepted articles was 72, among which all the continents were represented. It was assumed that economically similar countries and countries in close geographic proximity had comparable health parameters. Therefore, 17 of the accepted papers compared prices for countries located in different continents (2, 5–10, 12–14, 16, 17, 32–35, 37), whereas four performed multicountry comparisons within the same continent (1, 11, 15, 36). While studies written in Western European languages were considered, only studies written in English were found. All 21 accepted papers had been published in 1986–2009.

Countries and geographic areas were compared using various baskets of drugs, including generic and brand name pharmaceuticals, as well as novel and essential drugs. Many of the studies examined a comprehensive basket of drugs while others did not state which drugs were used for the comparison (see table in supplementary materials). Thirteen studies explicitly named the drugs that were compared (2, 6, 10, 12–17, 34–37). As an example, the study by Cameron and colleagues clearly listed all the drugs investigated by both their generic and brand names (17). By contrast, the paper by Cohen and colleagues did not mention the drugs used in their comparison (9). However, only 1 of the 13 studies used a diverse and representative sample of drugs across all nations compared (6).

International comparisons also varied with the economic parameters used to convert prices into a common currency. The 17 studies that reported adjusted drug prices used different parameters in their comparisons, including PPPs ( $n = 6$  papers) (5, 7, 11, 13, 32, 33), currency exchange rates ( $n = 12$  papers) (1, 6, 10, 14–16, 32–37), and income adjustments ( $n = 4$  papers) (5, 7, 9, 34). In addition, five studies used multiple parameters within their comparison to provide separate or more accurate results (5, 7, 32–34). However, four studies did not

**FIGURE 1. Flowchart depicting the search for international drug-price comparison studies and results for each step used in applying the inclusion/exclusion criteria**



adjust their prices, but used price ratios as an alternative for their comparisons (2, 8, 12, 17).

Furthermore, the analyzed articles displayed different methods of presenting prices. The recorded data were reported from the studies either in price indices, dollars, price ratios, or as a percentage difference in prices, which were all acceptable methods. Some researchers ( $n = 5$  papers) presented their results as price indices; however, the types of indices used and the economic parameters used to adjust the index were not always stated (1, 5, 7, 11, 36). Six publications used different price ratios to compare the data (2, 6, 8, 12, 17, 33). Ratios were consistently used to compare the price differentials between brand name and generic drugs and between countries.

Manufacturing decisions, including packaging and production, can also affect price comparisons (1). In most of the studies ( $n = 13$ ), researchers used a standard strength for each drug in order to draw an accurate price comparison (2, 6, 8, 12–17, 34–37). Although some articles used specific pharmaceuticals resulting in relative doses throughout the compar-

ison, others did not identify whether the drugs used were of different indications for different countries. Some of the articles also used a price-per-unit dose or a price-per-standard-unit of strength (14, 15). However, others did not make adjustments or indicate any discrepancies in the price data due to manufacturing issues (1, 5, 7, 9–11, 33). The presence of the six quality criteria in the accepted studies is summarized in Table 1. A single study was found that fulfilled all of the quality requirements for conducting a robust comparison (6).

### Results reported by the studies

Obtaining identical information across all the international comparisons of drugs was not possible. Most of the comparisons had few countries in common and few or no drugs in common within the basket of comparisons. Thus, it was not possible to derive a single number summarizing the differences in drug prices among the countries. However, the data collected were used to describe similarities among the papers in order to draw a conclusion.

**TABLE 1. Quality assessment of 21 international drug-price comparison studies accepted for review, 2009**

Study (reference)	Similar countries	Representative sample of drugs	Specific price category	Manufacturing and packaging issues identified	Weights on price indices	Currency conversion (PPP, <sup>a</sup> exchange rate, income adjustments)
Andersson (1)	✓		✓		✓	✓
Baht (33)						✓
Cameron (17)			✓	✓		
Cohen (9)						✓
Danzon (5)			✓			✓
Danzon (7)						✓
Ford (10)			✓	✓		✓
Gelders (34)			✓			✓
Mrazek (11)	✓		✓	✓		✓
Nobrega (12)			✓	✓		✓
Nunn (35)			✓	✓		✓
PDCI <sup>b</sup> (36)	✓					✓
PMPRB <sup>c</sup> (32)						✓
Productivity Commission (6)	✓	✓	✓	✓	✓	✓
Roughead (13)			✓	✓		✓
Sasich (37)			✓	✓		✓
Simoens (14)	✓		✓	✓		✓
Spasic (15)	✓		✓	✓		✓
Szuba (16)			✓	✓		✓
Tafari (2)			✓	✓		
Wagner (8)				✓		

<sup>a</sup> Purchasing Power Parity.

