The London School of Economics and Political Science

Pharmaceutical prices 1999-2008: an exploration into global variation, comparative measures, and potential determinants

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Declaration

I certify that the thesis I am presenting for examination for the MPhil/PhD degree of the London School of Economics and Political Science is solely my own work other than where I have clearly indicated that it is joint work (in which case the extent of any work carried out jointly by me and any other person is clearly identified below).

I declare that my thesis consists of approximately 80,100 words.

Statement of conjoint work

I confirm that Paper 1 was jointly co-authored with Professors McGuire and Mossialos and I contributed 85% of this work.

Statement on pre-existing work

I confirm that all of the chapters in this dissertation reflect work that was undertaken for the purposes of this degree, during the registration period.

ABSTRACT

Despite globalization, major differences in access and affordability of pharmaceuticals remain across the countries of the world. This dissertation aims at quantifying the differences in the price of pharmaceuticals amongst countries, identifying the factors responsible for these differences, and examining the policy consequences.

Paper 1 compares prices in a large set of middle-income countries to some high- and low-income countries. It finds that prices of pharmaceuticals are inconsistently related to income, with many middle-income countries paying more than some high-income countries and some paying less than countries that are far poorer. Paper 2 confirms the belief that drug prices in United States are generally higher than in 20 other high-income countries, but shows that prices became more similar over the period 1999-2008. Using the values and the range of three price indices (Laspeyres, Paasche, and Fisher) calculated with multilaterally- and bilaterally-matched samples provides a nuanced understanding of these price differences and their evolution. Paper 3 combines price data from middle- and high-income countries to ascertain the social, economic and demographic factors that determine differences in pharmaceutical prices. It finds that prices in middle- and high-income countries are affected differently by competition and globalization and that the greater effect of demographic factors on prices in middle-income countries can give them an inherent disadvantage in early price negotiation. Paper 4 also examines possible determinants of price but in this case focusses on health system characteristics in OECD countries only. The study finds that whilst the overall health system type does not bear any significant relationship with price, governance structures do have a moderately strong relationship with the price and availability of pharmaceuticals. Based on these results, the Conclusion discusses the issue of horizontal and vertical equity in pricing across countries and highlights important policy themes emerging from this work overall.

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INTRODUCTION

Challenges in accessing medicines outside of the rich, industrial world are well-known, albeit not well understood. A critical question is whether the prices at which pharmaceuticals are offered are beyond the means of the populations in question. Arguments for pricing pharmaceuticals according to affordability amongst countries (cross-country differential pricing) and even locally (within-country differential pricing) are multiple and well justified on both normative and economic grounds (see Underlying Theory section for a discussion of the latter). However, there is little evidence that differential pricing is the dominant pricing strategy employed by pharmaceutical companies. This dissertation is an exploration into the degree to which differential pricing is taking place, ways of measuring price differences in the fairest possible manner given the immense diversity in products across countries, and what other factors might be playing into the level of price offered to different country markets. The final piece of the work explores the variation that exists in price and scope of availability even across the group of wealthiest countries and how this might be accounted for by the type of health system or underlying structures—governance, finance, or provision.

Paper 1 of this dissertation examines relative pharmaceutical prices in middle-income countries – the income group about which we know the least. The comparison is made through the construction of price indices, here Paasche and Laspeyres price indices. According to the World Bank, 70% of today's global population reside in middle-income countries (World Bank 2008) and the wealth of many of these countries is expected to rise very rapidly in the years to come. The E7 countries – Brazil, China, India, Indonesia, Mexico, Russia and Turkey – are expected to see real GDP triple from 2004 levels, their wealth relative to that of the G7 rising from 19.7% to 43.4% (PWC 2007). With economic growth, demand for pharmaceuticals is expected to increase significantly, especially amongst middle-income countries. Price Waterhouse Coopers expects that by 2020 E7 pharmaceutical sales alone will account for 19% of global sales in a $1.3 trillion global pharmaceuticals market (PWC 2007). According to IMS Health, 7 emerging markets—Brazil, India, Turkey, Mexico, Russia, South Korea, and China will soon even eclipse the once-dominant sales drivers, the United States, Europe and Japan (Hill 2009).

Although we know they are growing rapidly, relatively little is actually known about the pharmaceutical markets in middle-income countries, namely about price levels offered given

that they are not completely industrialized, have some remaining areas of extreme poverty, and are overall socially and demographically quite different from the group of high-income countries that are the traditional marketplace for high-volume sales of pharmaceuticals. To help fill in some of these important gaps in understanding, we constructed price indices to explore the relative price of pharmaceuticals in a number of middle-income markets and compared them to prices in both high- and low-income markets. The classification of countries by World Bank income category was included in order to most appropriately align with the real price negotiation process that takes place between pharmaceutical companies and countries (as well as both international and civil society organizations involved in health) when badly needed medicines fail to reach populations in need (for example with ARVs for the treatment of HIV/AIDS income category generally works as the tier at which prices are set). .

Our findings suggest that in fact national income category (income categories were employed in order to reflect the actual decision-making process undertaken by pharmaceutical companies whenever they undertake highly publicized global price tiering or "compassionate" pricing schemes to increase access to badly needed medicines -- e.g. ARVs, malaria, and TB drugs) is not consistently related to prices in the countries examined. Indeed the study finds that despite the generally accepted view that it would be statically and dynamically efficient as well as ethical to price pharmaceuticals according to relative income, that does not appear to occur consistently. The study finds a wide variability in pharmaceutical prices, with prices in some middle-income countries being similar to those in rich developed countries - for example Mexico compared to the United States or Morocco compared to France - regardless of the index and of the consumption volumes used, whilst in others they are low in comparison to the prices seen in low-income countries. Indeed for some middle-income countries the prices seem low even compared to much poorer countries, for example Egypt and India compared to western Africa.

Whilst our study conclusions were clear, the study does have some obvious limitations. The samples used to create these price indices include only a portion of medicines that are available on the respective country markets. Though we tried to maximise like-for-like price comparisons, we gave priority to the overall representativeness of the market. This means that whilst the respective country samples will match with the United States, for example, in molecule-indication (the identifying label), they may differ in their prescription status, level of competition, age, manufacturer, formulation, or other features. These characteristics should be

controlled for in an ideal analysis of price determinants. This was part of the rationale for exploring price determinants in Paper 3.

Our findings require care in interpretation given the sensitivity of relative prices to how they are measured. Indeed the use of different indices and different samples of pharmaceuticals lead to different relative prices. In this study all Laspeyres index values (which are weighted by base country consumption patterns) exceeded their Paasche index counterpart (which are weighted by the consumption patterns of the comparator country, or "own-weighted"), indicating that the correlation between relative price and volume changes was negative, as for most normal goods, that is goods whose physical consumption falls when their prices rise. In most countries pharmaceutical prices are regulated by government so this negative correlation could come from the regulation itself. Whilst this relationship is expected, the interplay between indices and the samples on which they were based did not feel sufficiently clear after the publishing of Paper 1 (published as 'The level of income appears to have no consistent bearing on pharmaceutical prices across countries' CM Morel, AJ McGuire, E Mossialos, *Health Affairs*, 30, no.8 2011 :1545-1552.). This was part of the rationale for exploring the relationship between indices in Paper 2.

In order to see how results differed by country sample, by base country, by unit of physical measurement, by type of index used, by matched sample, and by the effects of discounting, several additional analyses to those in Paper 1 were undertaken (see Appendix 1). For the most part the additional 30 analyses did not alter the main findings of Paper 1. Generally, when matching molecule-indications across all middle-income countries -- rather than bilaterally with the US—results did not change significantly. Except for the case of Mexico, all middle-income countries had prices less than half of US prices throughout the study period. Irrespective of the angle of comparison prices in middle-income countries were consistently below UK prices when using UK as the base country (although much closer to UK prices than US prices), with the exceptions of Mexico and Philippines. When looking exclusively at prices calculated using UK-specific consumption patterns, a number of middle-income countries had prices higher than UK prices in several years. These included South Africa, Tunisia, Brazil, Indonesia, and even western Africa in some years. Broadly speaking, pharmaceuticals that are important to the UK market had prices similar to several lesser (relative to the UK) developed countries. When focussing on middle-income country prices relative to France (another ex-colonial power) findings were similar, with a few more middle-

income countries, such as Poland and Morocco, having prices above French prices over several years when basing prices on French consumption patterns. Regarding the comparison of middle- to low-income countries overall the additional findings reinforce those presented in Paper 1, suggesting that many middle-income countries have prices below those attained in low-income countries. Beyond Egypt and India which were mentioned in the published version of Paper 1, results here suggest that Algeria and Tunisia were consistently far below those in western Africa over several years of the study, irrespective of the consumption patterns or sample used.

Paper 2 focusses on relative drug prices in high-income countries, quantifying and trying to understand the differences in pharmaceutical prices across high-income countries and how these differences evolved over a ten year-period, 1999 through 2008. As in previous studies, this is achieved by using price indices despite the fundamental difficulties in using such indices. As is well known, no single price index can provide a "true" quantification of relative prices when customers (or patients) in different countries exhibit different preferences. The use of price indices is particularly fraught in the case of pharmaceuticals, which come in presentations, dosages and compositions that vary from country to country. In addition drug prices are controlled in some way in most countries, and often not fully paid by the consumer as a result of private or national health insurance programs.

In view of these difficulties, this study takes a pragmatic approach and makes simultaneous use of several indices that respond differently to consumption patterns and to the variations in the prices of individual products. This approach has the double benefit of circumventing the inherent impossibility to define a true price index for pharmaceuticals and of providing useful information not only from the numerical values of the various indices and their evolution over time, but also from their differences.

This study analyses IMS data from 20 comparator countries from 1999 through 2008[1] relative to the US. The comparator countries are all high-income countries as defined by the World Bank: Australia, Austria, Belgium, Canada, Finland, France, Germany, Greece, Italy, Japan, Korea, Netherlands, Philippines, Poland, Portugal, South Africa, Saudi Arabia, Singapore, Spain, Sweden, Switzerland, Taiwan, and the United Kingdom. The analysis is made for two

[1] Data was available for years 1999 through the 3rd quarter of 2008, hence just under one full decade.

baskets of pharmaceuticals for each country: 1) a multilaterally-matched sample of about 150 "global" drugs that were available in all comparator countries and the United States in any given year, and 2) a much larger bilaterally-matched sample of drugs available in each individual country and the United States in each year (between 750 and 2600 drugs) that is more representative of the whole market in each country.

The analysis is conducted by calculating for each comparator country and for each year six separate indices, namely the Laspeyres, Paasche and Fisher indices calculated separately for the multilaterally- and bilaterally-matched samples: L_B, L_M, P_M, P_B, F_M and F_B. As a result of the inverse relationship between usage and price, the Laspeyres indices (which uses weights from the base country --the US in most of our study) are always larger than the Paasche indices (which use weights from the comparator country) and this effect is magnified when the sample size is larger such that $L_B > L_M > P_M > P_B$. This expected result was indeed verified for all years for all countries considered.

With very few exceptions the indices show that pharmaceutical prices in the comparator countries were lower than in the US for the period of the study. They also indicate a decrease in those differences with time for most countries with indices increasing from 1999 to 2008. Most notable exceptions were indices calculated for Saudi Arabia, which decreased over time, and for the United Kingdom, which remained nearly constant.

For several countries, Finland, France, Italy, Spain, Portugal, Greece and the Netherlands, the total range of the mean bilateral index values was relatively narrow with a difference $L_B - P_B < 0.25$. In that situation, the bilateral Fisher index, F_B, which is the geometric mean of L_B and P_B, provides a reasonable and practically useful single number approximation of relative prices of a large fraction of pharmaceuticals in two countries. On this basis, it can be said that, on average over the ten years of the study, the manufacturer-level prices of pharmaceuticals in these countries were between 40% and 50% of US prices. Based on small differences between mean multilateral indices ($L_M \approx P_M$), representative relative price of commonly used "global" pharmaceuticals (which constituted on average 33% of the various markets) compared to the US could be obtained by using the corresponding Fisher index, F_M, in more than half the comparator countries.

In a number of cases, the data showed unusual contrasts between the values of Laspeyres and Paasche indices based on the same sample, or between the same index based on multilaterally-

or bilaterally-matched samples, or in the relative evolution of these four indices over time. Such contrasts served as flags indicating unusual features of the pharmaceutical market in individual countries during the period of the study. In several instances, a detailed examination of the indices led to a likely explanation in terms of differences or changes in pricing or consumption patterns between the comparator country and the US. In all such cases a detailed examination of the individual data sets would help to positively ascertain the underlying causes.

Appendix 2 describes the samples used in Paper 2 and shows the results of the sensitivity analysis described in the paper.

Paper 3 looks at the combined middle- and high-income dataset in order to examine potential determinants of prices globally. After proving the quality, safety and efficacy requirements through pre-clinical and clinical trials, new pharmaceutical products undergo regulatory scrutiny by the regional authority (e.g. European Medicines Agency) and/or national agency (e.g. Food and Drug Administration, national authorities) in order to receive marketing authorization. Pricing and reimbursement negotiations then take place to determine price (except where there is truly free pricing) and reimbursement status. So whilst list prices are in theory set solely by the manufacturer or distributing company, they are really a result of potentially many other, including local, considerations. This study explores what some of these might be.

The paper focusses on the contribution of country-specific economic, social, and demographic characteristics, in addition to drug-specific properties such as quality and levels of competition in the market. The study utilizes data from 33 middle- and high-income countries over a 10-year period, and, as such, it is much larger than previous studies of medicine price determinants and is the first to consider the potential relationship of country social and demographic characteristics to pharmaceutical prices.

The study finds the price of drugs in all countries to be strongly negatively associated with the time since their global launch and positively associated with national income per capita (although this latter effect was less strong in middle- than in high-income countries). Prices offered to middle-income countries are particularly dependent on several socio-demographic variables rather than purely economic ones. In middle-income countries, the percentage of old people was the strongest determinant of drug prices, most probably reflecting a rapid increase

in demand. The length of time since launch of a drug in a country was strongly positively related with its price, likely a result of product recognition and associated marketing strategy and ensuing purchaser behaviour. Overall, results suggest that prices offered to purchasers in middle- and high-income countries are affected differently by globalization and competition and that social and demographic differences in middle-income countries give them a notably different negotiation predisposition (less leverage) that may deserve attention in global discussions surrounding fairer pricing and improving access to medicines. A description of each of the 13 samples used in Paper 3 can be found in Appendix 3.

Bringing in a new, yet related angle, Paper 4 explores possible relationships between the price of pharmaceuticals and health system type, using the best methods approach explored in previous sections (namely in Paper 2). The study finds no quantitatively detectable relationship between overall health system type and pharmaceutical prices or market take-up in OECD countries. However, it does find a moderately strong relationship between regulation and both price and availability of pharmaceuticals in the national market. State dominance in governance if found to lead to slightly lower prices but also to a slightly more limited range of therapeutics available. These more subtle findings should be considered with caution due to the limited sample size. However, the overall greater importance of regulatory dominance than dominance of financing and provision may have implications for pharmaceutical as well as wider health policy. For example, privatization of provision (an effective transition from an National Health Service to a National Health Insurance system) in the name of budget constraints or achieving greater efficiencies does not necessarily translate to attaining more competitive prices in the pharmaceutical market.

Findings also suggest that allowing the devolvement of financing to sick funds (similar to what one would see in a transition from a non-profit National Health Service to an Etatist Social Health system) does not necessarily translate to a loss of ability to contain prices. Such a transition would have little effect on pharmaceutical prices. Decentralization of regulation, finance, and provision (e.g. in a transition from an National Health Service or an Etatist Social Healht Insurance system to a Social Health Insurance system) would however limit the ability to contain prices--interestingly not due to any loss of monopsonistic (sole payor) leverage (there would be no change in financing dominance from ESHI to SHI)—where one would likely assume the greatest influence would stem from in a free market--but rather from the transition away from state governance. Interestingly a closer relationship was also detected

between the availability of pharmaceuticals and regulation than between availability and either financing or provision. Again the governance role appears to be a more important determinant of the number of therapeutics available than who finances them or who prescribes them. Here state dominance in governance leads to slightly more limited range of therapeutics available. Appendix 4 provides background material supporting Paper 4.

In the name of comprehensiveness Appendix 5 aggregates price data across all countries (including all income levels) using optimal methods. Although the aggregation of data from such different parts of the world limits the size of the sample that can be analysed (down to approximately 100 for the multilaterally-match sample) and is arguably less fair given the inherent differences in the market (see Paper 3), there was value to be gained in such an exercise, namely as a type of sensitivity analysis for the overall work.

STRUCTURE OF THE DISSERTATION

Paper 1: 'The level of income appears to have no consistent bearing on pharmaceutical prices across countries' CM Morel, AJ McGuire, EA Mossialos (2011) *Health Affairs*, 30, no.8: 1545-1552.

Paper 2: 'Comparison of pharmaceutical prices amongst high-income countries using multiple indices' CM Morel (submitted for publication)

Paper 3: 'Global pharmaceutical prices and country development: How do economic, social, and demographic factors affect prices and how do middle- and high-income countries compare?' CM Morel (submitted for publication)

Paper 4: Pharmaceutical markets across OECD countries: How do the markets differ and what role do health system structures have in determining such differences? CM Morel (to be submitted for publication)

Appendix 1: Includes technical material not included in the paper, full results (a limited number of results could be published in the paper itself), additional study limitations, and additional results examining how results differed by country sample, by base country, by unit of physical measurement, by type of index used, by matched sample, and by the effects of discounting.

Appendix 2: Includes the description of samples used in each of the analyses and results of the sensitivity analysis testing for changes in base country and discounting. It also rebases prices to help examine evolution over time.

Appendix 3: Includes summary statistics for the variables of each of the models 1-13 described in Paper 3.

Appendix 4: Includes background material supporting Paper 4. It provides a picture of the relative size of the individual country markets by molecule presentation (also a decent proxy for variability) and the degree to which the samples used in calculating the indices were representative of the individual country markets.

Appendix 5: Includes additional price indices constructed for all countries together using optimal methods, using the US as the reference case. Also calculates global indices using other countries—including from other income classes--as the reference case.

METHODS SUMMARY

All papers are based on the same IMS dataset of ex-manufacturer prices from the decade 1999 through 2008[2].

Paper 1 constructs Paasche and Laspeyres price indices to explore price variation across a set of 14 middle-income countries, 3 high-income countries and an aggregate low-income country zone (made up of 10 countries in western Africa).

Paper 2 constructs Paasche, Laspeyres, and Fisher price indices to explore price relatives in 20 high-income countries compared to the United States.

Paper 3 examines the determinants of prices across 33 middle- and high income countries, looking at the association with country development indicators in addition to characteristics of the pharmaceuticals themselves.

Paper 4 constructs Fisher price indices to explore price relatives across OECD countries and investigates possible relationships between these price relatives and the type of health system in place as well as the underlying health system structures (in particular focussing on the actor dominating regulation, financing, and provision within the system) using pairwise correlation.

DATA DESCRIPTION AND PREPARATION

A very large dataset was acquired for this project from IMS Health. Data came in the form of an IMS-specific "Dataview" format, including monetary sales and unit sales volume data from the decade 1999 through the third quarter of 2008, including from the following country markets: Algeria, Australia, Austria, Belgium, Brazil, Canada, Egypt, Finland, France, Germany, Greece, India, Indonesia, Italy, Japan, Korea, Malaysia, Mexico, Morocco, Netherlands, Philippines, Poland, Portugal, South Africa, Saudi Arabia, Singapore, Spain, Sweden, Switzerland, Taiwan, Thailand, Tunisia, Turkey ,UK, United States, and a commercially aggregate West African zone including Benin, Burkina Faso, Cameroon, Republic of the Congo, Cote d'Ivoire, Gabon, Guinea, Mali, Senegal, and Togo. Data were extracted and loaded into STATA where they were reshaped, variables named and grouped

[2] Only the first three quarters of data were available for 2008

where appropriate, and categorical variable values coded. Duplicates in terms of all variables were dropped. Combination products were dropped.

Positive sales (in terms of thousands of USD) were summed across all country-ATC3-molecule combinations by quarter, conversion from local currency having been undertaken by IMS Health using exchange rates in effect at time of sale (converted by quarter). Sales data for quarter 4 in 2008 (missing data) were calculated as the average of the first 3 quarters of that year. Positive unit sales (in terms thousands of standard units[3] and kilograms) were summed across all country-ATC3-molecule combinations by quarter. Unit sales data for quarter 4 in 2008 (missing data) were calculated as the average of the first 3 quarters of that year. Pharmaceuticals with very small (smallest 3% by volume in terms of standard units) were dropped. Sales and unit sales were then converted to years. [Data outlay: Each ATC3[4] category had at least one molecule within in, usually several. Each molecule fell within one indication, sometimes more than one. Pharmaceuticals were defined as ATC3-molecule combinations, allowing any multiple indications to be counted separately.] Prices were calculated by dividing sales by unit sales and deflated (to 2005 dollars) using World Bank estimates of the annual GDP deflator for each country. Here the GDP price index is preferable to the Consumer Price Index (CPI), a better known general index, for a several reasons. Most importantly here, the composite CPI only covers approximately 60% of the economy, omitting government purchases, rural consumers, and investment goods. With the high proportion of health care expenditures—including pharmaceuticals--coming from federal and state governments it becomes particularly important to use a price index, such as the GDP deflator, that more broadly reflects the whole economy (MEPS 2014).

The data include all drugs sold to the retail market. As such it does not include those sold to hospitals, except in the case of hospital private pharmacies that purchase through retail channels. (Together the retail and hospital sectors comprise the complete formal pharmaceutical market within each country.) It should be noted that the implications of omitting pharmaceuticals destined for hospitals may include a selection bias in that hospitals

[3] Standard units are the small common dose unit. For oral solid forms this is one tablet or capsule, for syrup forms this is 5 ml, and for injectable forms this is one ampoule or vial. Defined Daily Doses were not available.

[4] The 3rd Anatomic Therapeutic Class (which classifies with 3 to 4 digits).

use a greater number of intravenous drugs, a greater number of drugs for serious diseases and diseases with pathogens resistant to first/second-line therapies. This may suggest that the database used for the analyses had a downward bias in prices due to a cheaper selection of drugs. However, hospitals are also known to be price sensitive and thus to switch quickly to generic substitutes as soon as they are on the market. This, on the contrary, would suggest that in omitting pharmaceuticals in the hospital channels the dataset utilized may have suffered from an upward selection bias if compared to the overall price (whole market) in the respective country markets. Prescribed drugs as well as OTC drugs are both included in the dataset.

In the creation of the price indices (Chapters 1,2, and 4), drugs are collapsed by molecule-indication combinations. This means that there may be some variation across all other attributes from country to country, including in quality. So indeed the drugs matched across countries may have some differences in terms of their quality. This method of matching drugs is meant to be as inclusive as possible given that there is so much variation in the other attributes of the drugs available across different countries or even local markets. Inclusiveness in this case was traded off against an exact like-for-like comparison as the latter would have dramatically reduced the sample size. In Chapter 3 quality was able to vary across countries as the data did not have to be collapsed down as it did in the index calculations. In this case quality pertained to each drug by way of several proxies (e.g. level of global penetration, molecule age).

Prices were weighted by sales volumes across all products, pack-sizes, forms, and strengths. Prices represented ex-manufacturer prices for medicines being sold to the retail market except in the case of a few countries for which distribution pathways are not delineated between retail and other[5]. Data from the United States were based on drugstore, food store and mail service distribution channels.

[5] Singapore and Sweden prices include those for medicines destined for retail and hospitals. Indonesia and Malaysia prices include those destined for retail, hospitals, and dispensing doctors.

Copies of base country price and volume data were made and renamed for use as separate weighting variables. Level of global presence was calculated for ATC3-molecule combinations for multilateral matching across country groups of interest. In an identical, separate file only ATC3-molecule combinations matching with the US were kept in order to create bilaterally-matched indices. Samples were then created to calculate the price indices.

Calculation of price indices was undertaken using the following formulas. The Laspeyres index, L, for a comparator country, C, weights prices according to consumption patterns of the base country, i.e., the United States in most of the study:

$$\mathrm{L}_C = \frac{\Sigma(Q_{M,USA})(P_{M,C})}{\Sigma(Q_{M,USA})(P_{M,USA})}$$

Where $Q_{M,USA}$ is the quantity weight of the pharmaceutical sold in the USA, and $P_{M,C}$ and $P_{M,USA}$ are the prices of the pharmaceutical per standard unit in the comparator country and in the USA , respectively.

Paasche index, P, weights prices according to consumption patterns of the comparator country (sometimes called "own-weighting"):

$$\mathrm{P}_C = \frac{\Sigma(Q_{M,C})(P_{M,C})}{\Sigma(Q_{M,C})(P_{M,USA})}$$

Where $Q_{M,C}$ is the quantity weight of the pharmaceutical sold in the comparator country, and $P_{M,C}$ and $P_{M,USA}$ are the prices of the pharmaceutical per standard unit in the comparator country and in the USA, respectively.

Fisher price indices were also calculated for each country.

$$Fisher = \sqrt{\mathrm{P} * \mathrm{L}}$$

Where P is the Paasche index value and L is the Laspeyres index value. (Fisher indices are the geometric mean of Paasche and Laspeyres Indices.)

As part of a separate but related branch of this project a regression model was estimated using panel data with random effects.

$$\ln P_{mit} = \alpha_i + \sum \beta Z_{it} + \sum \gamma X_{mt} + \varepsilon_{mit}$$

for molecule m, in country i, in year t.

The vector *Z* represented the country-specific predictor variables, whilst the vector X represented the drug-specific predictor variables. Log transformations were used for prices (ln P) and characteristics, reflecting proportional effects as they were not normally distributed. Full variable descriptions are provided in Paper 3 itself.

Paper 4 constructs Fisher indexes (described above) for the entire pharmaceutical market within each OECD country, also utilizing the IMS price/volume dataset. The same is then done for originator and generic pharmaceuticals individually in order to detect differences in price trends in these sub-markets. The three sets of price relatives are then used in multiple simple pairwise correlations to test for relationships to health system type and the actor dominant in regulation, financing, and provision within the health system.

n.b. There were some problems encountered with the original IMS data. Indeed upon hearing of major omissions IMS re-uploaded and re-sent new versions of the database (this occurred twice). However, some problems with the data were never resolved. For example, many UK prices for the year 2007 were negative (IMS failed to provide an explanation for this but it is assumed that some change in their methodology changed that year). Price data expressed per kilogram also contained major errors from the year 2004 on. Again, IMS was approached about this but gave no explanation. A representative did however informally suggest that there may have been some conversion errors when creating the database. Therefore, whilst numerous price indices were constructed using kilograms as the volume measure, none of these was used as the basis for the studies presented here.

UNDERLYING THEORY

DIFFERENTIAL PRICING

Pharmaceutical companies that are geared towards research and development often provide innovative products to the market. In some cases such new products may even introduce an entirely new class of therapeutics. If there are no therapeutic alternatives from the same therapeutic class or from another class with similar application, then such a product can, in theory, command a very high price (premium price) in a free market. In this sense innovative pharmaceutical companies can function much like monopolies in that they are a single supplier of a product. Given that access to innovative products can represent life or death for a patient or can significantly prolong life, the issue of monopoly pricing and the level to which it restricts access is at the forefront of any debate over health system financing (e.g. the ability of single or multiple payors to negotiate prices down), intellectual property protection, and, of course, equity in access.

In normal monopoly pricing strategies, prices are set at a level above a socially optimal point and only populations that are relatively well off and have low price elasticity of demand can purchase the goods. Under such conditions, both consumer and producer surpluses are foregone. The principles of differential pricing according to elasticity of demand (also known as Ramsey pricing or Boiteux-Ramsey pricing[6]) allow for a product to be offered at more than one price level, commensurate with the respective elasticities of those consumers who could not afford the product under normal monopoly pricing. Such an approach follows an inverse-elasticity rule according to which higher prices are offered to consumers with lower price elasticity of demand and lower prices to those with higher price elasticity of demand. It is often applied by utility firms in the electric and telecommunications industries, as well as railroads, airlines and other deregulated industries (Shepherd 1992). The fairness argument underpinning such pricing strategies ("vertical equity"; see below) hinges upon the idea that

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[6] William Baumol was actually the one responsible for attaching Ramsey's name to the work although Ramsey's one paper on the subject (published in 1927) actually dealt with optimal rates of taxation. Ramsey had noted that the inverse-elasticity rule was appropriate in that context in order to minimize the loss of efficiency from taxing alternative goods. Baumol applied this idea to utility pricing (Shepherd 1992)

The structure of Boiteux pricing (1956) and Ramsey pricing (1927) are very similar and, as such, the strategy is often referred to as Boiteux-Ramsey pricing.

poorer populations will be offered essential products at prices in line with their level of affordability and they will not be simply priced out of the market as in the case of pure monopoly pricing. Beyond the equity argument, differential pricing strategies are also considered to offer advantages in terms of economic efficiency. For example, rather than offering one high price to the small population that can afford the product, differential pricing strategies offer the product (often with slight differences in branding or formulation) at different price points in order to be able to sell to more price elastic markets. In theory sales can be increased until all demand is saturated out towards the equilibrium point where supply equals demand. The net result is to maximize both total output and consumer surplus, thus improving static efficiency.

The version of differential pricing referred to as Ramsey pricing is not without controversy. Ramsey pricing advocates often claim it to be "the one superior, automatic, and effective device for efficient results" and use it to argue for a complete hands-off approaches, particularly in debates on deregulation and privatization. A primary example is that of formerly monopolistic utility firms that are evolving toward full competition. Ramsey pricing advocates argue that such dominant firms should be permitted total freedom in pricing and to discriminate at will, stressing that it will result in a set of efficient prices that will not, on the whole, exploit customers.

A key argument against Ramsey pricing is that price discrimination can be used to under-price smaller competitive firms and to prevent their growth and innovation. In retaining greater dominance, the former natural monopolistic firm is able to control and limit innovation, in some cases considerably (Shepherd 1992). By using differences in demand rather than cost as the basis for prices, Ramsey pricing has in principle no lower limit, not even long-run marginal cost, a condition that can violate basic notions of fair competition. As stressed by Shepherd, this situation could be tolerable if Ramsey pricing assured an efficient outcome. But he argues that it does not because a quasi-monopolistic company cannot be trusted to abstain from reaping excess profits, and hide the fact that it does (Shepherd 1992).