<sup>b</sup> Palmer D'Angelo Consulting Inc., Ottawa, Canada.

<sup>c</sup> Patented Medicine Prices Review Board, Ottawa, Canada.

The studies consistently showed Germany, Sweden, the United States, and the United Kingdom as having drug prices higher than the other countries to which they were compared and relative to other comparisons, suggesting that higher drug prices exist in high-income countries (1, 5–8, 11, 14, 16, 33, 36, 37). Although prices in the United States were the highest in all the comparisons in which it was included, the other developed countries (i.e., Germany, Sweden, and the United Kingdom) would alternatively occupy the position of having the second highest priced. These results were derived only from the studies that compared exchange rates or PPPs (1, 2, 5–8, 10–17, 32, 33, 35–37), but not affordability issues.

An unexpected finding was that when compared to the lower income countries, the more affluent countries' higher prices were more affordable (5).

Although the United States had, on average, the highest absolute prices, when compared to other countries using a common currency and adjusting for income, it had one of the lowest average drug prices. After adjusting for income, Brazil, Chile, and Mexico had the highest prices compared to the other countries

with which they were compared, such as Australia, Canada, France, Germany, Italy, Japan, Spain, the United Kingdom, and United States (5). In addition, when comparing price ratios of generic drugs to brand name, low-income countries had the widest variations (17).

## DISCUSSION AND CONCLUSIONS

The methodological issues in multinational price comparisons and results reported were the principal focus of this review. As seen in the reviewed literature, drug price comparisons differed mostly due to the methodology that was used to assess the data. For example, many researchers used different economic parameters, ones they believed were best suited for conducting their research. However, such discrepancies may cause the data found within different studies to become heterogeneous. In 1993, Andersson published a methodological approach to comparing prices accurately (1). This procedure, however, was intended primarily for policymakers to set socially correct prices that would compare equally with countries that had similar policies and economies. With a general price comparison, the

overall objective is to strip away economic restrictions in order to get a comparable price that is measured in a common currency between two or more countries.

First, Andersson suggested that selecting similar countries in the comparison is essential for obtaining accurate comparative information (1). However, this criterion was deemed unnecessary for studies that were comparing prices across borders in order to assess affordability and/or to gather information on countries of different income levels. However, where the intent is, for example, to set new pricing policies, countries with similar socioeconomics should be compared.

Second, correctly comparing prices across countries and removing bias can only be accomplished if the selection of drugs is from a representative sample of all countries compared. Therefore, it is recommended that the top 100–200 drugs by sales in each country be compared so as to reflect consumer preferences within nations (1). One of the papers reviewed used this approach (6); whereas all others focused on specific types of drugs, an approach that imposes a significant methodological limitation.

Third, selecting which available type of drug price should be used is another methodological issue. Several different prices are set during the drug distribution chain including a manufacturer, wholesaler, and retailer price. Retail prices should not be used within drug price comparisons because they tend to skew the data. Some countries impose taxes, such as value-added taxes, that may cause an unjust comparison (7).

Fourth, identifying and correcting problems within drug comparability is necessary for an accurate comparison. Package sizes, forms, strengths, indications, and ways of distributing drugs vary among countries (1). Some of the studies showed the strengths of the drugs; however, some did not suggest that the packaging of the drugs would affect the price of the product (i.e., non linear price per dose strength). An alternative approach is the use of standardized measures, such as defined daily doses (DDDs). DDDs are the recommended doses for a specific drug used for its most common indication.

Fifth, weighting prices is essential when indices are used to compare prices. Three types of indices have been sug-

gested to measure the difference in prices: Laspeyre's, Paasche's, and Fisher's (1). These indices apply weights to the prices to adjust for the consumption patterns (i.e., sales volume) within the pharmaceutical markets (1). The quantity demanded for a pharmaceutical product is the number of drugs that a community consumes or is willing to pay for at a certain price. Therefore, the quantity demanded displays the value placed on the drug and influences the price of each product. Weights must be placed on the prices because the variety of drugs within the compared drug basket may not be representative of the most consumed pharmaceuticals between two countries, thus creating a bias in the results.

Converting drug prices to a common currency (i.e., U.S. dollars or Euros) is the sixth and final criterion that is necessary for generating an accurate comparison. The dilemma is choosing between the utilization of PPPs or exchange rates. The theory behind PPPs is that in two similar nations, the identical basket of goods (minus transportation and transactions costs) should have the identical price after converting to a standard currency, such as U.S. dollars (38). However, an identical price is not usually the result. PPPs take into account inflationary pressures on nominal exchange rates, which force prices to become different within the two countries.