The debate over the use of Ramsey pricing has focussed primarily on utilities and seemingly created a rift between those "for" and those "against." In this dissertation, which deals with the pharmaceutical industry instead of utilities, the issue of price discrimination requires a nuanced approach. There is, of course, a basic similarity in the economic structure of utility and pharmaceutical companies that makes Ramsey pricing arguably suitable for both: marginal

costs are well below average costs and thus across the board marginal cost pricing leads to financial loss (Shepherd 1992). In the case of the pharmaceutical industry, the immense costs associated with pharmaceutical research and development is in wide contrast with the very small cost of manufacturing an additional pill (especially in the case of synthetic compounds). As in the case of utilities, a fundamental reason for differential pricing of pharmaceuticals is to increase the global access to essential goods. This argument has particular weight when the accessibility to drugs can be a matter of life and death.

The possibility of excess profits resulting from Ramsey pricing clearly exists in the pharmaceutical industry as it does in others. This possibility is magnified by the simple fact that the complicated nature of investment in pharmaceutical companies, the different and purposeful way by which they discount and estimate the opportunity cost of capital, and the high level of secrecy they maintain regarding their finances make it effectively impossible to know their true internal costs. In theory, firms using differential pricing can increase sales and profits through finely tailored pricing bands that correspond closely to individual consumer affordability. (In reality, however, the practical number of possible pricing bands for pharmaceuticals may be more limited.) In middle- and low-income countries in which little was previously offered for a particular class of therapeutics, the potential size of the new market and the ensuing new revenues may be substantial. This is especially true for makers of innovative products that stand to expand into large new markets.

Nonetheless there are particular characteristics of pharmaceutical markets that militate in favour of differential pricing. First, whilst pharmaceutical firms may be effectively monopolistic in the case of drugs for which there is no clear alternative treatment, this situation is undermined as patents expire and competitors enter the market, or alternatives become available. More importantly, differential pricing of pharmaceuticals can be justified by the need to provide sufficient profits (from high prices to the populations that can afford them) to defray the very high costs of R&D (typically 20-30% of costs, compared to much lower proportions in other industries) whilst simultaneously providing access to essential goods to those with lesser means.

Differential pricing of pharmaceuticals can also offer benefits such as enforcing patents by helping to deter involuntary licensing. Firms are of course very fearful of licensing in that it puts immense downward pressure on prices towards marginal costs – a price level at which pharmaceutical firms are not financially viable over the longer term given their cost structure

characterized by high early sunk costs. In this sense differential pricing can be argued to improve dynamic efficiency.

However, for differential pricing to be efficient two things are required. First, sales into the various markets must be segmented with the separation determined by elasticities of demand. If there is leakage across markets, either across consumer groups within a country or across different countries, such that cheaper priced products become available in markets with lower elasticity of demand, then the strategy breaks down as firms are unable to accrue sufficient profits. For the pharmaceutical industry, the perceived threat of leakage and arbitrage are believed to be the primary reason that firms do not make their products available in many parts of the developing world. Second, in order to properly tier their prices, firms need to be able to divide customers into groups according to their respective elasticities of demand. This is no easy task, especially for sales into countries where the firm may have little experience. Short of being able to either directly observe behaviour or estimate willingness-to-pay for pharmaceuticals, firms are in most cases limited to using proxies for price elasticity of demand. In this situation national (or regional) income is usually the most convenient such proxy.

As mentioned above, a major motivation for differential pricing of pharmaceuticals has to do with "fairness." In economics this notion is generally discussed in terms of "horizontal" and "vertical" equity. Horizontal equity implies that people with the same financial situation should make similar contributions towards something. It implies that there shouldn't be discrimination on the grounds of differences in personal background, type of work, etc. Vertical equity implies that groups with a greater ability to pay should pay proportionally more. In this sense vertical equity is concerned with the redistribution of resources within society. Both types of equity are important in the case of pharmaceuticals. The most obvious justification for differential pricing of pharmaceuticals is founded in principles of vertical equity: people should be charged drug prices commensurate with their relative income. But the issue of relative contribution to global pharmaceutical R&D is a matter of horizontal equity: countries with similar income should make similar contributions to the common good that is pharmaceutical research. The question of the fairness of pharmaceutical prices being higher in the US than in other countries can be viewed in this framework. High US prices are not a result of prices being lower elsewhere; rather they are the prices that the US market will bear. So whilst overall pharmaceutical prices in the US may be higher than elsewhere, this shouldn't be viewed as being unfair in that US preferences are responsible for these price

levels. The amount of R&D made possible through high US prices should therefore be seen as a reflection of what is "fair or better" according the US's own view (a concept in line with Baumol's notion of "superfairness" (Baumol 1980).

Technical challenges in Medicine Price Comparison

Understanding the differences between medicine prices across countries can be important on several levels. For example, national (or even local) health and pricing strategies may need to be aware of the relative prices of medicines sold in a neighbouring country to better predict or prevent patient migration. National authorities may be interested in understanding relative differences to better manage parallel imports and their impact on local availability. Payors are interested in relative prices in order to leverage price negotiations with manufacturers, rebates, discounts, refunds, etc. Patients, especially those living near national borders, are interested in relative prices to inform their choice of where to seek care. The public and civil society organizations are interested in understanding the difference in medicine prices internationally to understand and indeed better fight for fairness in pricing and access to medicines. Indeed international medicine prices are a major issue across civil society and in geopolitics. (See Appendix 5 for an exploration of how these differing desires might be reflected in how the price comparisons are undertaken.)

When comparing prices across goods there is the desire to compare those of like-for-like products to achieve a meaningful comparison. In this sense price comparisons should have a sample that is defined according to clear criteria for matching medicines across countries and a common unit for measuring both price and volume. In reality however, the immense diversity in available medicines makes defining a sample for comparison challenging. Even within a single country, a given pharmaceuticals can be available with a variety of names reflecting significant variation in licensing status and marketing strategies. For example, they may have a known brand name, a generic brand name, or just a generic international non-proprietary name. Also, the same molecule may be used in many different products and be sold in a variety of different forms. For example, a given molecule may come as a traditional tablet, a slow-release tablet, a capsule, a suppository, an injection, etc. Often the different forms are launched by the same manufacturer but this is not always the case. Also, with respect to their prices, the different technology used to produce the different forms as well as the marketing strategies behind their sales can create significant variation in price amongst products with the same molecule. Further, within a single country medicine price can also vary by batch, which

is in turn affected by the scale of purchasing, pharmaceutical policies, and sales sector (e.g. retail, hospital, prescription, over-the-counter).

When price comparisons are done across countries, further complications are imposed. The comparison of medicine prices across national borders (or across sub-national areas of differing regulatory jurisdiction) is in some ways just like for other goods. However, given the enormous diversity in products on the market, indirect nature of purchases, and the rapid pace of technological progress in medicine, comparison can be more complex. Indeed medically-used molecules sold throughout the world come in a plethora of different names, product type, levels of patent protection and license status, therapeutic purpose, packaging, formulations/ combinations, and strengths. This can make comparisons using even the most sophisticated and specially-designed software very challenging. For example, products are launched at different times from country to country, thereby leading to often very different measures of time-on-market (sometimes used as measure of age) which has been found to have implications for price. The level of intellectual property protection accorded to a medicine also varies from country to country and may have important implications for price. In addition, variation in societal preferences has led to different products and strengths being dispensed as well as to different approaches to dispensing (e.g. pack-splitting) which also impact unit price and can make standardization difficult. Currency conversion poses further challenges for international price comparison. Whilst exchange rates are a common method of converting from one currency to another, as they are affected by often volatile financial market conditions, they too can fluctuate significantly. Purchasing power parities are meant to smooth out fluctuations in exchange rates since they are independent of financial market conditions, however, they are not actual transaction prices.

Given this immense diversity in product mix both within and across countries, standardization across samples imposes poses significant challenges. Whilst standard physical units such as grams, kilograms, litres, tablets, etc. as well as packs and prescriptions are common ways to measure volume of medicines, these units are only useful if the medicines being studied are uniform. Comparison involving drugs with even slightly different characteristics requires other units for standardization. If volume is standardized in terms of grams of active ingredient, drugs with low potency will comprise a larger fraction of the total than drugs with higher potency. The use of tablets as the unit of standardized measurement also presents problems due to their differing strengths. The price per pill or "standard unit" is often used but leads to

bias if the relation between unit price and volume is non-linear because of economies of scale in packaging or high-volume discounts.

In sum, medicine price comparison is a complicated process and implies numerous trade-offs. The more narrowly the sample is defined to ensure similarity of products, the more the sample is restricted and thus less representative of the country's medicine market as a whole. Also, the greater the number of countries included in the comparison, the more difficult it is to match identical products—thus decreasing the size of the comparison sample and further diminishing the representativeness of the sample. Given the inherent differences in and between drug markets, there is no single ideal measure of price differences. However, whilst none are perfect, certain methods are more appropriate than others. The methods chosen for the studies presented here purposefully tackle medicine price comparison from multiple angles in order to mitigate these problems and provide robust estimates for relative differences across as many products and countries as possible.

LACK OF AVAILABLE COMPARATIVE PHARMACEUTICAL PRICE DATA

Whilst some data can be laboriously extracted from reimbursement tables and National Formularies there are very few sources of data on drug prices (Mossialos and Mrazek 2003). Generally governments do not provide detailed price data to external researchers (Mossialos and Mrazek 2003). In the European Community an attempt was made in 1988 to compile drug price and reimbursement rates (along with other product information) across Member States. However, as explained by Mrazek and Mossialos (2003), the initiative ultimately proved too ambitious and by 2001 plans for the database were abandoned. The best available data for research are those tabulated by commercial organizations who do many (opaque) adjustments to the data in an attempt to make it more complete, representative of the whole market, and generally more standardized. For example, much of IMS data is disseminated as retail or hospital level data but in fact it is measured at another level of the distribution process and marked up or down based on numerous assumptions (see Appendix 1 for list of assumed price evolution from manufacturer to patient). Prices are often expressed as ex-manufacturer prices but taken to reflect retail price movements. The retail price of prescribed drugs normally includes a dispensing fee and some prescriptions include both a mark-up and a dispensing fee (CIHI 2001). The complexity in real transaction does put into doubt the validity of prices when such broad brush standardization practices are used.

A handful of countries have extensive experience in gathering drug prices and constructing drug price indices. For example, Statistics Canada tracks drug prices charged by manufacturers using a drug component of the Industrial Products Price Index. Canada's Patented Medicines Price Review Board also follows manufacturer price increases, but in this case only for patented drugs. The Canadian CPI health component includes sub-components for drugs. However, even in this context it is questioned how well the price changes are captured given that there are only a limited number of drugs included (listed by generic name) and that in some cases treatment patterns change very quickly (CIHI 2001). In sum, short of conducting one's own surveys, IMS data (the data used in the papers making up this dissertation) for comparing drug prices cross-nationally is not perfect but it is the best data we have.

PRICE INDICES AND THEIR USE IN POLICY MAKING

The difficult problem of comparing prices over time or across countries is an old one in economic theory. The major underlying difficulty is that not only the prices of individual goods or services vary over time or across countries, but the volumes consumed of those goods and services vary as well. These simultaneous variations in prices and volumes make the definition of a single measure of average price extremely difficult and has given birth to an extensive literature on index number theory.

Indices allow us to take vast amounts of price and sales volume information stemming from a large number of products, and summarize that information into a very small set of numbers. A price index is a measure of proportionate, or percentage, change in a set of prices over time (temporal indices) or across places, e.g. countries at a given point in time (spatial indices). In this dissertation, I make use of both temporal (in this case yearly) and spatial indices. However, the use of spatial indices is relatively new compared to that of temporal indices, which have been the topic of an extensive literature. Most of the succinct review of index theory that follows is thus largely based on the temporal index literature, although it applies equally to spatial indices, *mutatis mutandis*.

An Italian, G. R. Carli, is credited with developing the first index numbers in 1764, as part of a report on price fluctuations in Europe observed between 1500 and 1750. One of the first known uses of a price index, dating back to the 1780, was commissioned by a government agency in order to adjust the pay of soldiers just after the American Revolution, as the war had shifted prices of basic goods substantially (IMF 2010). The first industrial commodities index in the US was later produced in 1902, developed in response to a U.S. Senate Finance

Committee request for an investigation into the effects of tariff laws on prices of domestic and foreign agricultural and manufactured products. The index used an unweighted average of price relatives for 250 commodities.

It took until the beginning of the 20th Century for the collection and reporting of data in index form to become systematic (McGraw Hill 2004). In the 1920s several important developments occurred in index number theory, the most influential of which was the publication of Irving Fisher's monumental work, "The Making of Index Numbers" in 1922. This work was initially prompted by Fisher's interest in inflation and advocacy of the Quantity Theory of Money, in which changes in the money supply could be used to lead to corresponding changes in the price level. The work required a dependable measure of changes in the price level—in other words, it needed a good price index—leading Fisher to undertake a systematic investigation of the properties of hundreds of different kinds of possible formulas for price indices. (IMF 2010) The Consumer Price Index (CPI), the most widely known index today, was introduced in 1913 and since then many other indices have been compiled. The systematic collection of price information as products left factories began in the 1970s when Eurostat, the Statistical Office of the European Union (EU), began a programme to build producer price indices (PPIs), intended to measure the change in prices producers receive at the factory gate (IMF 2010). More recently the collection of PPI data has extended to service industries, which in many countries account for almost two-thirds of GDP (IMF 2010). Today, as emphasized by Diewert, the ability of indices to make sense of the overwhelming abundance of microeconomic information allows them to "intrude themselves on virtually every empirical investigation in economics" (Diewert 1993).

The calculation of price indices is very closely linked to policy-making. The best known index, the CPI, measures changes in the prices of goods and services that households consume over time, usually within a country. Price changes captured in a CPI affect the real purchasing power of consumers' incomes and their welfare. There is now a long history of using CPIs to guide the evolution of public payments – a practice known as index linking. Generally speaking, index linking means that payments are adjusted in proportion to the change in some specified price index (often the CPI), in order to maintain the real purchasing power of wages over the kinds of goods and services typically consumed by wage earners (IMF 2010). For example, numerous government payments are linked to indices to ensure their "appropriate"

increase or decrease over time. In many countries pensions and unemployment payments are linked to the CPI[7].

Whilst less obvious to the public because they influence on the lives of individuals only indirectly, macro-economic indices play an increasingly important role in geopolitics. For example, high-level aggregations of manufacturing goods are useful for observing and comparing macroeconomic trends, which can, amongst other things, help identify the effect of government intervention (IMF 2010). Aggregations of commodity prices can also be undertaken in order to explore the total impact of commodity price change on the economy (IMF 2010). Analysis of aggregate prices by commodity can reveal the impact of inflationary pressure from raw materials, an issue of global relevance as those materials are often priced on international markets and therefore outside the control of national-level agencies. In view of the central role of energy in modern economies, the price index of crude oil plays a particularly important role in national and international economic analysis and planning (IMF 2010) Productivity measures such as the PPI can be used to deflate the nominal value added of a given industry into a real value added. Industry measures of real value added can then be divided by labour input into the industry in order to estimate industry-specific labour productivity. Alternatively, the real value added in a given industry can be divided by an index of primary input usage in order to estimate industry total factor productivity (IMF 2010) Productivity increases are seen as a key driver of standard of living increases within a country and there is therefore an interest in identifying the industries that lead productivity improvements (IMF 2010)

Internationally index calculation measures have been, and continue to be, developed to allow for comparable data to be collected and published by international agencies such as (the statistical offices of) the United Nations, the International Labour Organization, the International Monetary Fund, or the Organization of Economic Cooperation and

[7] The CPI is often described as a cost-of-living index, however, technically this is inaccurate. A true cost-of-living index would measure changes in the cost of attaining a fixed level of economic well-being, or utility, whilst a CPI estimates the change in cost of obtaining a fixed basket of goods. The idea of a cost-of-living index (arguably impossible to accurately calculate) is a standard against which economists gauge biases in the CPI (Moulton 1998).

Development. However, despite efforts for standard-creation and adoption, variation does persist in data collection and aggregation practices. So whilst national statistics agencies supply the data to the international agencies, their subsequent publication by the international agencies is not—and should not be interpreted as—an endorsement of their reliability (IMF 2010).

Beyond allowing for the comparison of data amongst countries, international standards for index calculation are used by many countries as the norms for their own individual statistics (IMF 2010). Domestic pressure to avoid errors or biases (see below) led to a significant push to improve index calculation methods in the 1990s. Much of the current literature on price indices stems from the work of the International Working Group on Price Indices, established under the auspices of the UN Statistical Commission in 1994. This body of experts, known as the "Ottawa Group" is made up of public servants responsible for national statistics offices and leading academics, and meets every other year. Today research on index calculation methods continues on, primarily from the economic as well as the statistical perspective (e.g. in terms of sampling of goods).

FOCUS ON PRICE INDEX THEORY IN THE POLITICAL REALM

Price index theory is usually left to specialists. It is only when a suspicion arises that something is wrong and that there is a possibility of large political or fiscal benefits from fixing it, that the topic moves into the limelight (Deaton 1998). Much of the present day interest in inflation calculation dates back to the 1990s when details of CPI calculation methods in the United States went from being an academic issue to one of public concern. At that time, an influential part of the population, largely dominated the highly educated and highly informed group, feared that public payments would be adjusted downward, following the revelation of previous miscalculation of, or strong bias inherent in, the CPI. The potential consequences of adjusting for the bias were vast as much of the US economy is based on the CPI. An example of the potential effect of bias in the CPI given by Moulton (1998) considers that an annual upward bias of 0.7% (the lowest estimate of the CPI Advisory Commission) over 25 years would lead to the growth of real wages and other quantities deflated by the CPI to be understated by 19%. Using the upper estimate of the Commission of 2% would lead to the same quantities being understated by 64%. Our assessment of the growth of our economy and people's well-being is therefore substantially affected by index calculation methods and their biases (Moulton 1998).

American economists had noted for several decades that the CPI may have been overestimating the increase in the cost of living. However, the bias only became a newsworthy topic when the issue got tied up in the debate over the balancing of the budget, with Greenspan mentioning in 1995 that the overestimation of 1-1.5% was the equivalent to an overpaying of $55 billion over five years in federal programmes (Moulton 1998). This bias in the CPI was arguably the critical event that brought the issue of index calculation to the forefront of the political realm.

OPTIMIZING INDEX NUMBER CALCULATIONS TO SUPPORT POLICY-MAKING

How microeconomic information can be aggregated to quantify overall price differences is the "index number problem," a classic and long-standing problem in economics, which is the subject of an extensive literature (see for example Fisher 1922; Samuelson and Swamy 1974; Afriat 1978; and Diewert 1978). The choice of a particular method to calculate an index number can be optimized for a particular purpose. Even if such optimization takes place behind the scenes, there is increasing awareness that for such calculations to be justifiable and as robust as possible a number of key issues must be addressed.

The calculation of a price index is necessarily based on basic choices, including the following (ILO 2004):

1. which goods (and/or services) to include in the sample
2. how to determine item prices
3. which transactions that involve these goods should be included
4. how to determine the weights and from which sources they should be drawn
5. what formula or type of mean should be used to average the relative prices within the sample

Except for the last one, all these questions can be answered on the basis of the purpose of the index to be calculated. The aggregate value, V, for a given collection of items and transactions is computed as (ILO 2004):

$$V = \sum_{i=1}^{n} p_i q_i$$

where p_i is the price of the i^{th} good in national currency units, q_i represents the corresponding quantity purchased in the relevant time period and the subscript i identifies the i^{th} elementary item in the group of n items that make up the chosen value aggregate V. Within this aggregate definition is the specification of which items and transactions to include, as well as principles of the valuation and timeframe within which economic agents undertake the transactions, or the determination of prices. The choice of parameters p_i and q_i is therefore all dependent on the definition of the aggregate value being calculated whilst the choice of formula used to calculate a price index from V is not (ILO 2004).

APPROACHES TO THE OPTIMIZING THE CHOICE OF INDEX

> "The answer to the question what is the mean of a given set of magnitudes cannot in general be found, unless there is given also the object for the sake of which a mean value
>
> is required. There are as many kinds of average as there are purposes; and we may almost say in the matter of prices as many purposes as writers. Hence much vain controversy between persons who are literally at cross purposes". [Edgeworth (1888, p. 347)].

The two main approaches to determining the optimal formula for a price index are: i) the test, or axiomatic, approach, and ii) the economic approach. The test approach assumes that vectors of prices and quantities are regarded as independent variables, whilst in the economic approach the two price vectors are taken as independent but the quantity variables are seen as solutions to a variety of economic maximization or minimization problems (Diewert 2010). Whilst experts do tend to take either an axiomatic or economic perspective on index numbers, the approaches should not be perceived as mutually exclusive.

AXIOMATIC APPROACH

The axiomatic, or test, approach seeks to choose the most appropriate formula for an index based on the number of tests that the index satisfies. Examples of important axioms include the following (summarized here by IMF 2010)

- Positivity Test: The price index and its constituent vectors of prices and quantities should be positive.

• Identity Test: If the price of every product is identical in both periods, then the price index should equal unity, irrespective of what the quantity vectors are.

• Commensurability Test: The price index does not change if the units in which the products are measured are changed (invariance to changes in the units of measurement).

• Time (or country) Reversal Test: If all the data for the two periods (or countries) are interchanged, then the resulting price index should equal the reciprocal of the original price index.,

• Quantity Reversal Test: If the quantity vectors for the two periods are interchanged, then the price index remains invariant.

• Mean Value Test for Prices: The value of the price index lies between the highest and the lowest ratio of prices for all products.

• Paasche and Laspeyres Bounding Test: The price index lies between the Laspeyres and Paasche indices. Paasche (Pc) and Laspeyres (Lc) indices are described here:

$$\mathrm{P}_C = \frac{\Sigma(Q_{M,C})(P_{M,C})}{\Sigma(Q_{M,C})(P_{M,USA})}$$

Where $Q_{M,USA}$ is the quantity weight (volume) of the pharmaceutical sold in the USA, and $P_{M,C}$ *and* $P_{M,USA}$ are the prices of the pharmaceutical per standard unit in the comparator country and in the USA (the base country), respectively. Such weighting is often referred to as "own-weighting".

$$\mathrm{L}_C = \frac{\Sigma(Q_{M,USA})(P_{M,C})}{\Sigma(Q_{M,USA})(P_{M,USA})}$$

Where $Q_{M,C}$ is the quantity weight of the pharmaceutical sold in the comparator country, and $P_{M,C}$ and $P_{M,USA}$ are the prices of the pharmaceutical per standard unit in the comparator country and in the USA (the base country), respectively. Such weighting is often referred to as "base-weighting".

Some axioms are more important than others and, most index numbers satisfy several of them, including the most obvious ones For example, the commensurability test implies that

if milk were to be measured in litres instead of pints, the index should clearly remain unchanged. (IMF 2010) But even such obvious axiom does not always hold. For example, the Dutot index, defined as the ratio of the mean of unweighted individual prices at time t and time 0:

$$I_D^{0:t} = \frac{\frac{1}{n}\sum p_i^t}{\frac{1}{n}\sum p_i^0}$$

which was widely used in the initial stages of producer price index calculations, does not satisfy the commensurability test. The IMF PPI calculation manual (2010) uses the example of salt and pepper to illustrate the problem: Suppose the unit of measurement for pepper is changed from ounces to grams whilst that for salt remains unchanged (in either ounces or kilograms). Given that an ounce is equivalent to 28.35 grams, the absolute value of the price of pepper decreases by more than 28 times, whilst that of salt is unchanged. As a result, the weight of pepper in the calculation of the Dutot index decreases by more than 28 times compared to that of salt. Basically, when the products covered collectively by an index are heterogeneous and measured with different physical units the value of any index that does not satisfy the commensurability test depends on the arbitrary choice of units -- making the index conceptually unacceptable. (IMF 2010) A useful price index must necessarily include some weighting of the prices of individual products that quantifies in some way their quality attributes. And these attributes reflect necessarily the preferences of, or the values to, the consumers, which are linked to the units of measurement (e.g., caviar vs. potatoes). Thus, upon aggregation, the price variations per physical unit of the higher-priced varieties (e.g. the price of pepper or caviar per gram) must be appropriately tempered in the index calculation (IMF 2010). When prices are weighted by consumption, the problem of units effectively disappears.

The widely used Laspeyres and Paasche indices given above fail both the quantity reversal test and the time (country) reversal test. Obviously, inverting the quantity vectors in the formula of the Laspeyres index gives the corresponding Paasche index, and vice versa. Reversing the time (or the country) in the formula of the Laspeyres index gives the inverse of the corresponding Paasche index; and conversely, reversing the time (or the country) in the formula of the Paasche index gives the inverse of the corresponding Laspeyres index. There is thus an underlying symmetry between the Paasche and the Laspeyres indices that makes their

geometric mean, the Fisher ideal index particularly satisfying from the point of view of the axiomatic approach. In fact the Fisher index fulfils all the axiomatic tests listed above

Overall the axiomatic approach is not without its limitations. A perhaps obvious shortcoming is that the list of axioms is itself somewhat arbitrary (IMF 2010). Furthermore, a simple application of the axiomatic approach only signals which tests are failed by the index in question, without indicating the degree to which the index fails (IMF 2010). However, the importance given to the respective tests is not uniform and whilst failing a major test such as the Commensurability Test should be enough to rule out the use of a particular index, failing several minor tests may not necessarily rule out its use.

ECONOMIC APPROACH

Aside from the axiomatic approach, candidate indices can also be analysed using another lens, such as the economic approach, which seeks to develop index number formulas based on "reasonable" models of economic behaviour between actors in the economy. In contrast to the axiomatic approach, the economic approach acknowledges that quantities purchased or produced are in fact dependent on the prices. Indeed in practice, rational consumers and producers adjust the relative quantities they consume or produce in response to changes in relative prices (this concept is discussed in Paper 2).

The economic approach assumes that the consumer has a set of well-defined preferences for different combinations of goods. Each combination of goods is perceived as a positive vector and the consumer's preferences in favour of one set of goods over another are perceived as a continuous, non-decreasing, concave utility function. The consumer is assumed to minimize the cost of achieving the utility level within the period (or country in the case of spatial indices) – thereby solving the cost minimization problem. The equivalent for producer indices is the assumption of revenue maximization (ILO 2004).

The assumption of optimizing behaviour -- cost minimization or revenue maximization -- along with other assumptions, is used to derive a theoretical index that is "true" under these conditions. The approach then examines practical index number formulas such as Laspeyres, Fisher, Törnqvist, etc. to consider how they compare with "true" formulas defined under differing assumptions. Diewert used the term "exact" for indices that can be derived from an underlying utility, cost, production, revenue, transformation or profit functions (Diewert 1976).

Consumer Price Indices draw on the economic theory of consumer behaviour whilst Producer Price Indices draw on the economic theory of production (and the short-term rigidities in the production process). However, these two underlying economic theories are isomorphic and lead to similar conclusions regarding index number compilation (IMF 2010).

SUPERLATIVE INDICES

> "In mathematics disputes must soon come to an end, when the one side is proved and the other disproved. And where mathematics enters into economics, it would seem that little room could be left for long-continued disputation. It is therefore somewhat surprising that one economist after another takes up the subject of index-numbers, potters over it for a whilst, differs from the rest if he can, and then drops it. And so nearly sixty years have gone by since Jevons first brought mathematics to bear upon this question, and still economists are at loggerheads over it. Yet index-numbers involve the use of means and averages, and these being a purely mathematical element, demonstration ought soon to be reached, and then agreement should speedily follow." Walsh [1921; preface, as quoted in Diewert 2010]

Despite the vast number of possible index number formulas developed over the past two centuries, each with their champions, in practice the choice of index number formula has narrowed to only a very small class of indices. In some ways this confirms the prediction made in the Walsh (1921) quote above. Whilst historically important indices such as the Laspeyres and the Paasche indices are still widely in use, economists favour the use of a few indices with particularly useful properties according to both the axiomatic and the economic approach: the Fisher ideal index, the Persons-Törnqvist index, and the Walsh index. These indices are known as superlative indices (Diewert 2010).and they have been shown to closely approximate an exact cost-of-living index for any utility function (Moulton 1998).

$$Fisher = \sqrt{P * L}$$

Where P is the Paasche index value and L is the Laspeyres index value. (Fisher indices are the geometric mean of Paasche and Laspeyres Indices.)

$$\textit{Törnqvist} \quad = \prod_{i=1}^{n} \left(\frac{p_{it}}{p_{i0}} \right)^{\frac{1}{2}\left[\frac{p_{i0}\, q_{i0}}{\sum_{i=1}^{m} (p_{i0} q_{i0})} + \frac{p_{it}\, q_{it}}{\sum_{i=1}^{m} (p_{it} q_{it})} \right]}$$

which is effectively the geometric average of the n price relatives (current to base year) for n goods weighted by the arithmetic average of the volumes for the respective periods.

$$\textit{Walsh} \quad = \frac{\sum \left(p_t \cdot \sqrt{q_0 \cdot q_t} \right)}{\sum \left(p_0 \cdot \sqrt{q_0 \cdot q_t} \right)}$$

which is the weighted sum of the current period prices divided by the weighted sum of the base period prices with the geometric average of both period volumes serving as weights.

A characteristic feature of superlative indices is that they treat the prices and quantities in both periods or countries being compared symmetrically (see section below for further discussion of the importance of this symmetry). Further, superlative indices tend to provide very similar results and perform overall in very similar ways. (IMF 2010) The superlative index often perceived as the "best" is the Fisher index (IMF 2010). In practice, when other indices are chosen it is due to a lack of price or volume data. For example, the use of Laspeyres or Paasche indices only requires volume data from one time period or country whilst superlative indices require volume data for each time period or country in the comparison.

JUSTIFICATION FOR THE TYPES OF INDICES UTILIZED IN THIS DISSERTATION

As emphasized 40 years ago by Samuelson and Swamy (1974), given heterogeneity in preferences, we cannot hope for one ideal formula for the index number. Explicit choices have to be made. For spatial indices the natural choice is to utilize the volume weights (a reflection of preferences via consumption) determined by the preferences of one country or the other – the equivalent of fixed basket indices from the temporal price index counterpart. A common choice for such indices are the Paasche and Laspeyres indices, the former utilizing own-country weights (determined by the preferences of the country in question) and the latter utilizing base-country weights (the US is very often taken as the base country for international comparisons). Laspeyres indices are the most common type encountered, due largely to their more limited data requirements, as mentioned above. In the context of spatial comparisons this means that they only require volume data for the base country. Paasche indices, for their

part, require volume data of only the comparator country. Beyond mere data practicalities and resource minimization, some of their attributes make Laspeyres and Paasche indices clear contenders for answering some policy questions. For example the single country dominance (the fact that the index is constructed solely on the consumption patterns of one country) that is embodied within these two indices has benefits to address particular questions. For example, Laspeyres indices are arguably highly relevant for policy questions relating to the base country given that they are based on the consumption patterns of that country. However, in the application of Laspeyres and Paasche indices to inform policy requires attention to their methods of construction as noted by Danzon (Danzon and Chao 2000). For example, taking the view of the US as the base country, Danzon describes Laspeyres indices as lower-bound estimates of how much the US could potentially save if it were to adopt a comparator country's pharmaceutical prices, assuming constant US consumption patterns over time. Conversely, Paasche indices, for their part, provide an upper-bound estimate of potential savings, if US consumers were to adopt the comparator country's consumption patterns, assuming that such changes in US consumption volumes do not affect prices. Therefore, Laspeyres indices could be informative if the US were to be evaluating the potential use of price regulations or other, perhaps indirect, price-influencing policies utilized by other countries. In contrast the Paasche indices would be unlikely to be of great use in a US policy context, as the assumption of US consumers exhibiting comparator country preferences is arguably too far-fetched, due, in part, to the cultural origin of preferences.

In other words, the choice of a single country to base indices makes it difficult to dissociate indices from the country-specific context and draw broad conclusions about price differences across countries. In essence, price relatives are inextricably linked to their country policy context. One example, also taken from the pharmaceutical policy context, to illustrate this point is the question of whether or not the rest of the world is free riding on the high levels of R&D provided by high US pharmaceutical prices. The first issue one has to examine in attempting to answer this constantly arising question is which pharmaceuticals we are talking about. US consumers often hear of new pharmaceutical technologies through direct-to-consumer advertising and there is minimal state role for product comparison or cost-effectiveness analysis. US preferences therefore favour newer technologies, arguably in a manner dissociated from real product quality or effectiveness. So if the question of free riding is posed in the US policy context, then the answer should arguably be based on price relatives of a sample made up of pharmaceutical products purchased by Americans, therefore reflecting

the preference for newer pharmaceuticals. But European preferences may be different for cultural or other reasons such as: public payor reimbursement (based on health technology assessment or some form of cost-effectiveness analysis); prohibition of direct-to-consumer pharmaceutical advertising; limited advertising to prescribers; etc. If, as a result, Europeans tend to prefer more thoroughly proven (and often cheaper) pharmaceuticals then is it fair to ignore their preferences in determining their purported free riding behaviour?

Whilst useful for examining questions posed for national purposes, the index values provided by Laspeyres and Paasche indices are at once unsatisfying (in that they fail to give a concrete answer regarding cross-national price relativity) and too country-bound to provide fair answers to questions posed at an international for international purposes.

The effect of using a single country consumption to base indices can perhaps be best illustrated by examining their temporal counterparts. Using the Lasypeyres index—which uses the volume measures of the base year-- tends to overestimate the rise in the cost of living by not allowing any substitution between goods (e.g. from higher to lower priced goods) to occur. Conversely, the Paasche index—which uses current year volume measures—tends to underestimate the rise in the cost of living. Diewert's work (1983) has shown that the true cost of living index (whilst not observable) is between the Paasche and Laspeyres price indexes (which are observable). The key finding of this work was that some average of the Paasche and Laspeyres indexes should provide a reasonably close approximation to the underlying true cost of living. The Fisher index, the geometric average (square root) of the Laspeyres and Paasche indexes, is a strong candidate for such an average.

Importantly, the Fisher index is a superlative index, as noted above and treats prices and quantities being compared symmetrically. As stressed by Walsh (1901) such symmetric treatment of countries is required if they are to be given equal importance in the policy question at hand. Whilst the detachment from the base country context makes Fisher indices less relevant to country-specific policy questions, it is arguably more appropriate when the goal is broad comparison of prices across countries.

Fisher indices appear to dominate other indices from an axiomatic viewpoint. For example, Fisher indices satisfy four tests that are considered "minimal": positivity, time/country reversal, quantity reversal, and factor reversal. The other two symmetric indices, the Walsh and Törnqvist indices, do not do as well in testing. (IMF 2010) The geometric averaging of the

quantities in both countries results in an equal weight to the consumption patterns of each of the countries. In addition, the use of the Fisher index, rather than the other superlative indices, can be justified on grounds of economic theory, in particular the fact that it is consistent with revealed preference theory (Diewert, 1976).

In this thesis we aim to compare pharmaceutical prices amongst several countries and over time. Whilst it is clear from the above that the Fisher index is the best choice for such comparison, the aggregation of all the individual price and volume data into a single number necessarily eliminates useful information. As noted above, no single price index can provide a "true" quantification of relative prices when customers in different countries exhibit different preferences. The use of price indices is particularly fraught in the case of pharmaceuticals, which come in presentations, dosages and compositions that vary from country to country. In addition drug prices are controlled in some way in most countries, and often not fully paid by the consumer as a result of private or national health insurance programmes.

In view of these difficulties, this study takes a pragmatic approach and makes simultaneous use of several indices that respond differently to consumption patterns and to the variations in the prices of individual products. This approach has the double benefit of circumventing the inherent impossibility to define a true price index for pharmaceuticals and of providing useful information not only from the numerical values of the various indices and their evolution over time, but also from their differences. It must also be noted that the theoretical considerations of the necessary or useful properties of price indices that have fuelled much of the discussion regarding index theory (Fisher 1922; Samuelson and Swamy 1974; Afriat 1978; and Diewert 1978) are largely irrelevant in this pragmatic multi-index approach since it does not rely on the use of a single parameter.

This thesis takes advantage of the richness of the available data on pharmaceutical prices and quantities to calculate Paasche and Laspeyres indices, in addition to Fisher indices. Further these indices are calculated for data sets that are common for all countries considered (multilaterally matched samples) and for data sets that are common to only two countries being compared (bilaterally matched samples.) Such an approach provides useful information because the Laspeyres and Fisher indices are dependent on the size of the data-base from which they are calculated as a result of their sensitivity to consumption patterns: the larger the number of samples being considered, the greater the range of differences in consumption patterns being captured.

As will be seen, in several instances the calculated values of the Laspeyres and Paasche indices exhibited large differences. This occurs sometimes for indices calculated from the same data set or for those based on multilaterally or bilaterally matched samples. Such contrasts serve as flags indicating unusual features of the pharmaceutical market in individual countries during the period of the study. In several instances, a detailed examination of the indices points to to a likely explanation in terms of differences or changes in pricing or consumption patterns amongst countries. Conversely, when the values of Laspeyres and Paasche indices are close to each other, the corresponding Fisher indices must necessarily provide a good estimation of overall price differences between two countries or between two time periods. In essence, the difference between the values of the Laspeyres and Paasche indices provides a measure of how good an estimation of price differences is given by the Fisher index,

LITERATURE REVIEW

Overview

Whilst cross-national pharmaceutical price variation is a relatively new area of study, the methodological progress made over the past two decades has been significant. Starting with studies dating back to the early 1990s, one can see an effort over time to increase accuracy, representativeness, and policy relevance. Each of the key early studies is reviewed below. Whilst the policy context is not explicit in all of the papers, it actually informs much of the previous work. The early studies in cross-country price comparison focussed on a very limited selection of pharmaceuticals found in the United States and one, or sometimes a few, other countries. The goal of such studies was seemingly largely political, focussed on highlighting the discrepancy, generally seen as unfair, between drug prices in the US and in other countries. Indeed the issue of other countries "free riding" on the pharmaceutical R&D made possible through high US prices was seemingly never far from the minds of the authors of the early studies. Not surprisingly, the results of those studies tended to support this conclusion.

Interestingly, whilst most of the early studies were conducted as part of reports intended to be used in the political setting, they were not themselves policy-related documents. The description of the work remained largely technical with little explanation regarding its motivation or how it was going to be used. Nonetheless, in many cases, the policy intent can be inferred or, at the very least, the work can be placed into a political context. In some cases

the studies appeared to miss their mark—having been seemingly designed for a given political end but falling short as a result of technical choices. The technical underpinnings of these studies and their limitations are described in the timeline below. Importantly, it is the studies by Danzon and colleagues in 1999-2000 that brought to light the key limitations of the earlier comparisons. Although there have been only a few studies published since the Danzon work, one can see in those a more balanced approach to the question of relative pharmaceutical prices amongst countries. This dissertation can be seen in part as an updating and a very large expansion (to more countries and over a longer period of time) of the work of Danzon and colleagues.

Government Accounting Office 1992

Motivated by the sudden rise in pharmaceutical prices in the US in the 1980s, the US Government Accounting Office (GAO) 1992 compared factory prices of medicines bought in retail pharmacies in the US relative to their similarly purchased counterparts in Canada. They selected one single, commonly used US dosage form, dosage strength, and package size for each of the drugs in their sample. Of the 200 drugs in their study, they were able to match 121 by brand name, manufacturer, strength, and dosage form across the two countries. Overall the authors found that a basket of the 121 frequently dispensed drugs would cost 32% more in the United States than in Canada. Looked at independently, the large majority of the 121 pharmaceuticals they studied were more expensive in the US, median price differential per package estimated at 43%. The price differentials between the two countries varied widely, the per package price to wholesalers in the US ranging from 44% lower to 967% higher than the Canadian price. Although there was a wide range, most drugs studied were found to be more expensive in the United States. The same manufacturers were found to charge US wholesalers much more than Canadian wholesalers for identical products. In selecting pharmaceuticals with a single dosage form, strength and pack size that was common in the US, the GAO sample for comparison presented significant bias. Also, US prices were compared with imputed prices from similar packs in Canada (using the Ontario formulary) and prices per pack were imputed (by multiplying the per unit price by the number of units per pack) since most of the Ontario formulary prices were per unit. As highlighted by Danzon and Kim, this linear imputation is likely to understate prices in Canada, since formulary prices tend to be based on the largest pack size, which has the lowest unit price. Further, to calculate price the authors use the unweighted sum of prices in the US relative to the sum of prices in

Canada as well as the median of price relatives. Also highlighted by Danzon and Kim, the first measure is usually not invariant to the units of measurement, which is normally a desired characteristic of index numbers (which is why it is not often used). The latter price used also poses limitations in that the median is unstable across samples.

Government Accounting Office 1994

In their 1994 report the GAO compared US prices to those in the UK. They looked at a sample of 200 drugs most frequently dispensed in U.S. drugstores and compared them to those dispensed in the UK with the same manufacturer. These 200 drugs represented 55% of all prescriptions dispensed in U.S. drugstores in 1991. They selected a single, commonly used dosage, strength and packsize in the US. Of the 200 most frequently dispensed drugs, the authors were able to match 77 drugs by brand, manufacturer, strength, and form. Of the 77 drugs compared, 66 medicines were priced higher in the US whilst 11 were priced higher in the UK. Forty-seven (61%) of the 77 medicines in the US had a price more than double that in the UK. The most commonly dispensed drug at the time, Amoxil, was found to cost 40% less in the US than in the UK. But the 2nd, 3rd, 4th, and 5th most frequently dispensed drugs in the US--Premarin, Zantac, Lanoxin, and Xanax—were found to cost 197,58, 169, and 278% more respectively in the US than in the UK. Seventeen of the 21 brand-name medicines were priced higher in the US than in the UK, whilst 17 of the lowest US generic prices were lower than the corresponding UK brand-name prices. Perhaps spurred on by methodological challenges to their 1992 report, the GAO 1994 report used the manufacturer, per unit prices to construct volume-weighted indices. However, this expenditure weighting can be seen to have been merely approximate since the weights pertained to all packs whilst the price in each country was based on a single pack. This is believed to have resulted in significant selection bias. This bias is further compounded by the focus on leading products in one single country. The perspective of the GAO reports must also be borne in mind. These studies only considered drugs that were popular on the American market.

In reality the basket of drugs used in the 3 countries they looked at differ and, where the same drug is used across them, they are used differently, in different forms and dosages (Payer, 1998). The GAO price comparison effectively poses a narrow question of how the prices of pharmaceuticals popular in the US compare with those of less commonly used medicines in other countries. As emphasized by Comanor and Schweitzer (2007), this is a different question than asking whether pharmaceuticals in general cost more in the US.

US House of Representatives 1998 study: Prescription Drug Pricing in the 1st Congressional District in Maine: An International Price Comparison

In 1998 the 1st Congressional District of a large border state (importantly bordering Canada, a country with a significantly different health and pharmaceutical policy and where residents could in theory seek care), Maine, issued a minority staff report examining the differences between pharmaceutical prices across a handful of countries. The study considered prices of ten on-patent branded products with the highest 1997 sales under the Pennsylvania Pharmaceutical Assistance Contract for the Elderly, comparing their retail prices in pharmaceuticals based in several Congressional districts to prices from four Canadian pharmacies and three Mexican pharmacies. The report concluded that US pharmaceutical prices were 72% higher than in Canada and 102% than in Mexico. Aside from the extremely limited and thus biased sample used to draw broad conclusions, the study also had numerous other limitations. For example, it did not consider the use of the generic equivalent to the ten on-patent drugs. This was despite the fact that--as previously pointed out by Danzon (2000a), generics accounted for 46% of prescriptions in the US at the time, most managed care and Medicaid programmes allow for and indeed encourage generic substitution (e.g. through reimbursement caps or charging higher patient co-payments for branded products). Payors in the other countries also allow generic substitution. Indeed this was particularly surprizing given that, as of 1996, the US the Bureau of Labor Statistics has recognized bio-equivalence of branded and generic pharmaceuticals and included them as effective equivalents in price index calculations. Price comparisons that ignore generics over-estimate the average price of drugs in countries where generics are a large part of the market and tend to be sold at relatively low prices, like the US (Danzon 2000a). In addition, the study focussed on single packs of products, thereby ignoring important multipack discounts (Danzon 2000a). Finally, it should be noted that this study uses prices that are un-weighted by volume, effectively separating price calculations from actual consumption.

Danzon and Kim 1998

Danzon and Kim used data from 1992 to compare the prices of cardiovascular drugs, including all matching products, including generics, within the category of cardiovascular drugs. They used this data to demonstrate the sensitivity of international pharmaceutical price comparisons to the choice of sample used, the volume unit of measurement, the weight given to consumption patterns, and the method of currency conversion. In the context of their

findings they also stressed the need for any international price comparison to be representative of the market, to include generics and over-the-counter pharmaceuticals, all forms, strengths and packs. This was the first study to emphasize the failure of all preceding studies to achieve broad representation by limiting their focus to pharmaceuticals with the same manufacturer, brand, dosage form, strength, and/or pack size. With respect to the limitations of their own study, the authors highlighted that their inability to estimate the value of direct rebates granted to managed care providers and government purchasers had overstated US prices.

Danzon and Chao 2000

The authors compared prices using indices of manufacturer-level outpatient pharmaceutical prices for Canada, France, Germany, Italy, Japan and the UK. Pharmaceuticals were defined by molecule name and third Anatomic Therapeutic Category (ATC 3)[8]. Prices were measured against US prices and the sample was far more representative than in previous studies, for example incorporating over-the-counter drugs that substitute for prescribed drugs. In total 171 molecules were found to be present in all seven markets. For these "global molecules" the authors computed a weighted average price per kilogram and standard unit. Prices were averages across all products, formulations, strengths and packs for each molecule. The Laspeyres indices were US volume-weighted. They found that differences for comparator country to US differences to be: Canada +2.1%; Germany +24.7%; France -32%; Italy -13%; Japan -12%, and the UK -17% which were not as great as suggested by previous studies (which used small samples of only leading branded products and unweighted averages). They also matched molecules bilaterally across each of the countries independently and the US. This resulted in a larger sample size than for the global molecules, ranging from 365 molecules in the Japan–US comparison to 438 molecules in the Germany–US comparison. Generally the price indices for the bilaterally matched molecules show slightly greater price differences between countries than the indices based on the smaller, globally-matched samples. The authors find that price differences depend to a great extent on the framing of the comparison, in particular the choice of country used to determine consumption patterns to weight prices.

In an effort to examine the determinants of prices this study also constructed a fully interacted model that allowed quality and competition parameters to differ across 7 countries. Overall

[8] Which uses the 3 to 4 digit European Pharmaceutical Market Research Association (EPhMRA) classification.

regression results suggest that cross-national price differences reflect differences in product characteristics and in their implicit prices, which are a reflection of the regulatory regime in place. They conclude that strict price regulation systematically lowers prices for widely diffused molecules as well as for older ones and that generic competition lowers prices in less-regulated regimes.

Cabrales and Jimenez-Martin 2008

Cabrales and Jiménez-Martín looked at prices from 25 largely high-income countries from 1998-2003 to conduct multilevel regression analyses. Findings from the first stage country-specific regressions included the following:

> Market share of national products and concentration of local products had little effect on prices
>
> New products received a small premium in several countries, the largest being observed in the US. Product nationality does not command significant premium change for novel products with two exceptional cases (Italy, where new products from exclusively local producers receive an extra premium; Canada, where new product from local multinationals also receive a substantial premium)
>
> The effect of firm size on prices is either non-significant or negative but small (*ceteris paribus*), the largest effects being found in Denmark and the US.
>
> The number of generics in the molecule significantly reduces prices in many countries, the effect being greater in the case of Italy and Japan. (For the US the effect of the number of generics was found to be insignificant.)
>
> With the notable exceptions of Spain, US, and Germany, global prices were found to have very little independent effect

Key findings from second stage country-specific regressions included the following:

> Products from exclusively local corporations had lower prices in almost all countries (*ceteris peribus*). It was suggest that, in many cases, this may be at least partially due to the fact that they were perceived to be of lower quality. The effect of being a local multinational company was less clear. Multinational conglomerates seemed to receive a premium over small, local producers.

The single molecule effect was either non-significant or positive, especially in big pharmaceutical markets (notably Canada, Germany, Italy, Netherlands, Spain, Sweden, UK and the US), with the exception of Poland

Molecule diffusion positively affected prices in a large number of countries (Austria, Belgium, Brazil, Canada, Czech Rep., Egypt, France, Germany, Greece, Hungary, Japan, Poland, Portugal, Spain, Sweden, UK and the US)

n.b. The critique of this paper was limited by the lack of information regarding price calculation and model composition. (The paper was found within the grey literature. It was never formally published and the author did not provide any other information other than to say that the paper was never published.)

Department of Health 2006 (replicated in Office of Fair Trade 2007)

The DH compared manufacturer-level prices for branded medicines in the UK to those found in other European countries[9] and the US for the years 1999 to 2005. The study compares prices of the molecules comprising the top 150 branded products (matching across form and strength). It used all brands under which the product was sold. The DH sample included 211 brands, some with small sales volumes. Comparisons were conducted multilaterally using molecules matched across all countries as well as bilaterally using molecules matched across just the UK and the comparator country. In its multilateral comparison, the DH found prices consistently highest in the US. It also found that prior to 2005, UK prices were consistently higher than those in all European countries with the exception of Germany, in some cases substantially higher. However, with the 7% price cut in 2005 there was realignment, leading to the UK prices becoming the fourth highest amongst the ten European countries assessed, behind Germany, Finland and Ireland. However, as the DH study does not include post-2005 price, it is not possible to determine the long-term effect of the price cut on ranking. In its bilateral comparisons the DH found UK prices to be significantly lower than those in the US and higher than those in the other European countries except Germany and Ireland, where prices were found to be broadly similar. The relative ranking for UK and Ireland, however, was found to be sensitive to the exchange rate used. The DH price comparison has several

[9] European countries included were France, Italy, Germany, Netherlands, Spain, UK, Austria, Belgium, Finland, Ireland

limitations. First, price calculations do not take into account rebates which can be significant in some countries and thereby may overstate prices for countries in which rebates are a common method of overall price control. Also, in terms of its contribution to the understanding of relative average therapy prices, this study presents a serious drawback in its exclusion of generic drugs. Excluding generics leads to a systematic bias within the comparison as generics are almost always less expensive than their branded counterparts. Given that generics account for over one-third of prescription sales in some countries and an even larger proportion of overall medicines sales, this is a significant omission (as often stressed by Danzon and colleagues).

Anderson, Shea, Hussey, Keyhani and Zephyrin 2004

In a 2004 study commissioned by Health Affairs, Anderson and colleagues homed in on 30 leading drugs (in terms of highest total spending in US), comparing prices with Canada, UK and France. Their findings suggested greater discrepancies between US and foreign prices than those found by Danzon and Furukawa, a difference explained as possibly due to methodological differences (the main one being the focus on 30 leading products rather than across all drugs). Another reason was that the others used more recent data (2003 versus 1999) and that US prices had seen a more rapid increasing in the period 1999-2003 than in other countries. The authors find that compared to US prices, prices in Canada were 52% lower, 59% lower in France, and 47% lower in the UK. After incorporating US discounts prices were found to be 40% lower in Canada, 48% lower in France, and 34% lower in the UK. The differences between US prices and foreign prices measured in Anderson et al. are greater than those reported by the most comparable Danzon studies. However, it should be noted that in limiting the sample to 30 leading drugs, the Anderson study sought to answer a specific question that was posed: "..whether the adoption of some mechanism of to control pharmaceutical spending such as price controls would allow for the elimination of the 'doughnut hole'" in the Medicare drug benefit program. It thus explicitly chose a more standardized approach to medicine price comparison over the representative approach utilized by Danzon and colleagues (Anderson et al. 2004).

Background on the donut hole: Medicare beneficiaries pay $35 per month for prescription drug coverage that covers 75% of prescription drug expenses up to $2,250. There is then a gap in coverage from $2,250 to $5,100 (the "doughnut hole"). Above $5,100 coverage resumes with Medicare paying 95% of a beneficiary's prescription drug expenses. The

resulting gap originated from a desire to hold Medicare drug spending below a previously agreed target of $400 billion over a ten-year period and it was seen as a middle option intended to encourage people with small drug bills to enrol whilst also protecting people with really large drug expenses. The Anderson study concluded that indeed if the US were to impose price regulations that bring prices of leading pharmaceuticals (the 30 drugs that together represented 30% of US sales) in line with other rich countries (specifically if it could reach the benchmark of 3 other countries combined: Canada, France and UK) that the "donut hole" or coverage gap in prescription drug benefit of the Medicare programme could be filled and keep overall Medicare drug spending within the limits previously set by Congress. However, the authors also seemed convinced that the price controls considered would have knock-on effects on the level of R&D undertaken.

Schustereder and Jutting 2008

The 2008 study by Schustereder and Jutting looked at how the trade related intellectual property rights (TRIPS) impacted drug prices in seven middle income countries. They summarize "TRIPS and Public Health" as divided into two different camps: Those (generally civil society and non-governmental organisations) who argue that the big research-based pharmaceutical companies unfairly use trade-related intellectual property rights to charge higher prices for their products under patent (Baker, 2007; MSF, 2001; Myhr, 2000; Oxfam, 2002), thereby imposing a major barrier to accessing essential medicines. Major pharmaceutical companies and other proponents of TRIPS retort that a global respect for pharmaceutical patents is the essential precondition for drug developers to take on research and development at all (Bale, 2000). This group stresses that TRIPS do not actually have a major impact on local medicine prices in contrast to many country- specific factors such as tariffs, non-tariff barriers, taxes, and excessive wholesale and retail mark-ups. Mark-ups indeed are argued by many to have the biggest influence on local prices and thus accessibility (Bale, 2001; Bate et al., 2005; Bate et al., 2006; Levison, 2003). The authors use these arguments as background to examine the potential impact of TRIPS on the price of essential medicines in middle-income countries. The study focuses on the prices of drugs to treat HIV/AIDS and malaria across seven countries, including Morocco, Tunisia, South Africa, Jordan, Philippines, Thailand, and Malaysia. Using econometric analysis, complemented by exploratory methods the authors concluded that, thus far, the introduction of TRIPS had made no major impact on

the development of drug prices. Excessive procurement and marketing costs appeared to be more important determinants for observed high drug price levels.

Kanavos and Vandoros 2011

In their 2011 study Kanavos and Vandoros looked that the determinants of prices of 50 originator, prescription-only pharmaceuticals across 15 OECD countries[10] in the first quarter of 2004 and the irst quarter of 2007 respectively (32 of the products being common across the two years analysed). The study calculates volume-weighted prices for the retail sector and for those paid by insurers and looks at the influence of product-specific properties such as launch date and patent status as well as market dynamics and the regulatory context in which the products diffuse. Results suggest that prices are significantly different between the US and major European markets when ex-factory prices are compared but that these differences narrow down significantly when public prices are compared across countries. Public price differences between the US and European countries are found to be much greater for off-patent originator brand than for those that are still on-patent. Key findings highlight the importance of distribution fees and taxes as key contributors to public prices of prescription branded pharmaceuticals.

[10] Including the US, Japan, France, Germany, Italy, Spain, United Kingdom, Australia, Mexico, Austria, Portugal, Sweden, Greece, Slovakia and Belgium.

PAPER 1

THE LEVEL OF INCOME APPEARS TO HAVE NO CONSISTENT BEARING ON PHARMACEUTICAL PRICES ACROSS COUNTRIES

(This paper has been included in its published format as it was clear that this version was far more aesthetic and readable than any version the Candidate herself could produce.)

By Chantal M. Morel, Alistair McGuire, and Elias Mossialos

The Level Of Income Appears To Have No Consistent Bearing On Pharmaceutical Prices Across Countries

ABSTRACT **A generally accepted view is that it is more efficient and ethical if global pharmaceutical prices vary according to countries' relative income. To understand manufacturers' pricing strategies, we compared average pharmaceutical prices in fourteen middle-income countries to those in three high-income countries and a low-income region in western Africa from 1999 through 2008. We found that some middle-income countries pay more for pharmaceuticals than high-income countries—for example, prices in several middle-income countries exceeded those in the United Kingdom for some years of the study period. Other middle-income countries paid less than low-income countries—for example, average prices in India were consistently below prices in western Africa. These variations suggest that we need new policies on pharmaceutical pricing to improve access to pharmaceuticals around the world.**

According to the World Bank, 70 percent of the world's population today lives in middle-income countries, including Brazil, India, and South Africa.[1] The bank defines *middle-income countries* as those with an annual per capita gross national income of US$936–US $11,455 (using the bank's 2008 calculations).[2]

The International Monetary Fund predicted in 2011 that the world's emerging and developing economies—which generally correspond to middle- and low-income countries—will collectively grow by more than 50 percent between 2011 and 2016, based on current US dollars.[3]

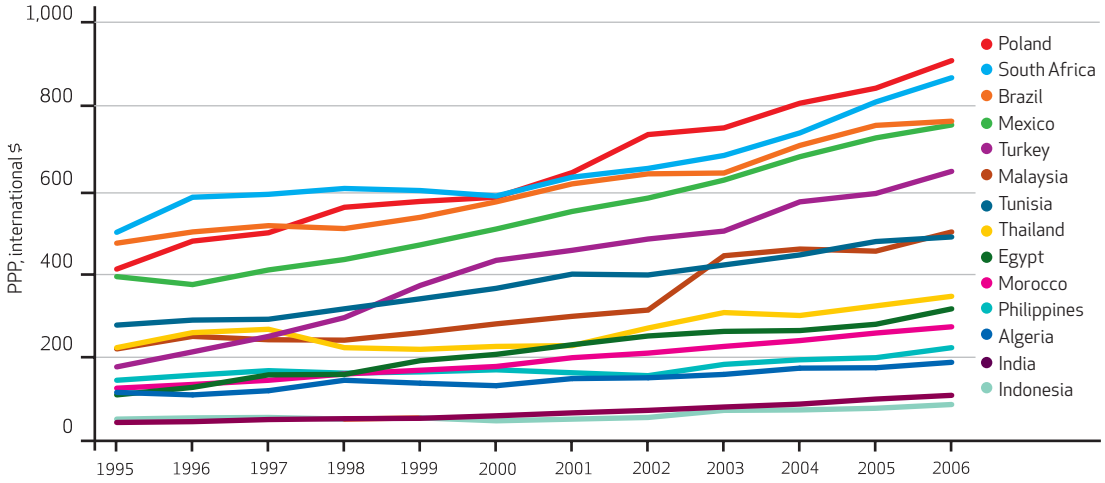
And PricewaterhouseCoopers estimated in 2011 that the recent global financial crisis had accelerated the shift in global economic power to what are known as the "emerging economies." The company estimated that the combined gross domestic product of the so-called E7 countries (Brazil, China, India, Indonesia, Mexico, Russia, and Turkey) would exceed that of the G7 countries (Canada, France, Germany, Italy, Japan, the United Kingdom, and the United States) sometime between 2018 and 2032, depending on the calculation method. By 2050 the E7 economies are predicted to be approximately 64–100 percent larger than the current G7 economies.[4]

Evidence from the fourteen middle-income countries in our study between 1995 and 2006 suggests that such economic growth will lead to increased expenditures on health care (Exhibit 1).