In addition to Andersson's six criteria mentioned above, two others should be considered in drug price reviews, as well as in comparisons. First, adjusting drug prices by average income should be part

of any price comparison to reveal the burden of drug prices on the average person. However, when prices are adjusted for income in low-income countries, there may be a skewed distribution (5). In most low-income nations, the Gini coefficient is usually very low, indicating that the wealth gap is large. The Gini coefficient measures income inequality within a nation and ranges from 0 (perfect equality) to 1 (complete inequality) (39). Therefore, prices tend to appear too high when adjusted for income. The high prices provide the assumption that they are set for citizens with a higher income within those countries. Twice-weighting prices by average income and the inverse of the Gini coefficient might be an alternative. Secondly, adjusting drug prices for inflation may provide different results depending on the year of the analysis. Comparisons could be skewed due to changing inflation rates over time. Therefore, drug prices compared between countries and reported from the selected studies could potentially be different in the current socioeconomic scenario than when originally published. Furthermore, continuous updates of international drug price comparisons are recommended based on changes in policy and economic variables among countries and over time.

Finally, despite all methodological discrepancies found in the published international price comparison literature, higher income countries were found to have more affordable drug prices than developing countries. This raises an important flag about access to pharmaceu-

ticals (both old or new) by individuals in developing countries. Reasons for such price and affordability discrepancy are many, including market need, socio-political pressure, permissive government regulation, poor country legislation, among others.

The studies retrieved in this review offered varied results on drug prices and affordability due to the different methods they used. The quality of most the studies was considered low—very few followed the ideal protocol and, therefore, could not present valid conclusions. A standard method of conducting international drug price comparisons would enhance the reliability of the results observed here. Proper recording measures and methods should be recognized and taken into consideration when conducting a study. Although recording measures can be easily corrected, the methodological issues are more difficult to overcome. Depending on the objective of the study, different methods of comparing prices can be used to generate and analyze data and associated conclusions.

In addition, higher drug prices compared using exchange rates or PPPs were found more frequently in affluent/developed countries. However, when adjusting for affordability, lower income countries (e.g., Brazil, Chile, and Mexico) had higher pharmaceutical prices compared to high income countries (e.g., United Kingdom and the United States). This inequity in drug affordability among economically different countries may point to potential influences on drug access that could negatively impact health.

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## RESUMEN

### Comparación internacional de precios de medicamentos: evaluación de la calidad

**Objetivo.** Resumir cuantitativamente los resultados (p. ej., precios y asequibilidad) presentados en estudios de comparación internacional de precios de medicamentos y evaluar su calidad metodológica.

**Métodos.** Se llevó a cabo una búsqueda sistemática en las bases de datos más importantes —Medline, Embase, International Pharmaceutical Abstracts y Scopus, desde la fecha de inicio hasta mayo del 2009— para identificar artículos de investigación original que comparaban precios de medicamentos entre distintos países. Se obtuvo y se registró la información sobre los precios de los medicamentos de los trabajos que fueron aprobados para ser incorporados en esta revisión. Para evaluar la asequibilidad se consideró la adaptación de los precios en función de los ingresos. Se evaluó la calidad de los estudios tomando como parámetro seis criterios: el uso en países similares, el uso de una muestra representativa de medicamentos, la selección de tipos específicos de precios, la descripción del tipo de envasado, las diferentes ponderaciones aplicadas a los índices de precios y el tipo de cambio empleado.

**Resultados.** De los 1 828 estudios encontrados, se incluyeron 21. Solo un estudio cumplió adecuadamente con todos los criterios de calidad. Se observó una amplia diferencia de calidad entre los estudios a causa de los diversos métodos empleados para comparar los precios de los medicamentos, tales como, diferentes índices, parámetros económicos, tipos de precio y canasta de medicamentos. Por lo tanto, se consideró que la calidad de los estudios publicados era deficiente. Si bien los resultados de los estudios son muy diversos, en general, los medicamentos fueron más costosos en los países de ingresos más altos. Sin embargo, una vez ajustados los precios en función de la asequibilidad, se observa que los países de ingresos más altos tienen precios más asequibles que los países de bajos ingresos.

**Conclusiones.** Se encontraron diferencias en los precios de los medicamentos y la asequibilidad entre los diferentes países. En los países de ingresos bajos, se registró un grado menor de asequibilidad, lo que origina posibles problemas de acceso a los medicamentos y, en consecuencia, tiene repercusiones negativas sobre la salud. Es necesario mejorar la calidad de los estudios dedicados a este tema.

## Palabras clave

Medicamentos bajo prescripción; precio de medicamento; comercialización de medicamentos; revisión.