The World Health Organization estimated in 2004 that expenditures on pharmaceuticals between 1990 and 2000 grew by $150 billion in high-income countries, $41 billion in middle-income countries, and $4 billion in low-income countries.[5] The fastest growth in this expenditure occurred among middle-income countries. With economic growth, demand for pharmaceuticals is expected to increase greatly in middle-income countries. PricewaterhouseCoopers expects that by 2020, the E7 countries will account for 19 percent—up from 8 percent in 2004—of the global pharmaceuticals market, which is projected to have $1.3 trillion of sales in 2020.[6] According to IMS Health—a provider of market

EXHIBIT 1

Per Capita Total Expenditure On Health In Fourteen Middle-Income Countries, 1995–2006



SOURCE World Health Organization. Global Health Observatory data repository [Internet]. Geneva: WHO; [cited 2011 Jul 14]. Available from: http://apps.who.int/ghodata. **NOTES** International dollars reflect how much a local currency unit is worth within the country and provide a more valid measure to compare standards of living than exchange rates. They are calculated using purchasing power parities (PPPs), which adjust currencies according to what they can buy in the respective country markets..

information to the pharmaceutical and health care industries—the E7 countries will soon spend more than the G7 countries on pharmaceuticals.[7]

Very little is known about pharmaceutical pricing levels in many of these middle-income countries. To address this issue, we constructed price indexes that measure the relative difference in pharmaceutical prices across different countries from 1999 through the third quarter of 2008. Such indexes normalize prices across countries to account for the different mixes of pharmaceutical consumption in different markets, as the Consumer Price Index adjusts for inflation to permit direct comparisons of the real prices of consumer goods within a country over time. Our pharmaceutical price indexes allowed us to estimate the prices of pharmaceuticals in a number of middle-income countries compared to prices in high- and low-income countries.

We wanted to see if pharmaceutical prices varied in any systematic way over the ten-year study period. A finding of systematic variation would suggest the need for further investigation of, for example, the global pricing strategies pursued by the pharmaceutical industry and further analysis of any underlying factors—such as income levels—that might explain the variation.

Income is of particular interest because many experts agree that income-related differential pricing among countries would be economically most efficient—that is, it would appropriately balance short-term desires to increase social welfare with long-term desires to sustain adequate levels of research and development—yet it is not clear that income has any bearing on pharmaceutical pricing strategies. Conversely, a finding of no systematic variation would suggest that analyses of price changes in individual countries would be useful.

Study Data And Methods

OVERVIEW We analyzed pharmaceutical prices in fourteen middle-income countries: Algeria, Brazil, Egypt, India, Indonesia, Malaysia, Mexico, Morocco, the Philippines, Poland, South Africa, Thailand, Tunisia, and Turkey. We compared prices in those countries to prices in three high-income countries: France, the United Kingdom, and the United States. These three are major pharmaceutical exporters, and it is logical to assume that manufacturers in those countries develop global pricing strategies to ensure adequate returns for future research and development, among other objectives.

We also compared the middle-income countries' prices to those in French West Africa, an aggregation by IMS Health of Benin, Burkina Faso, Cameroon, Côte d'Ivoire, Gabon, Guinea, Mali, Republic of the Congo, Senegal, and Togo. This is the sole source of pharmaceutical prices in low-income countries.

To resolve the inherent difficulties in comparing very different products within a market (in our case, the pharmaceutical market) and a

heterogeneous product mix across countries, we used an approach developed by Patricia Danzon and colleagues[8,9] to create broadly representative price indexes that were comparable for each country. We constructed indexes to describe the relative difference in prices for pharmaceuticals in middle-income countries compared to the base countries of France, the United Kingdom, the United States, and French West Africa.

We calculated Laspeyres indexes, which use the quantities of goods consumed in a chosen base country to weight—that is, to apply the appropriate level of importance to—prices of the different goods within the index calculation. We also calculated Paasche indexes, which use a country's own quantities of goods consumed as weights to calculate the price indexes. In other words, Laspeyres indexes apply weights to all other countries' consumption based on the pattern of consumption in the chosen base country, while Paasche indexes are based on consumption within the country of analysis. Using both indexes allowed us to see the impact that different weights for quantities of consumption (consumption patterns in the base country versus those of the country of analysis) had on our calculations of relative prices.

To ensure comparison of like-for-like products, many past studies of pharmaceutical prices have limited their analysis to products with similar formulations, strengths, brands, and manufacturers. However, given the vast differences in sales from one country to another because of variations in consumers' preferences or in pricing and reimbursement systems, these limited comparisons give only indications of overall prices. They are particularly unrepresentative when they exclude generic drugs, which can be a large proportion of the pharmaceuticals consumed.[9]

We broadened the analysis to include drugs based on the same molecule and used for the same purpose, but differing in formulation, strength, brand, and manufacturer across countries. We thereby increased the number of products that we could compare, as well as our chances of capturing a sample of pharmaceuticals that were representative of national markets as a whole.

DATA The data were provided by IMS Health and covered the period from January 1, 1999, through September 30, 2008.[10] Pharmaceuticals were identified according to molecule name and use. Prices were calculated from sales expressed in US dollars, using exchange rates in effect at the time of sale, and deflated to 2005 dollars (see the online Appendix for more details).[11] Sales were expressed in terms of standard units.[12]

Prices were weighted by the number of standard units sold, regardless of the specific product name, pack size, form, or strength. Within each Laspeyres or Paasche index, a given country's price per standard unit for a given drug was the volume-weighted average price per dose over all of the possible presentations in that country. The drugs in our sample had to have consistent molecule names and uses across all countries in the comparison in that given year. That is, the analysis is based on year-on-year comparisons even though a number of such comparisons are given across a number of years (see the online Appendix for more details).[11]

Drugs and uses were rematched for each year, allowing for the sample of pharmaceuticals being compared to change over time, in line with variations in availability and buyers' preferences, and innovations in the pharmaceutical sector.

COMPARISONS We compared drugs and uses bilaterally, between selected middle-income countries and selected base countries. We compared prices in the United States to those in all middle-income countries. We also compared prices in the United Kingdom with those in Egypt, India, Indonesia, Malaysia, Poland, South Africa, and Turkey; prices in France with those in Algeria, Morocco, and Tunisia; and prices in French West Africa to prices in all fourteen middle-income countries. We chose the former two comparisons based on potential lingering economic ties (originating in colonial times) that could affect pricing strategies. Because IMS Health's prices omit manufacturers' discounts in the United States, we assumed an overall discount of 8 percent in bilateral comparisons using that country's weighting.[10]

We used Spearman rank correlations, which test for a monotonic relation—for example, increases in prices as incomes or health costs increase—without assuming such a relation to be linear. We did this to examine the relationships between relative pharmaceutical prices and gross domestic product and between relative prices and one standard cost of health services—the cost per hospital bed day, as estimated by the World Health Organization.[13]

We also analyzed market structure, assuming the IMS Health data for pharmaceutical sales in each country were representative of the country's market as a whole. That is, we explored the degree to which the drugs in our analysis were representative of all products sold in the country markets in terms of the proportion of generic products, products that carry any type of brand, and those with original brand names. Product characteristics were not available for all categories in all countries.

We compared each sample in our analysis to

overall country data to assess the degree to which the sample represented the wider market in product type (including brands, whether it was over the counter or by prescription, and length of time since it entered the country's market).

LIMITATIONS Our findings must be interpreted carefully, given the sensitivity of relative prices to how they are measured. For example, the drugs that we used to create our price indexes represent only a portion of the medicines available in the respective country markets. Although we tried to compare prices of similar drugs, we gave priority to drugs that represented a country's overall pharmaceutical market. This means that although the sample drugs from other countries will match US samples in molecule and use (as shown on the identifying label of the drug package), they may differ in such features as formulation, manufacturer, length of time on the local market, and whether they are available in generic form. An ideal analysis of prices would control for these characteristics, but the methodology used to create the indexes does not lend itself well to such an analysis. Relative prices may also be very sensitive to other elements of study design (see the online Appendix for more details).[11]

This study has additional limitations from a policy perspective. First, it does not address the important issue of differences in price and access to pharmaceuticals within a particular country. Indeed, inequities in income and access to health care may well be worse in some middle-income countries than anywhere else in the world, and if drugs in those countries were merely to have a uniform price based on average national income, poorer citizens would still be unable to afford them. Far more needs to be done to bring in-country prices in line with local affordability. Policy makers are often reluctant to price-discriminate within countries for the benefit of the poor, because of political reasons or convenience.[14]

Second, IMS Health collects the data on which we based our analysis only through audits of formal distribution channels. This may produce inaccurate prices for countries with high levels of informal or black-market sales. Also, given that the prices exclude distribution-chain markups—markups added to the product at each step in the distribution chain—the price differences between countries may not accurately reflect differences in what patients pay (see the online Appendix for more details).[11]

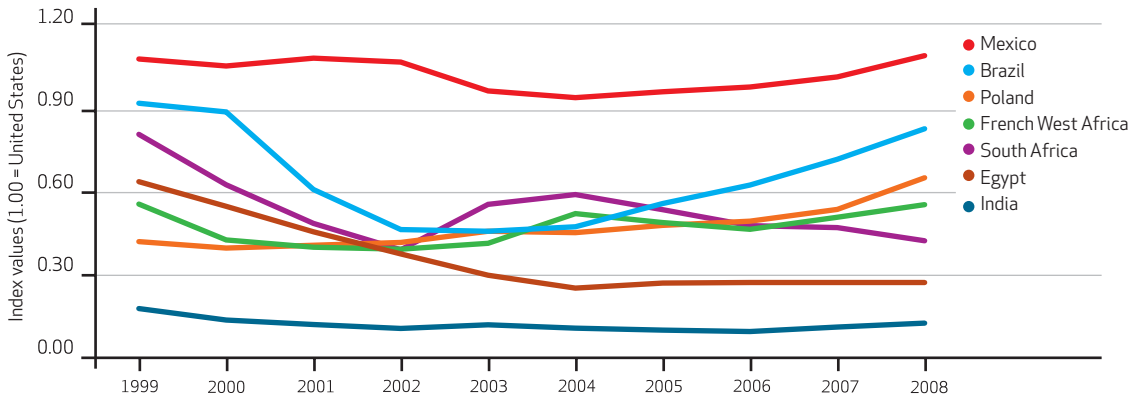
Study Results

Throughout the study period, prices in thirteen of the fourteen middle-income countries were below US prices. The exception is Mexico, where prices were similar to prices in the United States between 2003 and 2007, and higher than US prices during the other years when we used the Laspeyres price index (Exhibit 2). When manufacturers' price discounts are included (see the online Appendix[11]), Mexican prices exceeded US prices for all years. In addition, prices in the Philippines exceeded US prices in 1999 by 15 percent (data not shown).

Exhibit 3 presents similar comparisons using

EXHIBIT 2

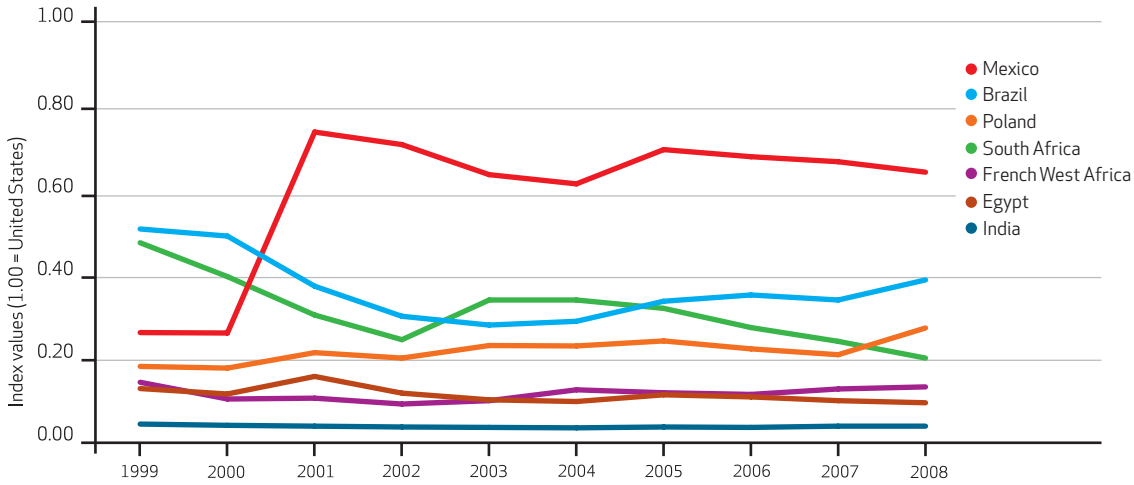
Pharmaceutical Prices In Selected Low- And Middle-Income Countries Compared To US Prices, 1999–2008, Using Laspeyres Price Indexes



SOURCE Authors' calculations based on IMS Health data (see Note 10 in text). **NOTES** See the text for explanations of the differences between Laspeyeres and Paasche price indexes. French West Africa is an aggregation of low-income countries constructed by IMS Health (see the text for a list of the countries). Brazil, Egypt, India, Mexico, Poland, and South Africa are middle-income countries. A fuller version of this figure appears in the online Appendix (see Note 11 in text).

EXHIBIT 3

Pharmaceutical Prices In Selected Low- And Middle-Income Countries Compared To US Prices, 1999–2008, Using Paasche Price Indexes



SOURCE Authors' calculations based on IMS Health data (see Note 10 in text). **NOTES** See the text for explanations of the differences between Laspeyeres and Paasche price indexes. French West Africa is an aggregation of low-income countries constructed by IMS Health (see the text for a list of the countries). Brazil, Egypt, India, Mexico, Poland, and South Africa are middle-income countries. A fuller version of this figure appears in the online Appendix (see Note 11 in text).

Paasche price indexes. These results suggest that prices in all of the six middle-income countries shown were below those in the United States, although prices in Mexico again were higher than those in the other middle-income countries (in this analysis, 62–74 percent of US prices after 2000).

Both Exhibits 2 and 3 compare prices in lower-income countries to those in the United States, based on the argument that the United States is the dominant source of pharmaceutical products. However, countries that were once colonies of the United Kingdom or France may have closer market relations to those countries than to the United States. Data from French West Africa were also used to assess price differences with low-income countries. Below we describe price comparisons between these "base" countries and middle-income countries, which we include in tabular form in the online Appendix.[11]

Results from comparisons with the United Kingdom based on both Paasche and Laspeyres price indexes suggest that pharmaceutical prices in several middle-income countries exceeded those in the United Kingdom for some years of the study period. Results of the comparisons with France suggest that prices in Morocco exceeded French prices in some years, when weighted according to French consumption volumes (using the Laspeyres price indexes). Both price comparisons with French West Africa suggest that several middle-income countries had prices consistently below those in that region.

As indicated above, we looked for associations between a country's Laspeyres and Paasche price indexes, its gross domestic product, and its cost of a hospital bed day.

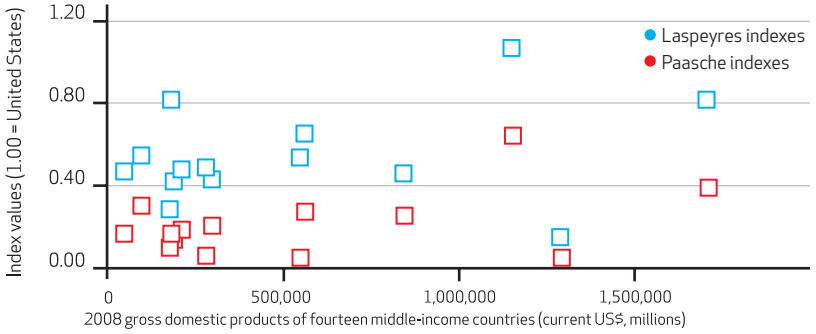
There is no statistically significant relationship between pharmaceutical prices in middle-income countries and their gross domestic products (Exhibit 4). Using the Laspeyres indexes gave a correlation of 0.1826 ($p = 0.5320$); using the Paasche indexes gave a correlation of 0.2203 ($p = 0.4492$). Pharmaceutical prices are much more closely associated with the cost of health care, such as the cost per hospital bed day (Exhibit 5), than with income. Here, the Laspeyres indexes gave a correlation of 0.4466 ($p = 0.1094$, almost significant at the 10 percent level). The Paasche indexes gave a correlation of 0.5771 ($p = 0.0307$, significant at the 5 percent level).

Discussion

This study sought to determine whether pharmaceutical prices varied systematically with income across a range of middle-income countries between 1999 and 2008. We found no such variation. Instead, we found wide variability in pharmaceutical prices around the globe, with prices in some middle-income countries (such as Mexico) being similar to those in industrialized countries (such as the United States) regardless of whether we used Laspeyres or Paasche indexes.

EXHIBIT 4

Price Indexes And Gross Domestic Products For Fourteen Middle-Income Countries, 2008



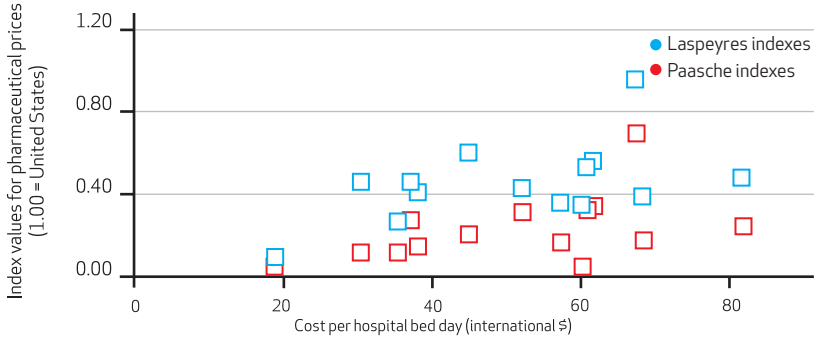
SOURCE Authors' calculations based on IMS Health data (see Note 10 in text) and World Bank Development Indicators (see Note 1 in text). **NOTES** The gross domestic products are as follows: Tunisia, $40,180; Morocco, $86,329; Egypt, $162,818; the Philippines, $166,909; Algeria, $173,882; Malaysia, $194,927; Thailand, $260,693; South Africa, $276,764; Indonesia, $514,389; Poland, $526,966; Turkey, $794,228; Mexico, $1,085,951; India, $1,217,490; and Brazil, $1,612,539. A fuller version of this figure appears in the online Appendix (see Note 11 in text).

Prices in other middle-income countries are low compared to prices in high-income countries, and even compared to prices in low-income countries. For example, prices in Egypt and India were lower than those in French West Africa (data not shown). This lack of association between prices and income generally confirms—although it is not identical to—findings of earlier studies.[15,16]

Exhibit 4 shows the lack of any clear association between a country's gross domestic product and its pharmaceutical prices. This figure shows 2008 data; the lack of association is similar for all years in the study period. The Spearman rank correlation reinforces this result.

EXHIBIT 5

Pharmaceutical Prices And Cost Per Hospital Bed Day In Fourteen Middle-Income Countries, 2005



SOURCE Authors' calculations based on IMS Health data (see Note 10 in text) and World Health Organization data (see Note 13 in text). **NOTES** For an explanation of international dollars, see the notes to Exhibit 1. The costs per hospital bed day are as follows: India, $18.75; Indonesia, $30.36; Egypt, $35.35; Morocco, $37.09; Algeria, $38.06; the Philippines, $44.92; Turkey, $52.14; Tunisia, $57.34; Thailand, $60.23; South Africa, $60.89; Brazil, $61.78; Mexico, $67.49; Malaysia, $68.46; and Poland, $81.89.

The lack of a clear relationship between pharmaceutical prices and gross domestic product is of particular interest because differential pricing across countries, relative to income, has been shown to be efficient on the grounds of both static and dynamic efficiency (that is, increasing social welfare and supporting long-term research and development).[12,17,18] Furthermore, the need to use such differential pricing to ensure access to pharmaceuticals may increase as developing countries make up a larger share of the global market for drugs.

For example, if countries are pushed to comply with the patent rules outlined in the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS; and in TRIPS-plus, which includes an even stricter application of intellectual property rules[19]), developing countries could have even greater difficulty in accessing pharmaceuticals than they do now, because of delays in generic drugs' entering the market. This further limiting of generic drugs' manufacturing would lead manufacturers of other drugs to adopt pricing strategies that can dictate more directly the prices that payers and patients will be charged. Thus, differential pricing driven by relative income may become increasingly vital to ensuring affordability in these markets.

Although we found no clear association between pharmaceutical prices and national gross domestic product (Exhibit 4), there does appear to be a link between pharmaceutical prices and other health care costs, represented in our study by cost of hospital bed day (Exhibit 5). The relationship holds for both 2005, shown in Exhibit 5, and 2000—the only years for which health services cost data were available. Spearman rank correlations between 2005 cost per hospital bed day and prices also suggest an association.

The relative prices paid for pharmaceuticals in middle- and low-income countries appear higher when the comparison is based on the volume of drugs sold in the United States (Laspeyres price indexes) than when it is based on the volume sold in the other countries (Paasche price indexes). This tendency for prices in each country to appear cheaper when the consumption patterns in that country—rather than those in the base country—are used to determine the relative importance of each drug in the overall index, regardless of the base country used, is known as the Gerschenkron effect. It may simply reflect a substitution effect, as consumers in each country purchase relatively more of those pharmaceuticals that are comparatively cheap there.[8] In our study, all Laspeyres index values exceeded their Paasche index counterparts, which indicates that as prices rose, the consumption of the drugs in our sample fell—confirmation that

the drugs we selected were not atypical products.

There appear to be simple explanations for some of the price differentials we found. For example, the dip in Brazilian prices in the middle years of the study period (Exhibits 2 and 3) may be due to that country's overall economic situation at the time. Brazil's gross domestic product declined from 2000 to 2002 and then rose very sharply, with income more than doubling between 2002 and 2008.[1]

The fact that Mexican prices were so close to US prices might be explained by the overlap of our study period with the implementation of major health system reforms in Mexico[20] that could have affected procurement and thus relative prices. And the sharp decline of prices in Turkey from 1999 to 2001 may be related to the banking and currency crisis that occurred in that country around this time (data not shown).[21] Further analysis of the effect of such events would be of interest.

Conclusion

The pricing of pharmaceuticals in markets around the world from 1999 through 2008 does not appear to have been systematically related to different countries' income category or gross domestic product. Despite the generally accepted view that it would be efficient—that is, it would produce an appropriate balance between meeting immediate social welfare needs and supporting future pharmaceutical innovation—and ethical to price pharmaceuticals in various markets according to relative income, manufacturers do not appear to use that approach consistently in setting prices. Some middle-income countries pay higher prices for pharmaceuticals than high-income countries, while other middle-income countries pay prices below those found in low-income countries.

This lack of association between prices and income suggests that we need policies to bring prices more in line with income, so that everyone has access to the pharmaceuticals they need. ■

NOTES

1 World Bank. World development indicators [Internet]. Washington (DC): World Bank; [last updated 2011 Apr; cited 2011 Jul 5]. Available from: http://data.worldbank.org/data-catalog/world-development-indicators

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PAPER 2

COMPARISON OF PHARMACEUTICAL PRICES AMONGST HIGH-INCOME COUNTRIES USING MULTIPLE INDICES

ABSTRACT

With major differences in disease treatment globally despite increasing global trade, there is growing attention to the relative prices paid for pharmaceuticals across countries. However, gaining an accurate picture of these price differences is very difficult due to variations in the presentation of pharmaceuticals and their local availability. Variations in consumption patterns as a result of social and cultural disparities also make the calculation of relative prices of relevant pharmaceuticals very challenging. This study aims at a quantitative understanding of the differences in the prices of pharmaceuticals amongst countries by using several indices that respond differently to consumption patterns and to the variations in the prices of individual products. It examines prices in the United States compared to 20 other high-income countries, and their evolution from 1999 to 2008, utilizing a much larger data set than ever used before. The results demonstrate how the different price indices provide a range of estimates for the relative prices of pharmaceuticals between two countries and how the differences between indices can be analysed to investigate differences in pricing or consumption patterns.

With few exceptions, drug prices in the comparative countries were lower than in the US but became gradually more similar to the US over the 10 years of the study. However, for only a few countries could the prices relative to the US be characterized by a single number based on similar values of the various indices. A good estimation of relative prices could be obtained for a much larger number of countries if the comparison was limited to "global" molecules (capturing on average 33% of the various markets). In cases where the indices were divergent, their differences provided useful insight into the underlying causes.

INTRODUCTION

With increasing global trade the value of cross-national price data increases. Understanding the differences between pharmaceutical prices amongst countries in particular can be useful on several levels. For example, to develop national (or even local) health strategies and trade policies may require awareness of the relative prices of pharmaceuticals sold in neighbouring countries to better predict or manage patient migration. National authorities may also be interested in understanding relative price differences to better manage parallel imports and their impact on local availability. Payers are interested in relative prices in order to leverage price negotiations with manufacturers to secure rebates, discounts, refunds, etc. Patients, especially those living near national borders, are interested in relative prices to inform their choice of where to seek care. The public and civil society organizations are interested in understanding the difference in pharmaceutical prices internationally to understand and indeed better fight for fairness in pricing and access to pharmaceuticals.

Quantifying differences in prices (or income or productivity) over time or amongst countries is a classic and long-standing problem in economics. There is an extensive literature dealing with the mathematical approaches to quantifying such differences with a single number, sometimes referred to as the Index Number Theory (see in particular Fisher 1922; Samuelson and Swamy 1974; Afriat 1978; and Diewert 1978). To make the problem tangible consider a simple two country-two product gedanken example: drug *alpha* costs $3 in country A and $1 in country B, whilst drug *beta* costs $1 in both A and B. Drug *alpha* represents 20% of the market by volume in A and 80% of the market in B, whilst *beta* represents 80% of the market in A and 20% in B. The pharmaceuticals in country B are clearly cheaper on average than in country A. But how much cheaper? To answer such questions, we rely on indices that measure overall differences in prices by comparing a comprehensive or representative sample of products that is appropriately weighted. Such indices summarize into one number a vast amount of price and sales volume information stemming from thousands of products. Indices make price differences more readily comprehensible and in recent decades they have become important tools for comparing prices and other important economic indicators across countries and regions. Indeed under the aegis of some of the major international organizations (and often carried out by national agencies) such international comparisons have become increasingly important in the geo-political landscape (Balk 2008).

The difficulty is that different indices can give widely diverging estimations of price differences between two countries. For example two prominent indices, which have been often used to compare the prices of pharmaceuticals, give very different answers to the relative drug prices in countries A and B in our gedanken example: prices in B are 71% of the prices in A according to the Laspeyres index but only 38% according to the Paasche index (see below for the mathematical definition of these indices). Which of these indices provide a true quantification of prices in A and B? Or is the true value some average of the two? Samuelson and Swamy gave the sobering answer 40 years ago: "…we cannot hope for one ideal formula for the index number: if it works for the tastes of Jack Spratt, it won't work for his wife's tastes" (Samuelson and Swamy 1974). In other words, heterogeneity in preferences makes the search for any single perfect price index *a priori* futile.

This study aims at comparing pharmaceutical prices in the United States and 20 other high-income countries. As in previous studies, this is achieved by using price indices despite the fundamental difficulties in using such indices, which are further magnified in the case of pharmaceuticals. Pharmaceutical products come in a dizzying variety of presentation, dosage and composition that vary from country to country such that it is inherently difficult to properly classify and compare like goods. Whilst the US pharmaceutical market is the closest the world has to a free market, all other countries use some form of price containment strategy or controls to manage prices, with the net result that the relation between price and consumption does not follow that expected of a free market. This phenomenon is exacerbated by private and national health insurance programs, which tend to dissociate price and consumption and, at the limit, can result in a marginal price of zero (Newhouse 1992). This makes it difficult to use the results of the literature that link "ideal" or "superlative" indices to some type of maximization of welfare or utility (see van Veelen and van Weide 2008, and references within). The difficulty of defining a proper price index for pharmaceuticals is greatly amplified when the objective is to compare prices amongst countries over time as is done in this study. This is so because preferences and prices in any given country co-vary over time in a manner that depends on the specifics of that country's pharmaceutical market.

In view of all these fundamental and practical difficulties, this study takes a pragmatic approach and makes simultaneous use of several indices that respond differently to consumption patterns and to the variations in the prices of individual products, as explained below. This approach has the double benefit of obviating the inherent difficulty in defining a

true price index for pharmaceuticals and of providing useful information not only from the numerical values of these indices and their evolution over time, but also from their differences. It must also be noted that the theoretical considerations of the necessary or useful properties of price indices that have fuelled much of the discussion regarding index theory (Fisher 1922; Samuelson and Swamy 1974; Afriat 1978; and Diewert 1978) are largely irrelevant in this pragmatic multi-index approach since it does not rely on the use of a single parameter.

PREVIOUS STUDIES

Cross-national price differences have been examined by a handful of authors in the past. Previous work on the construction of drug price indices has considered within country price variation (Berndt ER., Griliches Z., Rosett JG 1993; Griliches and Cockburn 1994) and cross-country variation (GAO, 1992, 1994; OFT, 2007, Minority Staff Report 1998). These early studies all found US prices to far exceed foreign prices, feeding the popularly held notion that the rest of the world is effectively free-riding on the innovation made possible by US prices. However, these studies were limited in numerous ways. Problems have ranged from unrepresentative samples (e.g. omitted generics despite widespread local consumption), to failing to account for large-pack discounts (Danzon 2000). Some studies used prices unweighted by volume, thereby detaching them from consumption and making them extremely sensitive to the products included and thus limiting their reliability. (See Danzon and Kim 1998 for a discussion of the limitations of the earliest of these). To-date studies published by Danzon and colleagues present the most comprehensive and methodologically advanced comparison of prices cross-nationally. Prices were measured against US prices and the sample was far more representative than in previous studies. As a result, the Danzon studies brought into question the generally held view that US prices were much higher than elsewhere. These studies, however, covered only a relatively small number of countries (seven in Danzon and Chao 2000 and eight in Danzon and Furukawa 2004) and were each based on only one year of data (1992 in Danzon and Chao 2000, 1999 in Danzon and Furukawa 2004).

The Danzon and Furukawa 2004 study used the 1999 data to examine how drug prices had changed from the previous study based on 1992 data. Contrary to the Danzon and Chao 2000 study, this new study sought to account for important off-invoice discounts that manufacturers make to large public and private payers in order to give a more accurate picture of relative prices. Crucially Danzon and Furukawa demonstrated that restricting the sample to

presentations that match on form and strength severely reduces the proportion of a country's sales that are captured by the sample (limiting it to only 10-21% of sales in many countries). Matching molecules according to usage characteristics such as OTC was also demonstrated to be very limiting. In essence the Danzon and Furukawa (2004) study demonstrated the need for a large, representative sample to obtain accurate measures of relative prices.

In a 2004 study commissioned by Health Affairs, Anderson and colleagues homed in on 30 leading pharmaceuticals (in terms of highest total spending in the US), comparing prices with Canada, UK and France (Anderson, Shea, Hussey, Keyhani and Zephyrin 2004). Their findings suggested greater differences between US and foreign prices than those found by Danzon and Furukawa 2004. This discrepancy was explained as possibly due to methodological issues, including in particular the focus on only 30 leading products. Another reason proposed for the different finding between the two studies was the more rapid increase in US prices than in other countries between 1999, when the data used by Danzon and Furukawa were collected, and 2003, when the data used by Anderson et al. were collected.

The approach used in this paper extends the work of Danzon, Anderson and colleagues in several ways. First the data set that is used is much larger, covering ten years, twenty one countries and many more pharmaceutical products. The study also makes explicit use of two different indices, Laspeyres and Paasche, each calculated in two different ways: one based on about 150 samples matched each year for all countries, and another based on a many more samples (~ 1000 to 2500) matched each year for any two countries being compared. This approach provides a much richer description of the price differences amongst countries. In addition to using the values of the individual indices as indications of price differences, this study explores how the differences between the two indices calculated from two different data bases (a total of four indices) may be diagnostic of the underlying causes of the price differences. In several instances, the Fisher Index, which is the geometric mean of the Laspeyres and Paasche indices, provides a useful quantification of price differences and it is used here for both the multilaterally and the bilaterally matched samples, bringing the total number of indices used to six.

METHODS

This study analyses IMS data from 20 comparator countries from 1999-2008[11] relative to the US. The comparator countries are all high-income countries as defined by the World Bank: Australia, Austria, Belgium, Canada, Finland, France, Germany, Greece, Italy, Japan, Korea, Netherlands, Philippines, Poland, Portugal, South Africa, Saudi Arabia, Singapore, Spain, Sweden, Switzerland, Taiwan, and the United Kingdom. The pharmaceutical prices analysed represent deflated manufacturer prices (which exclude wholesaler and pharmacy markups and taxes) for pharmaceuticals sold in the retail market except in the case of a few countries for which distribution pathways were not delineated between retail and other outlets[12]. Prices from the United States were based on drugstore, food store and mail service distribution channels. In a first analysis, US prices assumed no off-invoice discounts to allow for comparison with previous studies, in particular those of Danzon and Chao 2000 and of Anderson et al. 2004. But in a second analysis an overall average discount of 8%, was assumed, in line with Danzon and Furukawa (2004). Pharmaceuticals were defined by molecule name and indication, here the third Anatomic Therapeutic Category (ATC 3)[13]. All other characteristics were allowed to vary (e.g. brand name, pack-size, strength, form, etc.). A table describing the sample data is included in Appendix 2.

In the first instance pharmaceuticals were matched across all 21 countries (multilateral comparisons) in each year. This limited the analysis to only about 150 pharmaceuticals (depending on the year) that were available in all comparator countries, providing a common basis for price comparison. Pharmaceuticals were then matched between each individual country and the United States (bilateral comparisons), allowing for a much larger sample (between 750 and 2600 samples depending on the comparator country and the year) that was more representative of the whole market in each country. Prices in comparator countries could in this case only be compared to the base country, not across comparator countries. The product mix across the multilateral samples and bilateral samples respectively were the same but the volume weights differed according to the consumption patterns of the base country. Pharmaceuticals with very small sales volumes (lowest 3% in terms of sales measured in terms

[11] Data was available for years 1999 through the 3rd quarter of 2008, hence just under one full decade.
[12] In Singapore and Sweden prices include those for pharmaceuticals destined for retail and hospitals.

[13] Which uses the 3 to 4 digit European Pharmaceutical Market Research Association (EPhMRA) classification.

of standard units[14]) were excluded to minimize small number errors. Conversion from local currency was done by IMS Health using exchange rates in effect at the time of sale.

Methodologically the comparison of pharmaceutical prices across national borders (or across sub-national areas of differing regulatory jurisdiction) is in principle just like price comparison for other goods. However, given the enormous diversity in products on the market, the indirect nature of purchases, and the rapid pace of technological progress in pharmaceuticals, price comparison in this market are more difficult in practice. Medical molecules sold throughout the world come in a plethora of different names, product type, levels of patent protection and license status, therapeutic purpose, packaging, formulations/combinations, and strengths. This can make data analysis quite difficult even when using the most sophisticated and specially-designed software. For example, products are launched at different times thereby leading to often very different measures of time-on-market (sometimes used as measure of age) which can have implications for price. The level of intellectual property protection (also linked to age) accorded to a pharmaceutical also varies from country to country and may have important implications for price. In addition, variation in societal preferences has led to different products and strengths being dispensed as well as to different approaches to dispensing (e.g. pack-splitting) which also impacts unit price and makes standardization difficult. Dispensing policies also differ across countries or jurisdictions. For example, generic substitution or equivalent brand substitution is common in some markets but less so in others. There is also variation in the political and regulatory environment. For example, some governments show preferential status to local manufacturers, allowing them to charge higher prices (Anderson et al. 2004).

Availability of products is also not uniform and can thus limit the ability to match samples. For example, in their 2004 study of the relative prices of 30 leading pharmaceuticals, Anderson and colleagues initially examined the top 50 pharmaceuticals (in terms of highest total spending) in order to find 30 that were sold in all 4 countries used in the comparison.

This study aims at resolving the trade-off between the desirability of comparing only identical products and the need to compare a truly representative sample of a country's pharmaceutical market. This is achieved by 1) defining pharmaceuticals across therapeutic category and molecule combinations, and 2) conducting both multilateral (limiting the sample to only

[14] Standard units are the smallest common dose unit. For oral solid forms this is one tablet or capsule, for syrup forms this is 5 ml, and for injectable forms this is one ampoule or vial.

globally-relevant pharmaceuticals) and bilateral comparison of prices (vastly increasing the sample size but narrowing the comparative analysis between countries).

Overall the methodology used in this study is similar to the one developed by Danzon and colleagues. It includes branded as well as generic products, and considers all formulations, pack-sizes, and strengths. Some small changes were made to reflect changes in the form of the available data and the application of the methodology was different in that this study looks at pricing over a much longer time period (10 years as opposed to 1 year in the Danzon studies and the Anderson study) and incorporates many more countries for comparison.

The particular basket of pharmaceuticals used in the sample for each year was determined by availability. For indices based on bilaterally-matched samples the basket was made up of all molecule-indications that matched between the comparator country and base country. For indices based on multilaterally-matched samples the basket was made up of only those molecule indications that matched across all HICs.

As the importance of individual pharmaceuticals for patient treatment varies, price indices are weighted by actual consumption patterns—in this case proxied by volume sold. As alluded to above, a key concern in the building of indices is the fact that the consumption patterns in the countries being compared are a result of numerous contextual factors such as cultural preferences, demographics, relative prices, availability of goods and related services, and income levels. As a result, the consumption patterns of the two countries can be quite different. To take these differences into account, this study utilizes two indices that weight prices according to consumption patterns from each country. The Laspeyres index, L, for a comparator country, C, weights prices according to consumption patterns of the base country, i.e., the United States in most of our study:

$$\mathrm{L} = \frac{\Sigma(Q_{M,USA})(P_{M,C})}{\Sigma(Q_{M,USA})(P_{M,USA})}$$

Where $Q_{M,USA}$ is the quantity weight of the pharmaceutical sold in the USA, and $P_{M,C}$ *and* $P_{M,USA}$ are the prices of the pharmaceutical per standard unit in the comparator country and in the USA, respectively.

In contrast, the Paasche index, P, weights prices according to consumption patterns of the comparator country (sometimes called "own-weighting"):

$$P = \frac{\Sigma(Q_{M,C})(P_{M,C})}{\Sigma(Q_{M,C})(P_{M,USA})}$$

Where $Q_{M,C}$ is the quantity weight of the pharmaceutical sold in the comparator country, and $P_{M,C}$ and $P_{M,USA}$ are the prices of the pharmaceutical per standard unit in the comparator country and in the USA, respectively.

We note that for a given comparator country C, P is the inverse of L calculated for the US with C as the base country. One may consider L as quantifying how much the US would save if it adopted the prices in country C with no effect on consumption patterns. And one may consider P as quantifying how much less country C pays than it would if its drug prices were the same as US prices with no change in consumption pattern (Danzon and Chao 2000). However, as discussed later, the prices and consumption patterns are of course inter-related, rendering these conditions purely imaginary.

Using two ways of weighting prices for two different baskets of goods yields four distinct indices to compare drug prices between two countries. In what follows, the Laspeyres and Paasche indices based on multilaterally matched samples are denoted as L_M and P_M, and those based on bilaterally matched samples as L_B and P_B. In addition it is convenient to use the Fisher Ideal Index (Fisher 1922) which is the geometric mean of the Laspeyres and Paasche indices. This index –henceforth the "Fisher Index" although it is one of thousands of such indices proposed by Irwin Fisher (1922)—has been shown to provide an approximation of an "ideal" or "exact" index under some conditions (Samuelson and Swamy 1974; Afriat 1978). In a practical way, this index must necessarily provide a reasonably good estimation of overall price differences between two countries when the Laspeyres and Paasche indices are close to each other. The Fisher indices based multilaterally and bilaterally matched samples are denoted F_M and F_B, respectively:

$$F_M = (L_M \cdot P_M)^{1/2}$$

$$F_B = (L_B \cdot P_B)^{1/2}$$

In order to gauge HIC price differences independently from the US (although still linked through the US dollar conversion rate used by IMS), additional L and P indices were calculated using UK and France as base countries and multilaterally- as well as bilaterally-matched samples.

RESULTS

The calculated Laspeyres, Paasche and Fisher indices based on multilaterally matched samples and on bilaterally matched samples with the US, L_M, P_M & F_M and L_B, P_B & F_B for all the comparator countries and for the 10 years of the study are presented in Tables 1-6 and Figures 1-6. A summary presentation of the 10-year means of L_M and P_M, L_B and P_B is also given in Figure 7. The values of the indices for a given country are generally consistent over the whole data set with only six suspiciously high numbers: L_B for Austria in 1999, for Japan in 1999 and 2000, and for Canada in 2003 and 2004, as well as L_M for Japan in 2000.

TABLE 1. L_M: PRICES RELATIVE TO UNITED STATES PRICES BASED ON MULTILATERALLY-MATCHED SAMPLE, LASPEYRES PRICE INDICES (US=1)

	2000	2001	2002	2003	2004	2005	2006	2007	2008
AUSTRALIA	0.45	0.39	0.39	0.48	0.53	0.55	0.54	0.66	0.75
AUSTRIA	0.44	0.40	0.41	0.47	0.50	0.48	0.51	0.60	0.70
BELGIUM	0.53	0.46	0.49	0.57	0.61	0.57	0.56	0.65	0.75
CANADA	0.55	0.51	0.50	0.55	0.61	0.65	0.70	0.84	0.92
FINLAND	0.46	0.42	0.44	0.50	0.53	0.50	0.49	0.61	0.71
FRANCE	0.42	0.39	0.39	0.47	0.52	0.51	0.51	0.60	0.67
GERMANY	0.45	0.43	0.43	0.50	0.56	0.54	0.56	0.64	0.73
GREECE	0.35	0.33	0.34	0.42	0.49	0.46	0.50	0.63	0.75
ITALY	0.53	0.49	0.50	0.56	0.59	0.56	0.56	0.66	0.72
JAPAN	3.05	0.60	0.59	0.64	0.68	0.67	0.64	0.74	0.92
KOREA	0.45	0.38	0.37	0.38	0.40	0.45	0.53	0.62	0.61
NETHERLANDS	0.54	0.49	0.48	0.55	0.55	0.52	0.53	0.63	0.67
PORTUGAL	0.50	0.45	0.45	0.51	0.55	0.54	0.55	0.63	0.73
SAUDI ARABIA	0.71	0.69	0.63	0.56	0.53	0.54	0.56	0.57	0.52
SINGAPORE	0.52	0.41	0.40	0.42	0.41	0.40	0.44	0.52	0.60
SPAIN	0.40	0.37	0.37	0.45	0.46	0.45	0.48	0.61	0.69
SWEDEN	0.52	0.44	0.45	0.49	0.51	0.50	0.49	0.60	0.67
SWITZERLAND	0.74	0.70	0.74	0.83	0.90	0.85	0.78	0.83	0.99
TAIWAN	0.49	0.44	0.40	0.40	0.42	0.43	0.46	0.49	0.53
UNITED KINGDOM	0.54	0.49	0.48	0.51	0.55	0.48	0.50	0.57	0.56

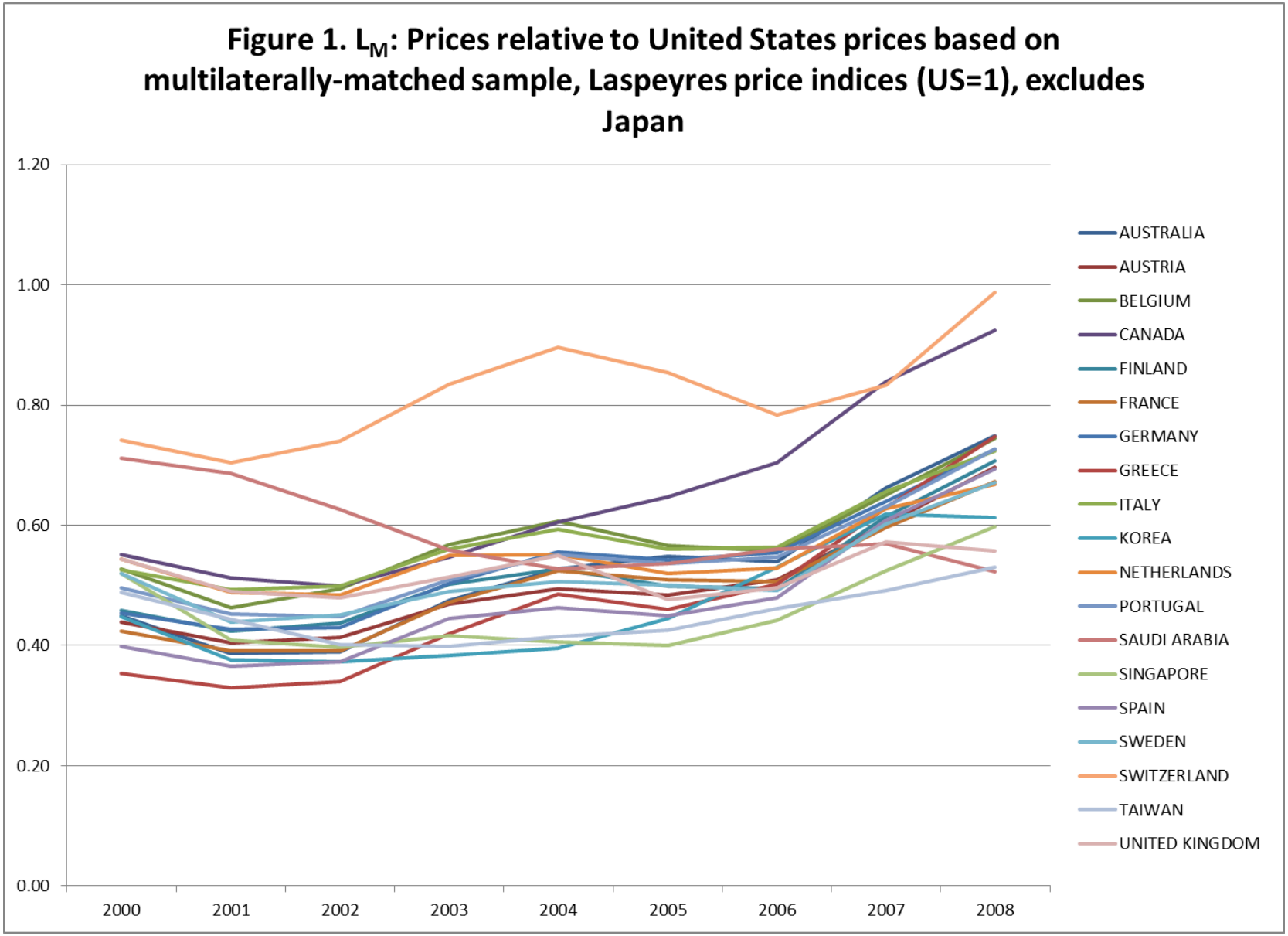
Figure 1. L_M: Prices relative to United States prices based on multilaterally-matched sample, Laspeyres price indices (US=1), excludes Japan
1.20
1.00
0.80
0.60
0.40
0.20
0.00
2000
2001
2002
2003
2004
2005
2006
2007
2008
AUSTRALIA
AUSTRIA
BELGIUM
CANADA
FINLAND
FRANCE
GERMANY
GREECE
ITALY
KOREA
NETHERLANDS
PORTUGAL
SAUDI ARABIA
SINGAPORE
SPAIN
SWEDEN
SWITZERLAND
TAIWAN
UNITED KINGDOM

TABLE 2. P_M: PRICES RELATIVE TO UNITED STATES PRICES BASED ON MULTILATERALLY-MATCHED SAMPLE, PAASCHE PRICE INDICES (US=1)

	2000	2001	2002	2003	2004	2005	2006	2007	2008
AUSTRALIA	0.33	0.29	0.29	0.36	0.41	0.41	0.39	0.45	0.47
AUSTRIA	0.38	0.34	0.34	0.41	0.43	0.41	0.42	0.37	0.50
BELGIUM	0.45	0.39	0.40	0.47	0.51	0.48	0.47	0.55	0.68
CANADA	0.49	0.24	0.38	0.48	0.53	0.54	0.61	0.66	0.59
FINLAND	0.39	0.36	0.38	0.43	0.45	0.42	0.39	0.46	0.50
FRANCE	0.35	0.33	0.33	0.40	0.44	0.44	0.44	0.45	0.51
GERMANY	0.36	0.36	0.36	0.43	0.46	0.43	0.46	0.37	0.53
GREECE	0.32	0.31	0.33	0.39	0.44	0.46	0.49	0.46	0.64
ITALY	0.45	0.42	0.42	0.47	0.50	0.48	0.49	0.42	0.48
JAPAN	0.43	0.41	0.42	0.45	0.44	0.44	0.43	0.47	0.63
KOREA	0.28	0.27	0.32	0.32	0.32	0.39	0.47	0.56	0.39
NETHERLANDS	0.44	0.41	0.40	0.46	0.45	0.42	0.43	0.52	0.53
PORTUGAL	0.44	0.41	0.40	0.45	0.50	0.48	0.48	0.49	0.63
SAUDI ARABIA	0.68	0.70	0.65	0.58	0.53	0.56	0.63	0.35	0.41
SINGAPORE	0.29	0.28	0.26	0.24	0.20	0.23	0.24	0.34	0.32
SPAIN	0.36	0.32	0.32	0.38	0.41	0.40	0.42	0.40	0.49
SWEDEN	0.41	0.34	0.34	0.37	0.37	0.37	0.37	0.44	0.48
SWITZERLAND	0.54	0.54	0.58	0.66	0.71	0.68	0.61	0.47	0.69
TAIWAN	0.27	0.28	0.29	0.29	0.31	0.36	0.34	0.31	0.35
UNITED KINGDOM	0.44	0.40	0.41	0.44	0.47	0.40	0.39	0.44	0.41

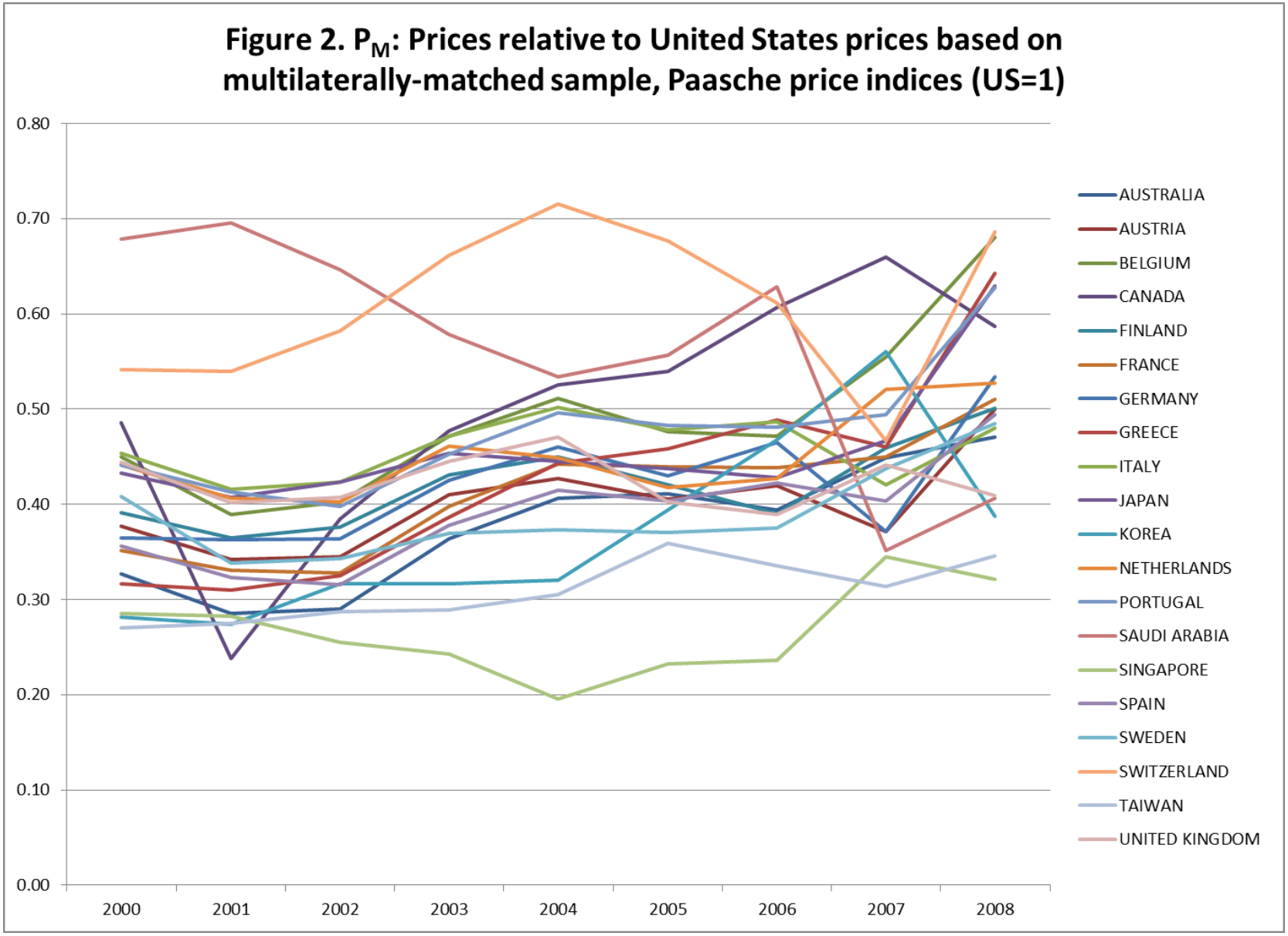
Figure 2. P_M: Prices relative to United States prices based on multilaterally-matched sample, Paasche price indices (US=1)
0.80
0.70
0.60
0.50
0.40
0.30
0.20
0.10
0.00
2000
2001
2002
2003
2004
2005
2006
2007
2008
AUSTRALIA
AUSTRIA
BELGIUM
CANADA
FINLAND
FRANCE
GERMANY
GREECE
ITALY
JAPAN
KOREA
NETHERLANDS
PORTUGAL
SAUDI ARABIA
SINGAPORE
SPAIN
SWEDEN
SWITZERLAND
TAIWAN
UNITED KINGDOM

TABLE 3. L_B: PRICES RELATIVE TO UNITED STATES PRICES BASED ON BILATERALLY-MATCHED SAMPLE, LASPEYRES PRICE INDICES (US=1)

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
AUSTRALIA	0.87	0.71	0.56	0.56	0.65	0.74	1.21	1.05	1.14	1.15
AUSTRIA	1.40	0.89	0.76	0.74	0.61	0.64	0.56	0.58	0.78	1.06
BELGIUM	0.72	0.56	0.51	0.53	0.64	0.67	0.68	0.69	0.86	1.22
CANADA	0.72	0.67	0.61	1.11	5.89	4.76	1.57	1.65	1.39	1.34
FINLAND	0.55	0.46	0.43	0.45	0.54	0.57	0.56	0.54	0.69	0.94
FRANCE		0.45	0.41	0.41	0.49	0.54	0.54	0.53	0.58	0.64
GERMANY	1.18	0.85	0.73	0.74	0.79	0.82	0.83	0.78	0.94	1.50
GREECE	0.46	0.36	0.36	0.39	0.47	0.53	0.53	0.55	0.64	0.70
ITALY	0.64	0.54	0.50	0.49	0.56	0.57	0.54	0.57	0.76	1.08
JAPAN	2.30	2.35	0.98	0.92	0.87	0.86	0.86	0.79	0.91	1.23
KOREA	0.56	0.48	0.40	0.41	0.41	0.42	0.48	0.52	0.56	0.53
NETHERLANDS	0.67	0.55	0.49	0.51	0.60	0.62	0.58	0.57	0.64	0.68
PORTUGAL	0.62	0.50	0.45	0.46	0.52	0.56	0.54	0.52	0.56	0.61
SAUDI ARABIA	0.82	0.74	0.72	0.70	0.62	0.56	0.60	0.60	0.62	0.55
SINGAPORE	0.62	0.60	0.53	0.51	0.52	0.49	0.43	0.45	0.49	0.54
SPAIN	0.52	0.43	0.39	0.41	0.47	0.49	0.47	0.48	0.55	0.61
SWEDEN	0.60	0.53	0.44	0.47	0.55	0.58	0.58	0.61	0.79	1.10
SWITZERLAND	1.01	0.79	0.78	0.82	0.92	0.97	0.83	0.77	0.81	0.91
TAIWAN	0.48	0.51	0.46	0.42	0.42	0.43	0.45	0.44	0.45	0.47
UNITED KINGDOM	0.79	0.65	0.57	0.57	0.59	0.65	0.59	0.58	0.64	0.61

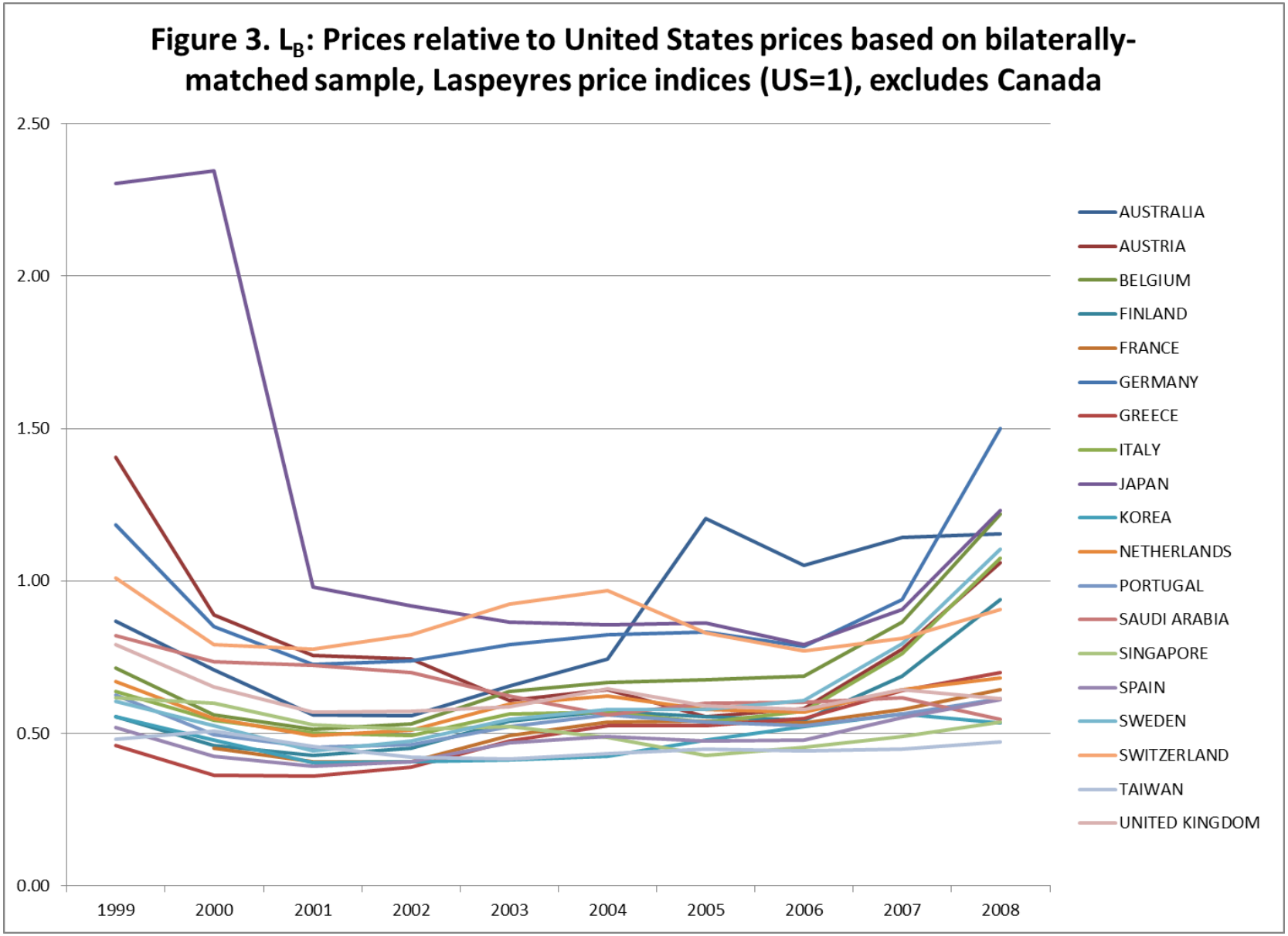
Figure 3. L_B: Prices relative to United States prices based on bilaterally-matched sample, Laspeyres price indices (US=1), excludes Canada
2.50
2.00
1.50
1.00
0.50
0.00
1999
2000
2001
2002
2003
2004
2005
2006
2007
2008
AUSTRALIA
AUSTRIA
BELGIUM
FINLAND
FRANCE
GERMANY
GREECE
ITALY
JAPAN
KOREA
NETHERLANDS
PORTUGAL
SAUDI ARABIA
SINGAPORE
SPAIN
SWEDEN
SWITZERLAND
TAIWAN
UNITED KINGDOM

TABLE 4. P_B: PRICES RELATIVE TO UNITED STATES PRICES BASED ON BILATERALLY-MATCHED SAMPLE, PAASCHE PRICE INDICES (US=1)

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
AUSTRALIA	0.33	0.28	0.26	0.24	0.28	0.32	0.33	0.30	0.32	0.31
AUSTRIA	0.37	0.25	0.33	0.34	0.40	0.43	0.41	0.40	0.38	0.43
BELGIUM	0.38	0.33	0.35	0.36	0.43	0.47	0.46	0.43	0.26	0.49
CANADA	0.24	0.27	0.28	0.37	0.42	0.47	0.49	0.51	0.45	0.46
FINLAND	0.23	0.22	0.29	0.31	0.35	0.40	0.42	0.39	0.42	0.45
FRANCE		0.19	0.26	0.26	0.30	0.35	0.35	0.35	0.36	0.38
GERMANY	0.29	0.24	0.35	0.33	0.43	0.48	0.47	0.48	0.45	0.55
GREECE	0.19	0.18	0.23	0.25	0.30	0.36	0.38	0.40	0.41	0.48
ITALY	0.43	0.38	0.37	0.37	0.42	0.44	0.42	0.41	0.38	0.40
JAPAN	0.32	0.35	0.33	0.31	0.34	0.36	0.35	0.32	0.31	0.34
KOREA	0.16	0.12	0.17	0.21	0.22	0.25	0.31	0.35	0.40	0.30
NETHERLANDS	0.42	0.33	0.37	0.37	0.43	0.45	0.44	0.43	0.48	0.48
PORTUGAL	0.38	0.33	0.33	0.35	0.40	0.45	0.44	0.42	0.43	0.47
SAUDI ARABIA	0.30	0.38	0.52	0.46	0.46	0.42	0.40	0.39	0.29	0.26
SINGAPORE	0.24	0.23	0.24	0.25	0.25	0.24	0.26	0.27	0.29	0.29
SPAIN	0.31	0.27	0.28	0.29	0.35	0.38	0.38	0.37	0.37	0.41
SWEDEN	0.27	0.24	0.29	0.31	0.36	0.39	0.40	0.40	0.26	0.43
SWITZERLAND	0.49	0.42	0.42	0.46	0.53	0.59	0.58	0.52	0.48	0.56
TAIWAN	0.15	0.15	0.15	0.13	0.14	0.16	0.16	0.16	0.14	0.14
UNITED KINGDOM	0.34	0.32	0.33	0.35	0.37	0.41	0.38	0.36	0.40	0.37

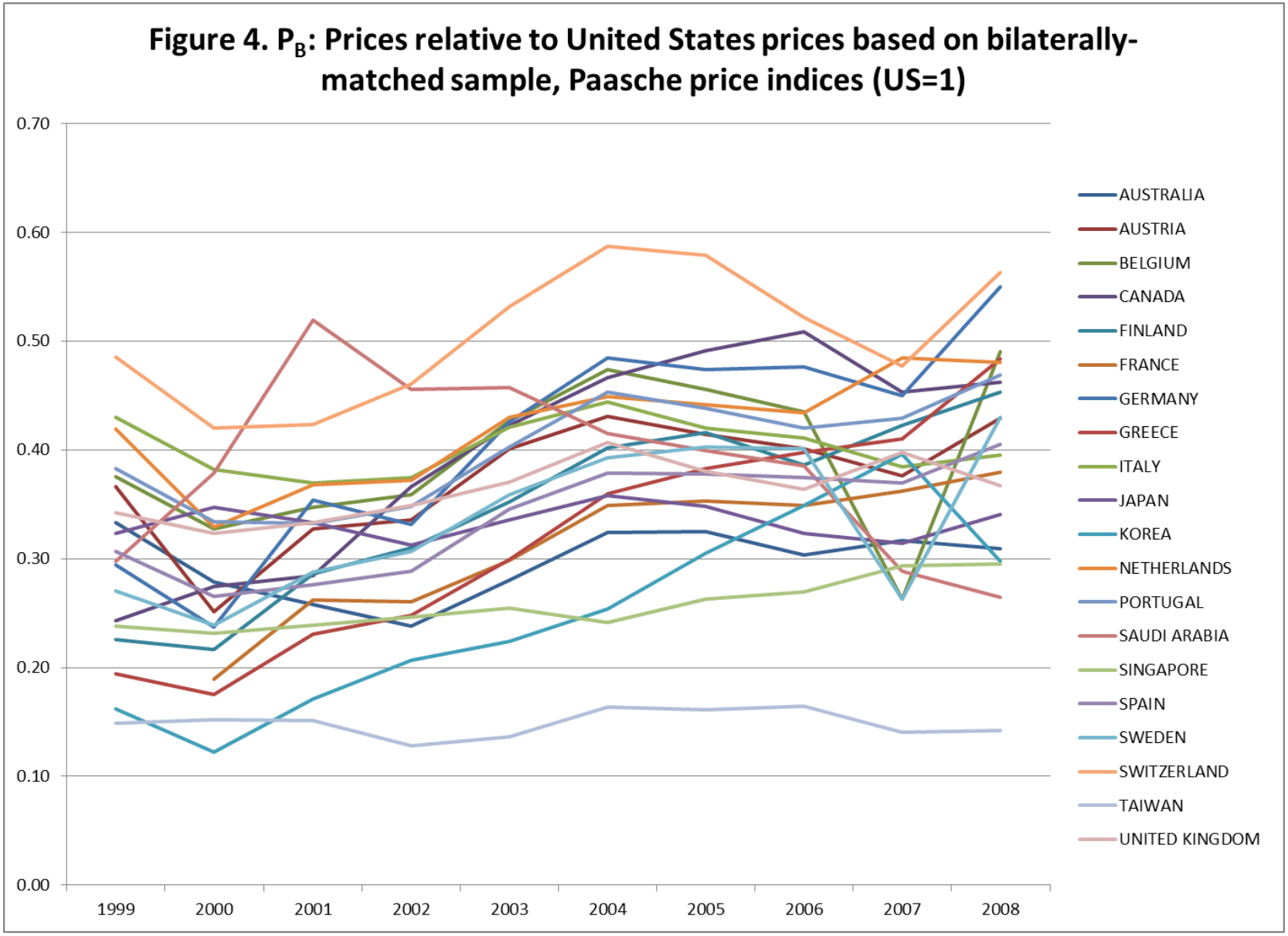
Figure 4. P_B: Prices relative to United States prices based on bilaterally-matched sample, Paasche price indices (US=1)
0.70
0.60
0.50
0.40
0.30
0.20
0.10
0.00
1999
2000
2001
2002
2003
2004
2005
2006
2007
2008
AUSTRALIA
AUSTRIA
BELGIUM
CANADA
FINLAND
FRANCE
GERMANY
GREECE
ITALY
JAPAN
KOREA
NETHERLANDS
PORTUGAL
SAUDI ARABIA
SINGAPORE
SPAIN
SWEDEN
SWITZERLAND
TAIWAN
UNITED KINGDOM

TABLE 5. F_M: PRICES RELATIVE TO UNITED STATES PRICES BASED ON MULTILATERALLY-MATCHED SAMPLE, FISHER PRICE INDICES

	2000	2001	2002	2003	2004	2005	2006	2007	2008
AUSTRALIA	0.38	0.33	0.34	0.42	0.46	0.47	0.46	0.54	0.59
AUSTRIA	0.41	0.37	0.38	0.44	0.46	0.44	0.46	0.47	0.59
BELGIUM	0.49	0.42	0.45	0.52	0.56	0.52	0.51	0.60	0.71
CANADA	0.52	0.35	0.44	0.51	0.56	0.59	0.65	0.74	0.74
FINLAND	0.42	0.39	0.41	0.47	0.49	0.46	0.44	0.53	0.60
FRANCE	0.39	0.36	0.36	0.43	0.48	0.47	0.47	0.52	0.59
GERMANY	0.41	0.39	0.40	0.46	0.51	0.48	0.51	0.49	0.62
GREECE	0.33	0.32	0.33	0.40	0.46	0.46	0.49	0.54	0.69
ITALY	0.49	0.45	0.46	0.51	0.55	0.52	0.52	0.53	0.59
JAPAN	1.15	0.49	0.50	0.54	0.55	0.54	0.52	0.59	0.76
KOREA	0.35	0.32	0.34	0.35	0.36	0.42	0.50	0.59	0.49
NETHERLANDS	0.49	0.45	0.44	0.50	0.50	0.47	0.48	0.57	0.59
PORTUGAL	0.47	0.43	0.42	0.48	0.52	0.51	0.51	0.56	0.68
SAUDI ARABIA	0.69	0.69	0.64	0.57	0.53	0.55	0.59	0.45	0.46
SINGAPORE	0.39	0.34	0.32	0.32	0.28	0.30	0.32	0.43	0.44
SPAIN	0.38	0.34	0.34	0.41	0.44	0.43	0.45	0.50	0.59
SWEDEN	0.46	0.39	0.39	0.43	0.43	0.43	0.43	0.51	0.57
SWITZERLAND	0.63	0.62	0.66	0.74	0.80	0.76	0.69	0.62	0.82
TAIWAN	0.36	0.35	0.34	0.34	0.36	0.39	0.39	0.39	0.43
UNITED KINGDOM	0.49	0.44	0.44	0.48	0.51	0.44	0.44	0.50	0.48

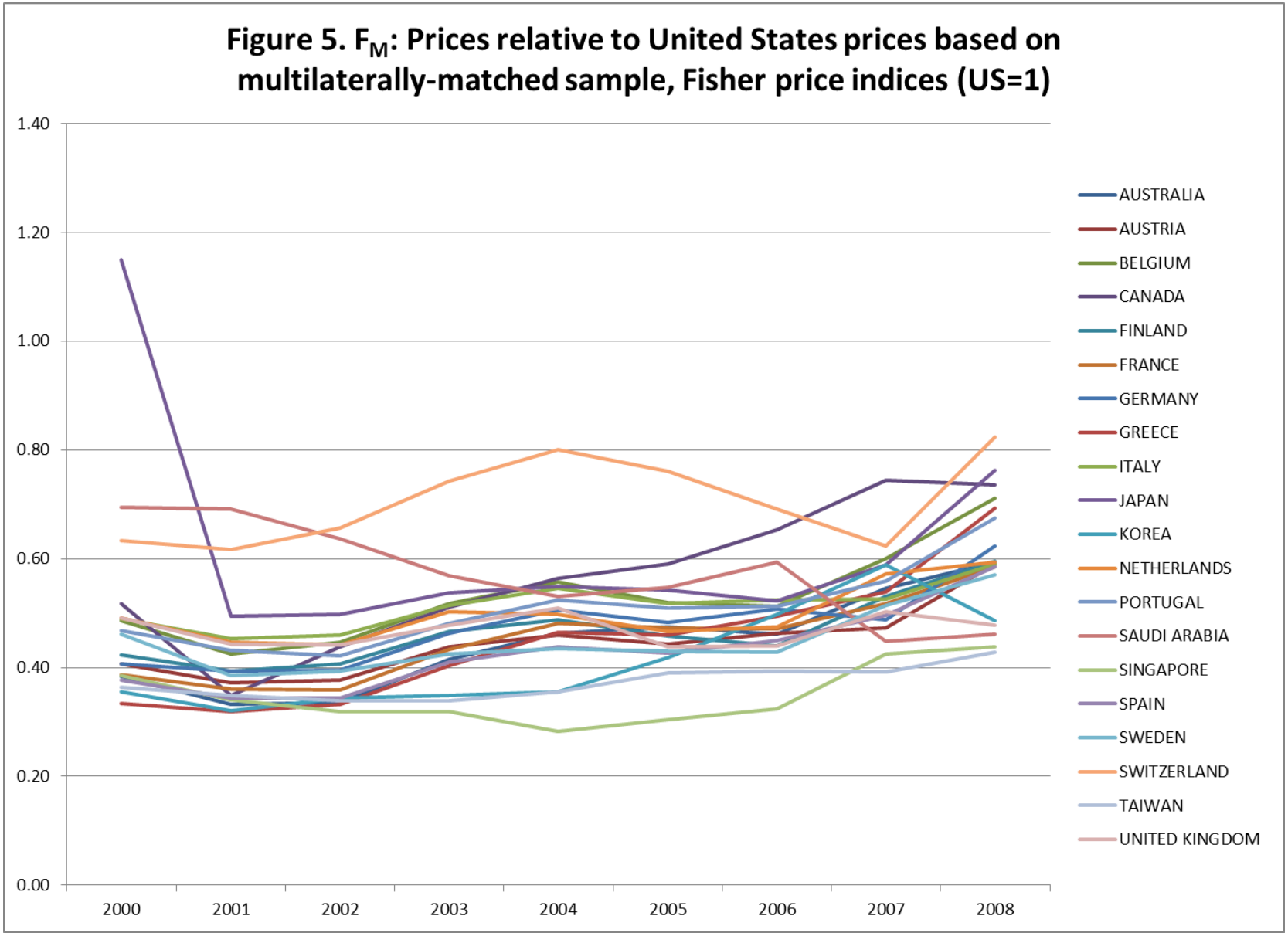
Figure 5. F_M: Prices relative to United States prices based on multilaterally-matched sample, Fisher price indices (US=1)
1.40
1.20
1.00
0.80
0.60
0.40
0.20
0.00
2000
2001
2002
2003
2004
2005
2006
2007
2008
AUSTRALIA
AUSTRIA
BELGIUM
CANADA
FINLAND
FRANCE
GERMANY
GREECE
ITALY
JAPAN
KOREA
NETHERLANDS
PORTUGAL
SAUDI ARABIA
SINGAPORE
SPAIN
SWEDEN
SWITZERLAND
TAIWAN
UNITED KINGDOM

TABLE 6. F_B: PRICES RELATIVE TO UNITED STATES PRICES BASED ON BILATERALLY-MATCHED SAMPLE, FISHER PRICE INDICES (US=1)

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
AUSTRALIA	0.54	0.44	0.38	0.36	0.43	0.49	0.63	0.56	0.60	0.60
AUSTRIA	0.72	0.47	0.50	0.50	0.49	0.53	0.48	0.48	0.54	0.67
BELGIUM	0.52	0.43	0.42	0.44	0.52	0.56	0.55	0.55	0.48	0.77
CANADA	0.42	0.43	0.42	0.64	1.58	1.49	0.88	0.92	0.79	0.79
FINLAND	0.35	0.32	0.35	0.37	0.44	0.48	0.48	0.46	0.54	0.65
FRANCE		0.29	0.33	0.33	0.38	0.43	0.44	0.43	0.46	0.49
GERMANY	0.59	0.45	0.51	0.49	0.58	0.63	0.63	0.61	0.65	0.91
GREECE	0.30	0.25	0.29	0.31	0.38	0.44	0.45	0.47	0.51	0.58
ITALY	0.52	0.46	0.43	0.43	0.49	0.50	0.48	0.48	0.54	0.65
JAPAN	0.86	0.90	0.57	0.54	0.54	0.55	0.55	0.51	0.53	0.65
KOREA	0.30	0.24	0.26	0.29	0.30	0.33	0.38	0.43	0.47	0.40
NETHERLANDS	0.53	0.42	0.43	0.44	0.51	0.53	0.51	0.50	0.56	0.57
PORTUGAL	0.49	0.41	0.39	0.40	0.46	0.50	0.49	0.47	0.49	0.54
SAUDI ARABIA	0.49	0.53	0.61	0.56	0.53	0.48	0.49	0.48	0.42	0.38
SINGAPORE	0.38	0.37	0.36	0.36	0.36	0.34	0.34	0.35	0.38	0.40
SPAIN	0.40	0.34	0.33	0.34	0.40	0.43	0.42	0.42	0.45	0.50
SWEDEN	0.40	0.35	0.36	0.38	0.44	0.48	0.48	0.49	0.46	0.69
SWITZERLAND	0.70	0.58	0.57	0.62	0.70	0.75	0.69	0.63	0.62	0.71
TAIWAN	0.27	0.28	0.26	0.23	0.24	0.27	0.27	0.27	0.25	0.26
UNITED KINGDOM	0.52	0.46	0.44	0.45	0.47	0.51	0.47	0.46	0.51	0.47

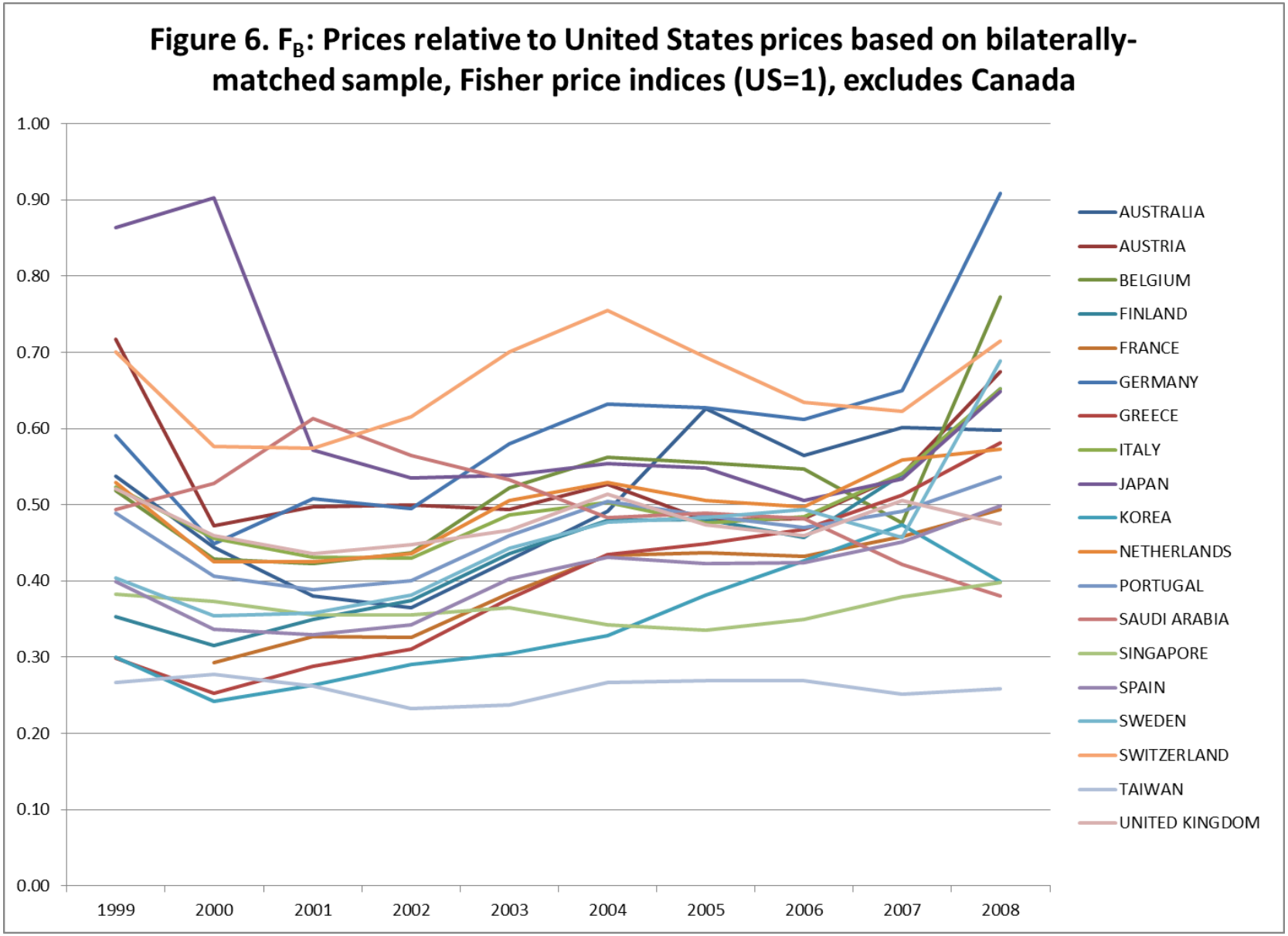
Figure 6. F_B: Prices relative to United States prices based on bilaterally-matched sample, Fisher price indices (US=1), excludes Canada
1.00
0.90
0.80
0.70
0.60
0.50
0.40
0.30
0.20
0.10
0.00
1999
2000
2001
2002
2003
2004
2005
2006
2007
2008
AUSTRALIA
AUSTRIA
BELGIUM
FINLAND
FRANCE
GERMANY
GREECE
ITALY
JAPAN
KOREA
NETHERLANDS
PORTUGAL
SAUDI ARABIA
SINGAPORE
SPAIN
SWEDEN
SWITZERLAND
TAIWAN
UNITED KINGDOM

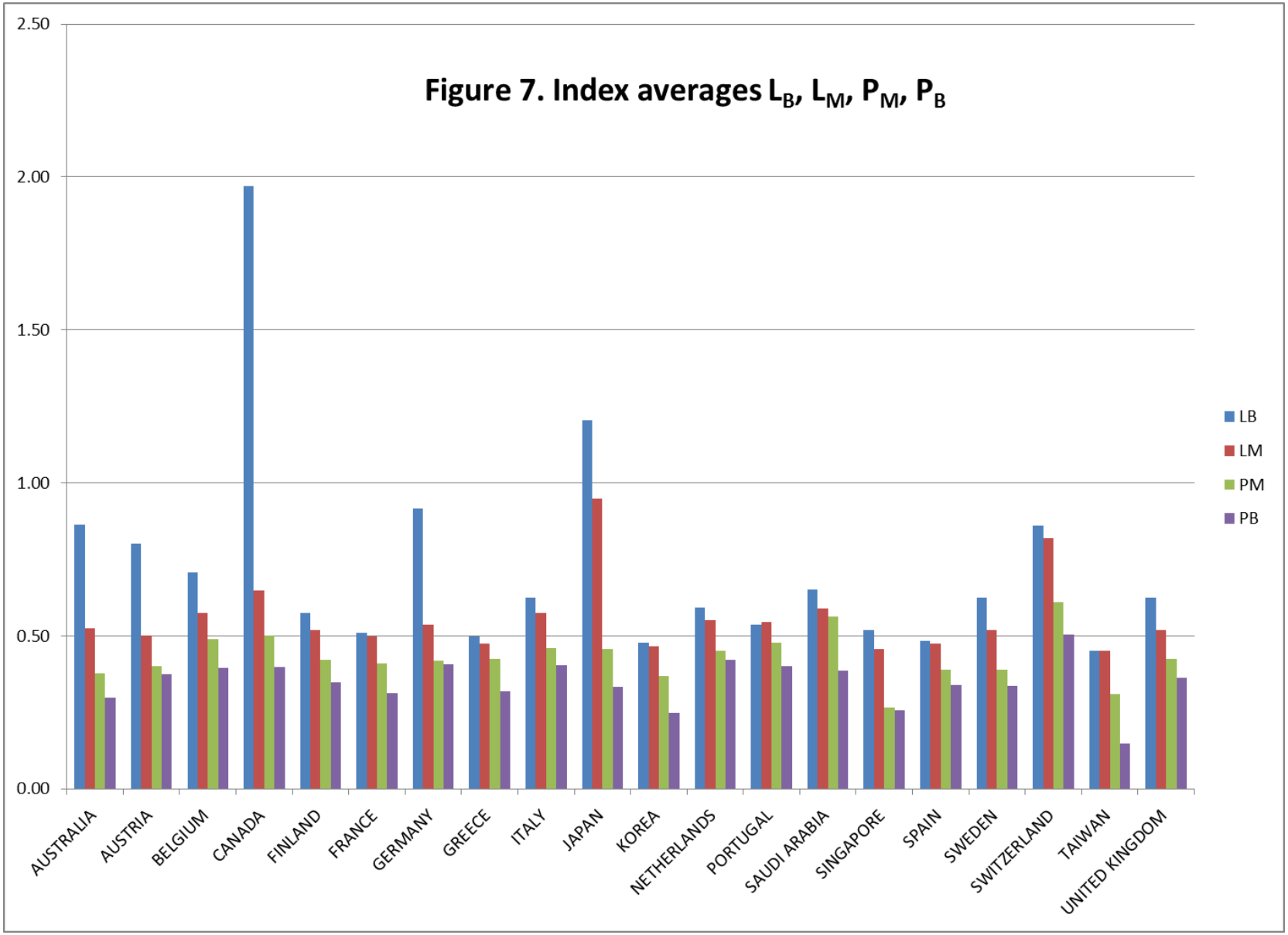
Figure 7. Index averages L_B, L_M, P_M, P_B
2.50
2.00
1.50
1.00
0.50
0.00
LB
LM
PM
PB
AUSTRALIA
AUSTRIA
BELGIUM
CANADA
FINLAND
FRANCE
GERMANY
GREECE
ITALY
JAPAN
KOREA
NETHERLANDS
PORTUGAL
SAUDI ARABIA
SINGAPORE
SPAIN
SWEDEN
SWITZERLAND
TAIWAN
UNITED KINGDOM

Looking at the general features of the data (and keeping a detailed examination of the differences amongst indices for the discussion) some general trends are readily apparent. With very few exceptions the indices show that pharmaceutical prices in the comparator countries were lower than in the US for the period of the study. Following a general decrease between 1999 and 2001, most of the indices increased from 2001 to 2008, indicating a lessening of the price differential with the US over time. As clearly seen in Fig. 7 and explained below, the Laspeyres indices are greater than the Paasche indices in all instances and the ranking $L_B > L_M > P_M > P_B$ remains throughout for all countries considered. As a result of this ranking, the Fisher indices based on multilateral and bilateral samples, F_M and F_B, for a given country (which are the geometric means of the corresponding L and P indices) remain numerically close to each other at nearly all dates and thus provide a first order quantification of relative prices and their evolution.

As seen in Table 5 and Figure 5, the Fisher indices based on multilaterally matched samples, F_M, in 2000 range from 0.33 for Greece to 0.63 for Switzerland (and a suspicious 1.15 for Japan). In 2008, the range in F_M is slightly elevated with a low value of 0.43 for Taiwan and a high value of 0.82 for Switzerland. The most common trend in F_M is a decrease from 2000 to 2001, followed by a gradual increase until 2007 and, in several instances, an abrupt increase in 2008. One country, Saudi Arabia, shows a decreasing F_M over time, and two countries, Taiwan and the United Kingdom, show very little change over the 9 years of data.

The results for the Fisher index based on the much larger data base of bilaterally matched samples, F_B, (Table 6 and Figure 6) are generally similar to those observed for F_M. In 1999, F_B ranges from 0.27 in Taiwan to 0.86 in Japan, and in 2008 from 0.26 in Taiwan to 0.91 in Germany. The variations in F_B over time confirm: 1) a general decrease in drug prices in comparator countries compared to US from 1999 to 2001; 2) a general increase from 2001 to 2007; 3) an abrupt increase in 2008 in a few countries; 4) a relative decrease in prices over time in Saudi Arabia; and 5) little change over time in the UK and Taiwan. In addition the F_B index indicates little change over time in the average price of the pharmaceuticals considered in the bilateral analysis for Singapore compared to the US.

Including a discount of 8% in the US prices automatically increases all the indices by 8.7% ($1/0.92 = 1.087$), bringing the cost of drugs in the US closer to that of other countries. Whilst significant, the resulting change in the average values of the indices (e.g., from 0.43 to 0.47 for P_M, 0.56 to 0.61 for L_M and 0.49 to 0.45 for F_M across all countries for all years) is actually much smaller than the difference between P_B and L_B (0.35 and 0.72, respectively

averaged across all countries for all years) both of which represent defensible measures of relative drug prices in comparator countries and the US.

Indices based on multilaterally-matched sample, L_M and P_M, using UK as a base suggest that prices in other HIC evolved to become relatively higher than UK prices over the course of the decade. Whilst the UK starts the decade in the middle of the group of comparator countries, by 2008 it ties for the position of lowest relative prices. Indices based on bilaterally-matched samples, L_B and P_B, using UK as the base suggested a similar overall trend as those based on the multilaterally-matched sample. (See Appendix 2 for these indices: L_M^{UK}, P_M^{UK}, L_B^{UK}, and P_B^{UK}.) This result is consistent with the fact that drug prices in the UK remain relatively stable compared to the US during the period of the study whilst they increase in other countries.

Indices based on a multilaterally-matched sample using France as the base suggest French prices fell in the bottom third of HIC prices. Austrian prices dipped below French prices in one year, Saudi Arabia over 2 years, and Greece, Korea, Singapore, Spain, Taiwan, and UK over at least 4 years. Indices based on bilaterally-matched samples suggested that all other HIC had higher prices than in France during the period in question. Exceptions included Taiwan, Singapore, Korea and Spain in some years. See Appendix 2 for these indices: L_M^{FR}, P_M^{FR}, L_B^{FR}, and P_B^{FR}.

DISCUSSION

GETTING AN ACCURATE AND REPRESENTATIVE PICTURE OF PRICE DIFFERENCES AND THEIR TIME EVOLUTION USING MULTIPLE INDICES

As discussed in the introduction, the price differences in pharmaceuticals amongst countries are difficult to quantify because of variations in the availability of compounds and presentations and disparities in consumption patterns. To better understand how the Laspeyres (L) and Paasche (P) indices used together provide insight into the price differences amongst countries, it is useful to consider what factors affect the values of these two indices and the differences between them. There are two limiting cases in which the difference in prices between two countries is well-defined and can be captured in a single number: 1) when the factor of the prices between one country and another is the same for every pharmaceutical (e.g., all pharmaceuticals are 1.3 times more expensive in country A than in country B); or 2) when the consumption patterns for pharmaceuticals are identical in both

countries, such that an accurate quantification of overall relative prices is obtained by using the same relative quantity to weight each individual pharmaceutical price for both countries. In both of these limiting (and extremely unlikely) cases, the numerical values of the L and P indices are identical. The differences that are seen between these two indices stem from differences in consumption patterns and price sensitivity amongst countries: the more dissimilar the patterns of consumption for pharmaceuticals and the more responsive consumption is to price (or the price is responsive to consumption as a result of competition or regulation[15]) in the two countries being compared, the greater the difference between L and P. Because of the inverse relationship between usage and price, own-weighting provides a relatively lower average price, and the Laspeyres index is always larger than the Paasche index (L > P as can be seen in Tables 1-4). This result has been called the Serendipity Theorem by Samuelson and Swamy (1974).

As a result of their sensitivity to consumption patterns, the L and P indices are dependent on the size of the data-base from which they are calculated: the larger the number of samples being considered, the greater the range of differences in consumption patterns being captured. Because of the negative correlation between price and consumption, the net result is an increase in L and a decrease in P as the size of the data-base increases. Here we have considered multilaterally-matched samples, with a mean sample size of 146 (range 140 to 158), and bilaterally-matched samples, with a mean sample size of 1250 (range 745-2548). As can be seen in Tables 1-4, the Laspeyres indices based on bilaterally-matched samples are indeed always larger than those based on multilaterally-matched samples ($L_B > L_M$) and the reverse is true for the Paasche indices ($P_B < P_M$). The overall relationship $L_B > L_M > P_M > P_B$ for the indices averaged over 10 years is illustrated in Fig.7.

Together, the four indices, L_B, L_M, P_M and P_B, provide a useful estimation of the range of the overall differential in drug prices amongst countries. Further, the differences between the values of these four indices give some insight into the relative roles of consumption patterns and individual drug prices in causing the overall price differentials amongst countries. This is particularly useful when examining the relative evolution of drug prices over time. Consider, for example, the limit case in which all the prices in the US (or more generally in the reference

[15] The point here is that the relationship between price and consumption is not uni-directional. Prices can respond to changes in consumption as a result of competition (e.g. availability of several products with similar usage may drive down their prices) or as a result of regulation (e.g. because the pricing authority may force low prices on widely used drugs whilst allowing high prices on infrequently used drugs).

country) increase by the same factor λ, and all the prices in the comparator country, increase by a factor μ, from one year to another. Then, if there is no change in consumption patterns in the US and C, both the Laspeyres and the Paasche indices increase by the same factor μ/λ. Because consumption patterns change relatively slowly (i.e. there is typically less difference in the consumption patterns from year to year within a country than between two countries at any given time), similar relative increases in the values of the two indices are suggestive of relatively uniform differentials in price increases amongst countries. In contrast, differences in the relative increases in L and P from one year to another suggest a differential in the relative price increase of widely and sparsely used drugs, between the comparator country and the US.

COMPARISON OF MEAN LASPEYRES AND PAASCHE INDICES

Bilaterally-matched samples captured on average 85% of pharmaceuticals in a given country's market in any given year (ranging from 65% for France to 99% for Australia; see tables in Appendix 2). In eight countries, Finland, France, Italy, Korea, Spain, Portugal, Greece and the Netherlands, the total range of the bilateral index values is relatively narrow with a difference $L_B - P_B < 0.25$. In that situation, the bilateral Fisher index, F_B, which is the geometric mean of L_B and P_B, provides a reasonable and practically useful single number approximation of relative prices of a large fraction of pharmaceuticals in two countries. On this basis, it can be said that, on average over the ten years of the study, the manufacturer-level prices of pharmaceuticals were between 40% and 50% of US prices in Finland, France, Italy, Spain, Portugal, Greece and the Netherlands and somewhat lower in Korea (34%; see Table 6). For all other countries, the substantial differences in the values of L_B and P_B are indicative of disparities in consumption patterns that make the use of a single price ratio problematic if not meaningless for the basket of drugs included in the bilateral comparisons.

To the extent that the pharmaceuticals included in the multilaterally-matched samples represent an important part of the international market, the corresponding indices provide an interesting means of comparison between countries and the US. Multilaterally-matched samples captured on average 33% (ranging from 16% for Japan to 44% for Finland) of total country markets (by volume) in each year of the comparison. When the two multilateral indices, L_M and P_M, are close to each other, their mean value is indicative of the overall price differences for this important basket of pharmaceuticals. For all the countries except three – Japan, Singapore and Switzerland-- the average difference between L_M and P_M is less than or equal to 0.15. In this situation the corresponding Fisher index, F_M, provides a useful measure

of the price differential with the US. Accordingly, over the ten years of the study, the manufacturer prices of the pharmaceuticals included in the multilaterally matched samples for 16 countries -- Australia, Austria, Belgium, Canada, Finland, France, Germany, Greece, Italy, , Korea, Netherlands, Philippines, Poland, Portugal, South Africa, Saudi Arabia, , Spain, Sweden, and the United Kingdom-- were on average between 40% and 50% of the US prices, with only Taiwan below at 37%. Within a few percent, these price differences for "global" molecules are independent of whether they are weighted by US or domestic consumption patterns and they can thus be used for international policy decisions.

In one country, the L and P indices based on multilaterally matched samples show a very large mean difference: L_M-P_M = 0.49 for Japan. The most likely explanation for this singularity is that Japan and the US exhibit very large differences in their patterns of consumption for pharmaceuticals (which of course engenders differences in prices); this explanation is consistent with the very low fraction (16%) of the Japanese drug market that is included in the multilaterally-matched samples. Differences may be attributed to geographical barriers and the predominantly domestic nature of the Japanese market.

Effect of data-base (multilaterally- vs. bilaterally-matched samples) on indices

As discussed above, because larger data sets capture more differences in consumption patterns and price, the effect of the negative correlation between price and consumption on the corresponding indices is magnified. The net result is that the bilateral Laspeyres indices are always larger than the corresponding multilateral Laspeyres indices ($L_B > L_M$), and, vice versa, the bilateral Paasche indices are always smaller than the corresponding multilateral Paasche indices ($P_B < P_M$).

The differences between L_B and L_M are relatively small in several instances: the ten year average values of L_B and L_M are within 10% of each other for 12 out of 20 countries. This agreement indicates that, despite the relatively small data-base of the multilaterally-matched samples, the values of L_M provide a reasonably robust integration of the consumption patterns for comparing the pharmaceutical prices of many countries with US prices. Besides Japan (see above), four countries, Australia, Austria, Canada and Germany, exhibit large differences in the average values of L_B and L_M. Whilst the underlying reason is unknown, a likely possibility is that some pharmaceuticals that are included in the bilateral but not the multilateral sample are widely used and much cheaper in the US than in these countries.

As Laspeyres price indices use US weighting, the increase from L_M to L_B must be particularly sensitive to the negative relation between price and volume in the US. Vice-versa because P is using own-weighting for the comparative country, C, the decrease from P_M to P_B must depend chiefly on the negative relation between price and volume in country C. The generally larger difference observed between L_M and L_B than between P_M and P_B (Fig. 1) thus reflects in part the larger price elasticity in the free pricing US than in other countries. This result may be falsified in countries where price regulations are particularly effective at controlling the prices of highly used drugs. According to the study results this situation may obtain in France, Greece, Korea, Portugal, Spain and Taiwan, where the mean difference between L_M and L_B is smaller than between P_M and P_B (Figure 7).

In four countries, Korea, Japan, Saudi Arabia and Taiwan, there is a large difference between P_M and P_B. These are countries where the pattern of drug use is likely very different from the US as a result of cultural differences. In addition, in the case of Japan, the bilateral sampling only captures a small fraction of the market such that the corresponding indices are poor indicators of drug prices compared to the US.

In contrast in three countries, Germany, Singapore, and Austria, the difference between P_M and P_B is quite small; in other words there is little sensitivity to the change from multilateral to bilateral sampling when using own-weighting. The fraction of the pharmaceutical market captured by the multilateral sampling in these countries (31, 35, 30% respectively) is not particularly different from that of other countries (mean across all countries 33%) and the corresponding mean values of P_M are within the range of other countries (except for Singapore for which the mean P_M is low). The explanation for the similarity between P_M and P_B in these three countries must thus lie in the prices and consumption patterns of the drugs included in the bilateral samples and not in the multilateral samples. A likely explanation is that the drugs that are not included in the multilateral samples and are heavily used in these countries must have prices approximately P_B times cheaper than the US prices. It is interesting that in the case of Austria and Germany $P_M \approx P_B$ whilst $L_B >> L_M$. Some drugs that are not included in the multilateral samples must be more widely used and much cheaper in the US than in these two countries.

GENERAL EVOLUTION OF INDICES OVER TIME

As can be seen in Figures 1-4, the Laspeyres and Paasche indices show a generally increasing trend over time. As explained above, the relative changes in these indices over time provide

insight into the underlying evolution of consumption patterns and individual drug prices. It is thus convenient to normalize the indices to their value in a given reference year to study the change of drug prices relative to the US over time. Because 2001 is generally the year in which the indices were lowest, it was chosen as the reference year for our calculations. This choice avoids the complication posed by very large (and possibly wrong) values of indices for Japan and Canada in 1999 and 2000. The four indices, L_B, L_M, P_M and P_B, normalized to their 2001 values are given in Appendix 2.

As can be seen in 2001-based indices ($L_B^{2001base}$, $L_M^{2001base}$, $P_M^{2001base}$ and $P_B^{2001base}$, in Appendix **2**), for most countries, all four indices increase over time between 2001 and 2008 with a mean increase of about 50% for the Laspeyres indices and of 30% for the Paasche indices. The two exceptions are Saudi Arabia and the United Kingdom. In Saudi Arabia, all four indices decrease systematically over time whilst in the UK, all the indices remain approximately constant. In other words, whilst the drug prices in most high income countries increased compared to the US between 2001 and 2008, they decreased in Saudi Arabia and remained relatively constant in the UK. In the case of the UK this would be suggestive of an overall containment pressure from the combination of policy tools in place at the time, including health technology assessments and the Pharmaceutical Price Regulation Scheme (previous model), as well as policies promoting generic prescription and dispensing.

Differential increases in Laspeyres and Paasche indices

In most countries the relative increase in the Laspeyres indices, both L_B and L_M, are somewhat larger than the increases in the corresponding Paasche indices, P_B and P_M. This is what is expected as the negative relation between price and consumption tends to buffer the increase in the price average in each country calculated using the country's own weighting. The result is a relatively large increase in L because of the relatively small increase in US prices weighted by US consumption, and a relatively small increase in P because of the relatively small increase in the comparator country prices weighted by this country's consumption.

Interestingly, the relative increase in P_M is markedly larger in Canada than the relative increase in L_M and the same is true of the relative increase in P_B compared to L_B in Korea. A possibility is that some drugs that are widely used in these countries but not in the US may have become relatively more expensive in these countries compared to the US over time. Such an effect may be caused by changes in price regulations in Canada and Korea compared to free market forces in the US.

In five countries, the Netherlands, Portugal, Spain, Sweden and Taiwan (plus the UK), the relative increases in L_B and P_B are close to each other, possibly indicating a fairly uniform relative increase across all drugs compared to the US as explained above. The same is true for the relative increases in L_M and P_M in a subset of these countries --the Netherlands, Sweden and Taiwan-- plus Japan (and the UK), indicating a similar uniformity of relative price increases for the basket of about 150 global pharmaceuticals in these countries. In all these cases the increases in the corresponding Fisher indices provide good measures of the changes in drug prices relative to the US: a range of no increase (Taiwan) to a near doubling (Sweden, 0.36 to 0.69) for the bilaterally matched samples, and a more muted range from 23% (Taiwan, 0.35 to 0.43) to 46% (Sweden, 0.39 to 0.57) increase for the multilaterally matched sample.

DIFFERENTIAL INCREASES IN INDICES BASED ON BILATERAL AND MULTILATERAL SAMPLES

As can be seen in Appendix 2, no general pattern can be seen in the comparison of the relative increases of the Laspeyres indices based on multilateral and bilateral samples: for some countries L_B increases more than L_M over time whilst the opposite is true for other countries. This presumably reflects a wide range in the comparator countries pricing of some drugs that have a sizeable effect on the average prices weighted with US consumption patterns. Often these increases in Laspeyres indices likely reflect relative price increases in the comparator countries of drugs that are widely used in the US; in some cases these drugs are part of the basket of global (multilaterally matched) drugs; in some cases they are not.

In contrast, the relative increases of the Paasche indices based on multilateral and bilateral samples are rather consistent with each other: for many countries the relative increase in P_B over time is within 10% of the relative increase in P_M. The most likely underlying reason is that the relative increases in prices (compared to the US) for the relatively small basket of global pharmaceuticals and for the much larger baskets of drugs included in the bilateral samples were similar, and that the consumption patterns changed relatively little over time.

There are three countries in which the increases of P_M and P_B diverged markedly over time: P_M increased more slowly than P_B in Korea and faster in Canada and Taiwan. In the case of Canada and Korea, this unusual pattern is to be compared with the unexpected larger increase of Paasche indices over Laspeyres indices noted above. These interesting observations may reflect either unusual changes in prices of drugs that are widely used in these countries (presumably as a result of changes in price controls), or, possibly, a significant change in

consumption pattern. A detailed examination of the individual data sets is required to pinpoint the underlying causes.

Price Discounting

As competitive forces of the free market are the primary cause of downward pressure on prices in the US (i.e. there is relatively limited direct price regulation) and IMS data is limited to list price, an overall average off-invoice discount was assumed. Discounting of US prices was not assumed in the first instance in order to make this study comparable to previous studies (e.g. Danzon and Kim 1998). However, the fact that IMS prices do not include the numerous types of discounts offered in the US market results in an upward bias in US prices (the author confirmed that they had already been accounted for in the list prices of other countries). Whilst fragmented and difficult to reliably document on a country-wide basis, wholesale discounts to large payers, including pharmacy benefit managers (PBM), Medicare, Medicaid etc. are known to be very common across the US pharmaceutical market. Omitting discounts also leads to unrealistic differentials between US and foreign prices in that the downward pressure on prices felt through price regulation (utilized in most other HIC markets) is captured in IMS prices in that they affect prices pre-listing. As previous authors have noted in the past, discounting in the US market can be significant. In one of their analyses, Anderson and colleagues assumed a 20% discount in their study of the 30 pharmaceuticals with the highest total spending in the US (that were also sold in the comparator countries), based on the upper end of the discounts that private insurers negotiated with pharmaceutical companies within the context of the Medicare drug benefit programme[16]. Indeed leading pharmaceuticals are often very highly discounted (Danzon 2000). This study however used the Danzon and Furukawa estimate of 8% as the sample drew from a much broader basket of pharmaceuticals[17]. The estimate came from a study that looked in detail at the discounts offered by payor group in the US and is based on the average that the study found for all drugs across the US market. As explained in the Results section, the net effect of such discounting of US prices is to increase all indices by 8.7%. Whilst significant, such an increase does not change the broad features of our results, as can be seen from the results of the sensitivity analysis (see Appendix 2) where most of the indices would simply increase by 0.04 to 0.06. Nonetheless, if one takes the Laspeyres index based on

[16] The Anderson analysis assumed that Canada, France, and the United Kingdom paid the full average wholesale price.
[17] Danzon and Furukawa estimated adjustment for off-invoice discounts overall reduces U.S. prices by approximately 8%, which they found to also be comparable to previous estimates.

bilateral comparisons, L_B, as the measure of relative prices, discounting results in a change in ranking in 2008: when US off-invoice discounts are included the US falls to the position of 4th highest payer by 2008 in the global sample and becomes part of a general upper tier within the HIC group.

COMPARISON TO PREVIOUS STUDIES

Using undiscounted 1992 prices, Danzon and Chao concluded, based on bilateral Laspeyres indices, that the percentage foreign/US price differences were (here expressed in a commonly used, more easily compared, format): Canada +2, Germany +25, France, -32, Italy -13, Japan -12, and UK -17. This compares to an average for these countries across the ten years of our data, L_B, of: Canada +97 (+13)[18], Germany -8, France -49, Italy -37, Japan +21, UK -37. The relative standing of US prices was thus similar—that US prices fell in the middle of the selected comparator countries—albeit with significant differences in calculated relative prices. These differences are largely attributable to the larger sample used in our study compared to the Danzon and Chao study. Price relatives using Paasche index methods, P_B, in our 10-year study were very similar to Danzon and Chao estimates for 1992: Canada -55, France -67, Germany -60, Italy -51, Japan -54, UK -44 from Danzon and Chao compared to Canada -60, France -69, Germany -59, Italy -60, Japan -67, UK -64. As expected based on our discussion, Danzon and Chao study found ubiquitous or what they call "global" molecules to demonstrate smaller price differences than those based on the larger bilaterally-matched samples, in accord with our results. As also expected and similar to our study, indices of ubiquitous pharmaceuticals showed P/L ratios closer to unity than did the indices based on the larger bilaterally-matched samples, reflecting a lesser degree of variation across consumption patterns for global pharmaceuticals than for those that are not globally accessible.

Using undiscounted US prices in the first instance Anderson and colleagues determined price relatives for 2003, quantified by the Laspeyres index based on a small number of core products as follows: Canada -52, France -59, UK -47. This study found price relatives for France and UK for 2003 to be similar[19]. When using an average discount of 20% for US purchasers these results changed to the following: Canada -40, France -48, UK -34. Our

[18] As mentioned in the Discussion, this high value for Canada stems from outlier price relatives for the years 2003 and 2004, drastically increasing the average for the decade. Omitting the values for Canada in these years leads to an estimate of +13.

[19] Canadian price relatives were estimated to be much higher in 2003 when looking at the market more broadly.

calculated values of L_M show very similar price relatives for France and UK for 2003. Overall these comparative results suggest that leading US products are sold at lower prices in Canada than in the US but that overall Canadian prices of pharmaceuticals available in both countries have been higher than US prices in many years – this study suggesting an overall trend of Canadian prices starting below US prices 1999 and significantly surpassing them by 2008 (when determined by US consumption patterns, arguably of more relevance to policy-making in the US than in Canada).

It should be noted that in limiting the sample to 30 leading pharmaceuticals, the Anderson study sought to answer a specific question that was posed: "..whether the adoption of some mechanism of to control pharmaceutical spending such as price controls would allow for the elimination of the 'doughnut hole'" in the Medicare drug benefit program. It thus explicitly chose a more standardized approach to pharmaceutical price comparison over the representative approach utilized by Danzon and colleagues (Anderson et al. 2004).

LIMITATIONS OF THE STUDY

This study sought to examine relative prices across many different countries over a decade. It deliberately chose a very large sample of many different types of pharmaceuticals in order to get a picture of the overall market, based on the idea that valid measures of average price levels can only be obtained from comparisons of a comprehensive or representative sample of products that are appropriately weighted and follow standard index number methods (Danzon and Kim 1998). Indeed matching molecules by manufacturer, strength, pack or other attributes had previously been found to significantly reduce the sample size to only a tiny fraction of the national market and was likely to biased results (Danzon and Furukawa 2004). However, choosing representativeness over standardization does present important trade-offs in that we are not necessarily comparing prices across completely identical products.

Molecule prices were weighted by sales volumes across all products, packsizes, forms, and strengths. This weighted average price per molecule assumes that there is perfect substitution across products in the same ATC-3 class. This may not be accurate in all cases but is based on the general idea of bio-equivalence and the fact that reimbursement price set by third-party payers in many countries (US, Canada, Sweden, UK, etc.) recognize this equivalence (Danzon and Chao 2000).

Finally, it should be acknowledged that the data used in the analysis are not very recent and thus that findings may not reflect today's price differences across markets. One difference between today's market and the 2008 market when the data ended could be that the US now uses a greater share of generics amongst all prescription pharmaceuticals. The US Census Bureau estimates that from 2008 to 2010 this share has increased from 64% to 71% (Census Bureau 2012) and this percentage may have increased further since. Changes may have occurred since the introduction of coverage for most pharmaceuticals under Medicare Part D, which came into effect in 2006 as part of the Medicare Modernization Act. These rebates have been significant. In 2008 the rebates were estimated to be approximately 10% of total gross Part D drug costs, or worth $63 billion (HHS 2008). Also, prices in Europe may have decreased in recent years due to greater price control and clamping down on pharmaceutical budgets due to the recession.

CONCLUSION

Differences in consumption patterns make the calculation of relative drug prices very difficult. We have shown that a first order quantitative understanding of the relative prices of pharmaceuticals amongst countries can be obtained by using several indices, namely the Laspeyres, Paasche and Fisher indices based on multilaterally and bilaterally matched samples: L_B, L_M, P_M, P_B, F_M and F_B. As a result of the inverse relationship between usage and price, the Laspeyres indices (which uses weighting for the base country --the US in most of our study) is always larger than the Paasche indices (which use weighting for the comparator country) and this effect is magnified when the sample size is larger such that $L_B > L_M > P_M > P_B$.

Using data from the United States and 20 other high-income countries, over the period 1999-2008 we found that drug prices in the comparator countries were lower than in the US with few exceptions. The prices in the comparator countries became more similar to the US over the 10 year of the study. For a few countries similar values of the Laspeyres and Paasche indices ($L_B \approx L_M \approx P_M \approx P_B$) meant that their geometric averages, the Fisher index, F_M or F_B, provided a good single estimate of drug prices relative to the US. Based on small differences between multilateral indices ($L_M \approx P_M$), representative relative price of commonly found "ubiquitous" pharmaceuticals (which captured on average 33% of the various markets) compared to the US could be obtained by using the corresponding Fisher index, F_M, in more than half the comparator countries.

In a number of cases, the data showed unusual contrasts between the values of Laspeyres and Paasche indices based on the same sample, or between the same index based on multilaterally or bilaterally matched samples, or in the relative evolution of these four indices over time. Such contrasts served as flags indicating unusual features of the pharmaceutical market in individual countries during the period of the study. In several instances, a detailed examination of the indices led to a likely explanation in terms of differences or changes in pricing or consumption patterns between the comparator country and the US. In all such cases a detailed examination of the individual data sets would help to positively ascertain the underlying causes.

PAPER 3

NATIONAL PHARMACEUTICAL PRICES AND COUNTRY DEVELOPMENT: HOW DO ECONOMIC, SOCIAL, AND DEMOGRAPHIC FACTORS AFFECT PRICES AND HOW DO MIDDLE- AND HIGH-INCOME COUNTRIES COMPARE?

ABSTRACT

This paper seeks to understand the determinants of global pharmaceutical prices, focusing on the contribution of country-specific economic, social, and demographic characteristics, in addition to drug-specific properties such as quality and levels of competition in the market. In analyzing data from 33 middle- and high-income countries (MIC and HIC) over a 10-year period, this study is much larger than previous studies of medicine price determinants and is the first to consider the potential relationship of country social and demographic characteristics to pharmaceutical prices. In all countries the price of drugs was strongly negatively affected by their age and positively by national income per capita (although this latter effect was less strong in MIC than in HIC). In MIC, the percentage of old people was the strongest determinant of drug prices, most probably reflecting a rapid increase in demand. The length of time since launch of a drug in a country was strongly positively related with its price, likely a result of product recognition and associated marketing strategy and ensuing purchaser behavior. Overall, results suggest that prices offered to purchasers in MIC and HIC are affected differently by globalization and competition and that social and demographic differences in MIC give them notably different negotiation predisposition (i.e. different levels of leverage) that may deserve attention in global discussions surrounding fairer pricing and improving access to medicines.

INTRODUCTION

Whilst it is generally understood that access to pharmaceuticals varies across countries, little is known about what determines the price paid in each country. Indeed, the opaque nature of pricing and the vast disparities in access support the call for greater clarity on pricing and the demand for fairer global pricing strategies. The increasingly global nature of the pharmaceutical market along with the strong growth and the ensuing greater ability to afford

pharmaceuticals amongst middle-income economies such as China and parts of India further enhance the need for price information. This study looks at the determinants of pharmaceutical prices in middle- and high-income countries (henceforth referred to as MIC and HIC respectively). In contrast to other studies that have looked at determinants of price variation across countries, this study hypothesizes that country development characteristics (economic, social, and demographic) may influence the price at which pharmaceuticals are sold by manufacturers to the respective country market. The country development variables used in this analysis vary by country and over the period of a decade. The study also takes into account the influence of characteristics of the products themselves such as quality and competition within the market. Overall findings may be relevant for policies intended to improve access to pharmaceuticals via price through better knowledge of what influences price.

THE EXISTING LITERATURE

Pharmaceutical prices are not a new area of academic research. Indeed a few previous studies have looked at the determinants of prices within a country or subset of countries. Older studies (argued to be more biased in their analysis) include a 1994 estimate by the US Government Accounting Office which looked at the impact of national level regulation and competition on medicine prices. The study findings suggested that price differences between the US and the UK could be primarily attributed to the regulatory constraints affecting the ability of manufacturers to price their products freely. They also found time-on-market to be a determinant of the wide variation in price differentials for brand-name drugs across the two markets. The effect of competition on prices has also been examined in several studies (Danzon and Chao 2000, Kanavos, Costa-Font, and Seeley 2008), generally finding that it helped keep prices low in less regulated markets and in particular when drugs were off patent. However, findings from many of these cross-country analyses have been questioned due to inherent bias. Indeed standardizing across medicines internationally in order to get a broadly perceived representative sample is a complicated process that implies numerous trade-offs. For example, the greater the number of countries included in the comparison, the more difficult it is to match identical products—thus decreasing the size of the comparison sample and reducing the representativeness of the sample. Also, the more narrowly the sample is defined to ensure similarity of products, the less representative of the country's medicine market as a whole.

Whilst no methodology for cross-national drug price comparisons are perfect, certain methods are more appropriate than others, depending on the purpose of the comparison. This study largely utilizes methods put forth by Danzon and colleagues in the most comprehensive of all existing studies, dating from 2000 (Danzon and Chao 2000), in an attempt to include as many products and countries as possible whilst minimizing selection bias. The 2000 study looked at the influence of drug quality and market competition parameters on outpatient drug prices in 1992 across 7 HIC. It found cross-national price differences to reflect differences in product characteristics including product age, formulation, strength, pack-size, and in their implicit prices, which were a reflection of the regulatory regime in place. The authors concluded that strict price regulation systematically lowered prices for widely diffused molecules as well as for older ones and that generic competition lowered prices in less-regulated regimes. Since the Danzon study others have also looked at the issue of cross national prices. A 2011 study (Kanavos and Vandoros 2011) found that prices for a basket of 50 leading, original, branded medicines in the years 2004 and 2007 (total of 100 products, 68 unique molecules) across 15 OECD countries were affected by product age (time from product launch) and regulation. The focus on public prices highlighted the importance of distribution costs and taxes on price.

This study builds on previous cross-national price determinant studies but includes a much more comprehensive set of data both in terms of the number of countries (33) and the time frame covered (10 years). In addition this study examines the impact of country-specific growth and development factors on prices, influences that have not previously been explored.

MATERIALS AND METHODS

DATA SOURCE

The study used data provided by IMS Health for 1999 through the third quarter of 2008. Countries included 14 MIC[20] (Algeria, Brazil, Egypt, India, Indonesia, Malaysia, Mexico, Morocco, Philippines, Poland, South Africa, Thailand, Tunisia, Turkey) and 19 HIC (Australia, Austria, Belgium, Canada, Finland, France, Germany, Greece, Italy, Japan, Korea, Netherlands, Portugal, Saudi Arabia, Spain, Sweden, Switzerland, UK, United States). The selection of countries was a function of availability at the time. Prices represented ex-

[20] Income levels as defined by World Bank in 2008

manufacturer list prices (thus excluding taxes, distribution charges, dispensing mark-ups, etc.) per pharmaceutical sold to the retail market except in the case of a few countries for which data were aggregated from multiple distribution pathways[21]. Conversion from local currency was done by IMS Health using exchange rates in effect at time of sale. Prices were deflated using International Monetary Fund (IMF 2009)-estimated deflators. Pharmaceuticals with very small sales volumes over the 10-year period (those in the lowest 3%) were excluded and those composed of more than one molecule were excluded to avoid double counting. Prices were calculated from sales and volume figures that were extracted in terms of US dollars and standard units[22] respectively. Prices from the United States were based on drugstore, food store and mail service distribution channels.

STUDY DESIGN

Prices were decomposed using volume-weighted prices for all countries to take into account the respective market share of each product and thus its relevance within the market to see how the indicators influence the prices of products in demand. The sample for analysis first included volume-weighted prices of all pharmaceuticals found in any number of the thirty-three MIC and HIC (Sample 1). A Chow test (partial F-test) was run in order to see whether the predictor variables had different impacts on prices in MIC and HIC and as such whether separate analyses would be necessary. Separate analyses were then conducted for MIC and HIC on their own. (See description of samples listed in Table 1.) Collinearity tests were conducted to explore the degree of correlation between predictor variables.

As part of a sensitivity analysis prices were also decomposed in their un-weighted form in order to see influences on general price levels attained within country markets regardless of the relative importance of those pharmaceuticals to treatment (Samples 4, 5). All analyses were also repeated using only pharmaceuticals that were internationally relevant – those that could be found in all of the relevant countries (Samples 5-8). These have been called "ubiquitous" pharmaceuticals, specified for MIC, HIC, or MIC/HIC (combined). Table 1 describes the samples used in each of the analyses.

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[21] Singapore and Sweden prices include those for medicines destined for retail and hospitals. Indonesia and Malaysia prices include those destined for retail, hospitals, and dispensing doctors.

[22] Standard units are the smallest common dose unit. For oral solid forms this is one tablet or capsule, for syrup forms this is 5 ml, and for injectable forms this is one ampoule or vial. Defined Daily Doses were not available.

TABLE 1. DESCRIPTION OF SAMPLES

Primary analysis

1. Drugs found in any number of the countries (MIC and HIC), using prices weighted by volume in each country
2. Drugs found in any number of the MIC, prices weighted by volume in each country
3. Drugs found in any number of the HIC, using prices weighted by volume in each country

Sensitivity analysis

4. Drugs found in any number of the countries (MIC and/or HIC), using unweighted prices
5. Only drugs found in all 32 countries (those found across all MIC and HIC), using unweighted prices
6. Only drugs found in all 32 countries (those found across all MIC and HIC), using volume-weighted prices
7. Only drugs found in all 13 MIC markets, using volume-weighted prices
8. Only drugs found in all 19 HIC markets, using volume-weighted prices
9. Drugs found in any number of the countries (MIC and/or HIC), using volume-weighted prices. Estimation using fixed effects and limited variable selection to control for unobserved heterogeneity.
10. Drugs found in any number of the MIC, using volume-weighted prices. Estimation using fixed effects and limited variable selection to control for unobserved heterogeneity
11. Drugs found in any number of the HIC, using volume-weighted prices. Estimation using fixed effects, limited variable selection.
12. Drugs found in any number of the countries (MIC and/or HIC), using volume-weighted prices. Similar to Sample 1 but without variables for population growth, rural population, and elderly population to examine effects of suspected collinearity.
13. Drugs found in any number of the MIC, using volume-weighted prices. Similar to Sample 2 but without variable for rural population to examine effects of suspected collinearity.

TABLE 2. DESCRIPTION OF PREDICTOR VARIABLES

Variable	Variable description	Source	Hypothesis[1]
Global penetration	Number of countries in which molecule is available (natural log of)	IMS[2]	+
Strength	Strength of molecule (milligram) (natural log of)	IMS	+
Forms	Number of forms each molecule comes in within each country (natural log of)	IMS	+
Manufacturers	Number of manufacturers producing each molecule within each country (natural log of)	IMS	-
Therapeutic alternatives	Number of molecules per ATC3 indication per country (natural log of)	IMS	-
Age1	Months from global launch of molecule to end of 2008 (natural log of)	IMS	-
Age2	Months from in-country of molecule to end of 2008 (natural log of)	IMS	-
Entry lag	Months between first launch within the indication and in-country launch (natural log of)	IMS	+
Older population	Proportion of population aged 65 and over	WB[3]	-
GNI per capita	Gross National Income per capita (natural log of)	WB	+
Population growth	Annual population growth	WB	-
Rural population	Proportion of population living in rural areas	WB	+
Trade	Trade as a proportion of GDP	WB	-
Death	Crude death rate per 1000 people	WB	-
Year	Year		

1. Direction of predicted relationship with price; 2. IMS Health; 3. World Bank

Specifications of the empirical model are given in the following section. Several country-specific variables were used to define the size and nature of the market and population. Time varying country characteristics included gross national income (GNI) per capita, demographics relating to the annual population growth, the proportion of the population 65 years of age and over, the death rate, the proportion of the population living in rural areas, and the level of international trade as a proportion of GDP. These indicators were thought to be important given their links to or representation of absolute and relative health status, access to general health care, and both access to and affordability of pharmaceuticals. Substantive variation amongst indicator values was expected across countries, especially across MIC. The expected positive or negative effect of these variables on pharmaceutical prices are indicated by + or – in the last column of Table 2.

It was expected that higher GNI per capita would be associated with greater funds available for the purchase of pharmaceutical products and thus greater ability to pay higher prices. It was expected that a rapidly growing population and an older population would also be associated with a greater demand and scale-related price negotiation resulting in lower unit prices. Greater levels of international trade were expected to lead to better capabilities to negotiate lower prices. An increasing death rate was expected to be representative of a more unhealthy population and thus also related to greater demand and lower unit prices. Proportion of the population living in rural areas--a proxy for physical access in low and middle income countries—was expected to be associated with higher prices resulting from lower demand as well as higher transport costs where purchasing is decentralized. The lag time between the first launch within the indication and in-country launch of the drug ("entry lag") was used as a proxy for (inverse of) openness of the market (red tape to accrue administrative and regulation-related costs) and hypothesized to be positively related to price. (See Appendix 3 for full summary statistics pertaining to the respective variables)

Drug-specific variables were chosen to represent the quality of the drugs and the competitiveness of the market for those drugs. Global penetration was included as a measure of expected therapeutic value (Danzon and Chao 2000, Barral 1995) and included in analyses that did not require ubiquitous presence (Samples 1-4, 9-13). Molecule age was included as an inverse measure of therapeutic value of the molecule (Danzon and Chao 2000). It was included both as the time-since-global-launch of the product as well as time-since-in-country-launch of the product. This is based on the idea that the demand-side factor that is most

important in determining medicine price is the degree of therapeutic advance as compared to products already on the market. Greater advances lead to greater willingness-to-pay and a resulting ability for sellers to set higher prices without driving customers away (Comanor and Schweitzer 2007). The number of available forms of the pharmaceutical was taken as a proxy for choice and convenience and therefore expected to be positively related to price (Danzon and Chao 2000). Molecule strength was also included. However, as it was expressed in differing, incompatible formats (e.g. milligram, millilitre, vial), strength was only included in the analysis where it was expressed in milligram, the predominant form (these represented 63-73% of the overall data, depending on the model).

Competition was expected to be negatively related to price. Competition was included in the form of variables for the number of manufacturers producing each drug within each country and for therapeutic alternatives, the number of drugs in the indication. Year is included as a variable in order to help account for time-related changes that may affect price levels such as macroeconomic trends, levels of innovation, etc. A country dummy variable was also included to help control for heterogeneity in health care finance, delivery, advertising and other regulatory aspects -- sometimes known as "cultural block dummies" (Yip 2007).

SPECIFICATION OF EMPIRICAL MODEL

A regression model was estimated using panel data with random effects.

$$\ln P_{mit} = \alpha_i + \sum \beta Z_{it} + \sum \gamma X_{mt} + \varepsilon_{mit}$$

for molecule m, in country i, in year t.

The vector *Z* represented the country-specific predictor variables, whilst the vector X represented the drug-specific predictor variables. Log transformations were used for prices (ln P) and characteristics, reflecting proportional effects as they were not normally distributed. See Table 2 for a description of these characteristics.

In many cases a Hausman test is used to help choose between fixed and random effects. In this study a Hausman test could not be performed to help inform the choice between (the model failed to meet the asymptotic assumptions)[23]. The choice was therefore based on other considerations. Generally fixed effects are seen to be simple in that they rule out

[23] Some experts argue that the Hausman test is in any case "neither necessary nor sufficient" (Clark and Linzer 2012) to guide this main methodological decision.

heterogeneity bias and the beta coefficients can be thought to represent the 'causal effect' (Bell and Jones 2014). As such they have become the "gold standard" in many disciplines (Schurer and Yong 2012). However, in assuming a correlation between the error term and predictor variables and in order to be able to assess the predictors' net effect, fixed effects remove the effect of time-invariant characteristics from the explanatory variables. Whilst this is very useful in many study contexts, it also means that fixed-effects do not work well with time-invariant variables or data comprising slow-changing variables over time (Torres-Reyna 2011). In controlling out time-invariant variables, fixed effects models effectively remove context that may be of great interest. Random effects, for their part, assume that the error term is not correlated with the predictors so time-invariant variables can play a role as explanatory variables. They also allow us to generalize the inferences beyond the sample used in the model. However, this type of model requires the specification of those individual characteristics that may or may not influence the predictor variables. This is problematic when some variables are not available, leading to omitted variable bias in the model (Torres-Reyna 2011).

The choice of random effects in this study was based primarily on the desire to maintain the effect of time-invariant variables (and not "throw the baby out with the bath water"). However, as the assumptions of random effects (e.g. no omitted variable problem, unobserved heterogeneity) may not hold, a fixed effects model was also run on the time-varying selection of variables (indeed in this case a Hausman test confirmed the preference for fixed effects when this more limited set of variables was used). Results provided by the estimation using fixed effects using only time-varying variables were very similar to those from the random effects model.

RESULTS

Results of the primary regressions for the MIC and HIC data sets together (Sample 1) and separately (Samples 2 and 3) are shown in Table 3. With few exceptions all variables were significantly associated with price at 1% significance level in the regressions run on the combined MIC and HIC dataset. The two dominant predictor variables were the time-since-global-launch and the GNI per capita, with coefficients of -1.25 and +1.09, respectively (i.e., corresponding to -1.25% and + 1.09% change in price for 1% increase in each variable). The time-since-in-country-launch also proved to be an important predictor variable, with a

coefficient of +0.63. Other variables with a noteworthy association with price were the proportion of population over 65, the population growth, the number of countries in which the drug is available and the number of forms. Chow test (partial F-test) results were significant (F=439.26, prob>F=0.000), suggesting that the coefficients estimated over the country income groups were unequal, and therefore that separate analyses could be necessary. Importantly, a conservative cut-off value of 10 for the variance inflation factor (VIF) suggested that the GNI variable could be presenting collinearity in regressions on Sample 1 (VIF = 15.64). Indeed notable coefficients of correlation were detected between GNI and three other variables: 1) the proportion of population over 65 (0.84), population growth (-0.67), and rural population (-0.80). The potential importance of the collinearity detected in Sample 1 is discussed below. When the analysis was repeated without these latter three variables (Sample 12, see results in Appendix 3) the results were largely unchanged except for a small decrease in the strength of relationship between per capita GNI and price.

Results of the regression for the MIC data set only (Sample 2) also showed most variable coefficients to be significant at 1%. The three dominant predictor variables were the percent of people 65 and over, the time-since-global-launch and the time-since-in-country-launch, with coefficients of +1.27, -0.98 and +0.96, respectively. The GNI, the annual population growth and the number of manufacturers were also important predictor variables, with coefficients of +0.62, +0.43 and -0.30, respectively. Collinearity tests on Sample 2 suggest some collinearity between GNI and rural population (VIF of 13.58, 10.37 respectively and coefficient of correlation of -0.80). When the analysis was repeated without the variable for rural population (Sample 13 in Appendix 3) the results were essentially unchanged.

Results from HIC data only (Sample 3) showed all variable coefficients to be significant at 1%. The dominant predictor variables were the time-since-global-launch and the GNI, with coefficients of -1.49 and +1.28, respectively. The time-since-in-country-launch and the number of countries in which the drug is available were also important predictor variables, with coefficients of +0.60 and +0.42, respectively. Other noteworthy variables were the number of forms and the proportion of rural population. VIF indicated that the predictor variables had no significant collinearity in the HIC only data set. The lack of collinearity amongst independent variables in the HIC analysis in contrast to notable collinearity amongst variables in the MIC analysis is discussed in the latter section.

TABLE 3. PRIMARY ANALYSIS RESULTS

SAMPLE:		1	2	3
		MIC/HIC	MIC	HIC
	Hyp.			
Global penetration	+	0.289***	-0.0641	0.423***
		(0.0267)	(0.0608)	(0.0336)
Strength	+	0.0425***	0.0606***	0.0331***
		(0.00550)	(0.00874)	(0.00699)
Forms	+	-0.240***	-0.0474	-0.275***
		(0.0184)	(0.0292)	(0.0235)
Manufacturer	-	-0.157***	-0.304***	-0.101***
		(0.0130)	(0.0197)	(0.0173)
Therapeutic alternatives	-	-0.0903***	-0.0201	-0.151***
		(0.0138)	(0.0223)	(0.0177)
Time-since-global-launch	-	-1.254***	-0.982***	-1.485***
		(0.0183)	(0.0260)	(0.0255)
Time-since-incountry-launch	-	0.632***	0.963***	0.597***
		(0.0145)	(0.0240)	(0.0185)
Entry lag	+	0.0483***	0.00374	0.128***
		(0.0159)	(0.0272)	(0.0196)
Older population	-	0.220***	1.273***	0.0568***
		(0.00683)	(0.0577)	(0.00874)
GNI per capita	+	1.091***	0.615***	1.284***
		(0.0250)	(0.0447)	(0.0323)
Population growth	-	0.233***	0.426***	-0.140***
		(0.0156)	(0.0376)	(0.0203)
Rural population	+	0.0633***	0.0168	0.198***
		(0.00546)	(0.0105)	(0.00923)
Trade	-	-0.0074***	-0.0095***	-.00220***
		(0.000542)	(0.00125)	(0.000665)
Death rate	-	0.154***	0.144***	0.159***
		(0.00760)	(0.0109)	(0.0133)
Year		-0.202***	-0.301***	-0.148***
		(0.00303)	(0.00911)	(0.00419)
Constant		371.1***	572.3***	262.4***
		(5.955)	(18.05)	(8.256)
Observations		396,914	114,485	281,926
Number of id		84,970	30,040	54,830
R^2 (overall)		0.1502	0.1917	0.1121

1. Drugs found in any number of the countries (MIC and HIC), using prices weighted by volume in each country

2. Drugs found in any number of the MIC, prices weighted by volume in each country

3. Drugs found in any number of the HIC, using prices weighted by volume in each country

TABLE 4. SENSITIVITY ANALYSIS RESULTS

Sample:	**4**	**5**	**6**	**7**	**8**
Global penetration	0.231***				
	(0.0128)				
Strength	0.179***	0.175***	0.0787***	0.0704***	0.0614***
	(0.00263)	(0.00395)	(0.00958)	(0.0120)	(0.0105)
Forms	-0.0114	-0.115***	-0.401***	-0.0109	-0.441***
	(0.00879)	(0.0127)	(0.0307)	(0.0362)	(0.0349)
Manufacturer	-0.406***	-0.304***	-0.0932***	-0.394***	-0.0322
	(0.00621)	(0.00987)	(0.0239)	(0.0284)	(0.0276)
Therapeutic alternatives	-0.254***	-0.378***	0.0682**	0.265***	0.0716**
	(0.00660)	(0.0135)	(0.0327)	(0.0410)	(0.0343)
Time-since-global-launch	-1.189***	-1.157***	-0.980***	-0.816***	-1.447***
	(0.00873)	(0.0134)	(0.0325)	(0.0410)	(0.0386)
Time-since-incountry-lnch.	-0.179***	-0.145***	0.592***	0.927***	0.674***
	(0.00677)	(0.0103)	(0.0254)	(0.0339)	(0.0282)
Entry lag	-0.070***	-0.076***	-0.184***	-0.285***	0.0994***
	(0.00763)	(0.00928)	(0.0224)	(0.0367)	(0.0224)
Older population	0.0455***	0.0505***	0.182***	1.088***	0.0598***
	(0.00113)	(0.00186)	(0.0111)	(0.0754)	(0.0124)
GNI per capita	0.453***	0.430***	1.214***	0.833***	1.272***
	(0.00410)	(0.00651)	(0.0390)	(0.0580)	(0.0449)
Population growth	-0.036***	-0.059***	0.338***	0.498***	-0.082***
	(0.00257)	(0.00408)	(0.0245)	(0.0486)	(0.0285)
Rural population	0.0918***	0.0934***	0.0787***	0.00667	0.217***
	(0.000903)	(0.00141)	(0.00838)	(0.0135)	(0.0127)
Trade	-0.010***	-0.0102***	-0.00452***	-0.00473***	-0.00117
	(8.90e-05)	(0.000142)	(0.000851)	(0.00162)	(0.000926)
Death rate	-0.012***	-0.0247***	0.147***	0.156***	0.0938***
	(0.00125)	(0.00196)	(0.0117)	(0.0141)	(0.0187)
Year	-0.021***	-0.0248***	-0.203***	-0.305***	-0.159***
	(0.000499)	(0.000785)	(0.00471)	(0.0118)	(0.00579)
Constant	40.00***	46.75***	373.4***	579.1***	285.9***
	(0.982)	(1.541)	(9.221)	(23.35)	(11.39)
Observations	398,338	157,118	156,552	65,925	140,155
Number of id	84,971	33,519	33,518	17,104	27,396
R^2 (overall)	0.4381	0.5127	0.1563	0.2016	0.1157

4. Drugs found in any number of the countries (MIC and/or HIC), using unweighted prices
5. Only drugs found in all 32 countries (those found across all MIC and HIC), using unweighted prices
6. Only drugs found in all 32 countries (those found across all MIC and HIC), using volume-weighted prices
7. Only drugs found in all 13 MIC markets, using volume-weighted prices
8. Only drugs found in all 19 HIC markets, using volume-weighted prices

TABLE 5. SENSITIVITY ANALYSIS RESULTS

Sample:	**9**	**10**	**11**
Older population	0.167***	1.030***	0.0230***
	(0.00383)	(0.0325)	(0.00463)
GNI per capita	1.098***	0.699***	1.360***
	(0.0136)	(0.0241)	(0.0180)
Population growth	0.152***	0.410***	-0.222***
	(0.00849)	(0.0189)	(0.0111)
Rural population	0.0304***	-0.0329***	0.124***
	(0.00287)	(0.00543)	(0.00489)
Trade	-0.00716***	-0.00744***	-0.00221***
	(0.000299)	(0.000674)	(0.000363)
Death rate	0.118***	0.140***	0.177***
	(0.00388)	(0.00544)	(0.00744)
Year	-0.199***	-0.317***	-0.153***
	(0.00158)	(0.00496)	(0.00216)
Constant	362.3***	604.0***	267.6***
	(3.123)	(9.899)	(4.271)
Observations	1,194,291	319,524	874,767
R-squared	0.045	0.092	0.036
Number of id	250,788	85,687	165,101

9. Drugs found in any number of the countries (MICs and/or HICs), using volume-weighted prices. Estimation using fixed effects and limited variable selection to control for unobserved heterogeneity.
10. Drugs found in any number of the MICs, using volume-weighted prices. Estimation using fixed effects and limited variable selection to control for unobserved heterogeneity.
11. Drugs found in any number of the HICs, using volume-weighted prices. Estimation using fixed effects, limited variable selection.

TABLE 6. SENSITIVITY ANALYSIS RESULTS

Sample:	**12**	**13**
Global penetration	0.297***	-0.0645
	(0.0268)	(0.0608)
Strength	0.0428***	0.0607***
	(0.00551)	(0.00875)
Form count	-0.248***	-0.0474
	(0.0184)	(0.0292)
Manufacturer count	-0.152***	-0.304***
	(0.0130)	(0.0197)
Therapeutic alternatives	-0.0886***	-0.0202
	(0.0138)	(0.0223)
Time-since-global-launch	-1.254***	-0.982***
	(0.0183)	(0.0260)
Time-since-incountry-lnch.	0.638***	0.963***
	(0.0145)	(0.0240)
Entry lag	0.0476***	0.00396
	(0.0159)	(0.0272)
GNI per capita	0.827***	0.590***
	(0.0239)	(0.0419)
Trade	-0.00219***	-0.00810***
	(0.000485)	(0.000882)
Death rate	0.176***	0.142***
	(0.00730)	(0.0108)
Year	-0.161***	-0.307***
	(0.00210)	(0.00843)
Older population		1.253***
		(0.0563)
Population growth		0.421***
		(0.0375)
Constant	295.4***	584.1***
	(4.010)	(16.50)
Observations	396,914	114,485
Number of id	84,970	30,040
R^2 (overall)	0.1484	0.1918

12. Drugs found in any number of the countries (MICs and/or HICs), using volume-weighted prices. Similar to Sample 1 but without variables for population growth, rural population, and elderly population to examine effects of suspected collinearity.
13. Drugs found in any number of the MICs, using volume-weighted prices. Similar to Sample 2 but without variable for rural population to examine effects of suspected collinearity.

Results of the sensitivity analyses are shown in Tables 4-6. When un-weighted prices (prices detached from their relative use) were used in the combined MIC/HIC dataset (Sample 4) the time-since-global-launch and the GNI per capita remained the two dominant predictor variables, although the coefficient for GNI decreased to +0.45 from +1.09 in sample 1. Interestingly, the coefficient for time-since-in-country-launch became negative: -0.18 compared to + 0.63 in sample 1. When the combined, un-weighted sample was restricted to only ubiquitous molecules (Sample 5 compared to Sample 4) small changes were detected such as a slightly weaker relationship between number of manufacturers to price and a slightly stronger relationship between therapeutic alternatives to price in the analysis of ubiquitous molecules.

Restricting the combined MIC/HIC, volume-weighted sample to ubiquitous pharmaceuticals only (Sample 6) resulted in some small changes in variable coefficients. For example, (comparing analyses of Sample 6 to Sample 1) form count became more closely associated with price, both measures of molecule age became less closely associated with price, entry lag became negative (in line with the study hypothesis) and more closely associated with price, population age became less associated with price, GNI per capita became more closely associated with price, population growth became more closely associated with price.

Restricting the MIC sample to ubiquitous molecules only (Sample 7 compared to Sample 2) led to the coefficient for entry lag becoming more strongly and negatively associated to price (result became statistically significant) and to therapeutic alternatives becoming more strongly and positive associated to price (and result became significant). All other coefficients stayed approximately the same. Restricting the HIC sample to ubiquitous molecules only (Sample 8 compared to Sample 3) led to small changes such as form count becoming more closely associated to price, number of manufacturers less closely associated to price, therapeutic alternatives became less strongly associated with price but this relationship became positive.

Differences between MIC and HIC ubiquitous samples (Sample 7 versus Sample 8) demonstrate a larger influence of several variables in high-income countries than middle-income countries. These include time-since-global-launch (price decreasing by 1.45% in high-income countries for every month compared to 0.81% in middle-income countries), GNI per capita (a 1.27% increase in price for one percent increase in per capita GNI in HIC versus 0.83% in MIC), and form count (0.44% versus 0.01% decrease in price for very one percent increase in form count). Variable coefficients that were on the contrary greater in MIC than HIC included elderly population (1.09% in increase in price for a one percent increase in

elderly population in MIC versus 0.06% increase in HIC) and population growth (0.5% increase in price for a 1% increase in population growth in MIC compared to a 0.08% *decrease* in price in HIC). Variable coefficients that were fairly consistent across MIC and HIC include drug strength, death rate and trade.

The more limited analysis focussing on the influence of only time varying, country-specific variables was also run using fixed effects (Samples 9-11, see descriptions in Table 1, see results in Appendix 3). As in the primary analysis of the study, all variable coefficients were highly significant and some notable differences were detected between MIC and HIC. For example, the relationship between the proportion of the population 65 and over and pharmaceutical price was much stronger in MIC than HIC (in the latter the relationship was weak). Per capita GNI was on the contrary much more closely related to price in HIC than in MIC. Population growth was found to have a positive relationship with price in MIC but a negative relationship with price in HIC. Proportion of the population living in rural areas was found to be negatively related to price in MIC and positively related to price in HIC, although neither of these relationships was particularly strong. Trade and death rate demonstrated a fairly consistent relationship with price across MIC and HIC. These results largely echoed the findings of the primary analysis.

DISCUSSION

Regressions on pharmaceutical price in this large, multi-country, multi-year dataset suggest that country development, in addition to the characteristics of the drugs themselves, had a significant influence on drug prices in MIC and HIC in the first decade of the 2000s. Generally there was a significant influence of economic, social, and demographic indicators across all samples analysed[24]. This suggests that many country- and population-specific factors—in addition to characteristics of the pharmaceuticals themselves--were significantly associated with the drug prices offered at the manufacturer level.

COMBINED MIC AND HIC RESULTS

Overall two predictor variables, time-since-global-launch and per capita GNI, had a particularly strong relation with price: as expected, the price of drugs generally decreased with

[24] Almost all variable coefficients were robust across all samples. Where there were exceptions at least one other indicator within the same proxy group (e.g. economic, social, or demographic) held within the sample.

their age and increased with purchasing power in a country (although this latter effect was less strong in MIC than in HIC as discussed below). Another very important predictor variable was the time-since-in-country-launch, but its relation to price was positive instead of negative as expected. One explanation for this surprising result may be the effect of patient and prescriber experience with known drugs, along with marketing and reputation building. This explanation is supported by the analysis with un-weighted prices for the combined MIC/HIC dataset (Samples 4 and 5) where the coefficient for time-since-in-country-launch became negative (-0.18/-0.15) as was initially expected. In other words it was the price of commonly used drugs (rather than widely available) that increased with time of use in a given country, driving the observed positive correlation. Greater product recognition over time (enhanced through product marketing) could be leading to greater willingness-to-pay. In some cases (especially in MIC) this may also coincide with limited availability, which in turn could increase expressed willingness-to-pay in the face of scarcity. It should also be noted that in-country launch may be conducted by a different corporation than global launch (which is usually done by the large, international mother company, generally based in HIC), especially in less familiar markets such as in MIC. This can lead to different pricing strategies overall. For example, products may launch at a relatively low price and be increased as they secure a position within formularies and generally amongst prescribers. Also, in cases where parallel importation or external reference pricing is a threat, prices may be kept elevated where competitive forces would normally have lowered them.

Two other country-specific predictor variables with noteworthy coefficients in the combined MIC and HIC data sets also had an opposite than expected relation to price: the percent of population 65 and over and the annual population growth both showed positive rather than negative correlations with drug prices. This result may not be meaningful as these variables exhibited high collinearity with GNI, a strong positive predictor of price. This collinearity is largely due to the large differences between these parameters in MIC and HIC: 6.8 ± 3.1% people 65 and over in MIC compared to 15.5 ± 3.7% in HIC, and a population growth rate of 1.3 ± 0.4% per annum in MIC compared to 0.50 ± 0.5% in HIC. It is noteworthy that the correlation between these parameters and price became much weaker when the sample was not volume-weighted (Samples 4 and 5), and the correlation with population growth even became negative. As in the case of the time-since-in-country-launch, it is the price of heavily used drugs that drives these positive correlations. (See below for differences between MIC and HIC.)

The negative correlation of the number of forms and the positive correlation of death rate with price were also contrary to the study hypothesis. In the case of the number of forms it is possible that the resulting availability of choice had a competitive effect to lower prices instead of reflecting quality. Although the coefficient for death rate was not particularly large (+0.15), the positive correlation suggests that the existence of a sicker population may have dampened the ability to negotiate lower prices and thereby put relatively less healthy countries at a price disadvantage. In both cases the coefficients became much smaller when the samples were not volume-weighted (Samples 4 and 5). Again, it is the price of heavily used drugs that was responsible for these counterintuitive correlations.

Differences between MIC and HIC

The results of the separate analyses on the MIC and HIC data sets showed interesting differences in the relative importance of predictor variables. Most notable is the strong correlation between population age and drug prices in MIC that is not seen in HIC, with coefficients relating drug prices and the proportion of the population 65 and over of +1.27 and + 0.06, respectively. Whilst this positive relation is in the expected direction, the difference between MIC and HIC is a key finding of this study (and one that is not an artefact of parameter collinearities). The explanation is likely linked to two key factors: 1) the very high demand for drugs by older people, and 2) the very rapid increase in the proportion of old people in MIC. As noted above, in HIC the proportion of people older than 65 is above 15% on average and increases slowly along with life expectancy. As a result the supply and demand in HIC pharmaceutical markets are in reasonable balance. In MIC, in contrast, the proportion of people 65 and over is on average less than 7% in 1999 and increases very rapidly, with a projection to surpass 15% around 2020 in many countries (WHO 2011). The very strong correlation between population age and drug prices in MIC thus likely reflects a rapidly increasing demand that is not matched by a corresponding level of supply. This situation is likely to persist in these countries until the proportion of old people begins to stabilize.

Another significant difference between MIC and HIC was the much weaker correlation with per capita GNI and price in MIC compared to HIC. This echoes previous work finding that national income was inconsistently related to pharmaceutical prices (Morel, McGuire and Mossialos 2011). This result likely reflects the much greater importance of demographic

variables[25] such as population age (see above) and population growth in determining price in MIC. Indeed the rate of population growth had a high positive correlation with price in MIC whilst it had a much weaker and negative correlation in HIC (and in our study hypothesis). These findings suggest that ageing and fast population growth stress the system in a way that ultimately hinders early price negotiation capabilities and, more broadly, that volume-related trends did not behave in a normal way and that basic price negotiation techniques were either not being used or were unsuccessful.

The relationships between the respective drug characteristics and price also differed between MIC and HIC. The contrasting relative importance of the two molecule age variables between MIC and HIC was interesting. Time-since-global-launch was found to have a substantially stronger relationship to price than time-since-in-country-launch in HIC whilst the reverse was found in MIC. The magnitude of these two variable age-related coefficients were approximately similar (although were inversely related as mentioned above) in MIC whilst in HIC the magnitude of the relationship of time-to-global-launch with price was much greater than the relationship of time-to-in-country-launch with price. Such findings may suggest differing effects of globalization on competition. Purchasers in MIC do not see the same price reductions that HIC do even when the drugs are no longer cutting-edge therapies. Future research should focus more closely on these relationships, perhaps as part of a country-by-country analysis. In addition, the number of manufacturers producing a pharmaceutical was found to have a stronger price dampening effect in MIC than HIC. This could have implications for policy strategies aimed at increasing access to pharmaceuticals through the expansion of licensing.

OVERALL EFFECT OF FOCUSSING ON PAN-AVAILABLE DRUGS

Restricting the sample to ubiquitous pharmaceuticals led to a smaller sample but also one that led to some more firm conclusions about the effect of product characteristics, especially in the case of MIC (Sample 7) [26]. Results suggest that MIC may be affected differently by globalization and competition. For example, findings from this more focussed sample suggest that the number of therapeutic alternatives were more closely related to price in MIC than in HIC. Interestingly the relationship between this variable and price switched from

[25] It should be noted that some collinearity was detected between per capita GNI and these demographic characteristics in the combined MIC/HIC sample, however, these were not detected when the sample was separated by income group.
[26] Almost all variables in the MIC analysis became statistically significant.

being negatively associated with price in the primary analysis (as was hypothesized) to being positively associated with price for both MIC and HIC when focussing in on ubiquitous pharmaceuticals. The magnitude of association was however weak in the case of HIC. Results from this more limited sample also suggest that entry lag was more closely and inversely related to price in MIC compared to HIC. The predicted negative association between entry lag and price in MIC compared to a positive association in HIC could suggest that manufacturers selling to MIC seek compensatory returns where they encounter red tape slowing market entry. The effect of form count remained weak for MIC but became more pronounced for HIC.

Overall effect of focussing on available drugs but not weighting them by volume

Interestingly leaving prices unweighted gave results that were closer to the original study hypotheses. The effects of the number of therapeutic alternatives, time-since-in-country-launch, entry lag, population growth, and death rate were all associated with price in the hypothesized direction. Compared to the results from the volume-weighted samples, therapeutic alternatives became notably more closely associated with price. Also, where it had been un-intuitively weak in all volume-weighted analyses, product strength became notably more closely associated with price when prices were left unweighted. GNI per capita became less closely associated with price. Aside from this last result these results are interesting in that they may suggest that the price of available pharmaceuticals do act in a fairly predictable manner. However, this predictability is limited to those that are available, not necessarily those that are routinely used. Indeed overall the findings from this study suggest that when looking at purchased pharmaceuticals (volume-weighted samples) the predictability of influence on price from product characteristics and country development indicators diminishes.

Study limitations

This study focuses on the price of products being sold to the retail market. As such it excludes others such as those sold directly to hospitals, for example. Prices reflect only manufacturer level prices, not prices paid by patients, the latter being influenced by other factors such as wholesaler and retailer distribution mark-ups, dispensing fees, taxation, etc. As such, policy relevance is limited to the more upstream aspects that determine accessibility of medicines to a country generally, not the downstream aspects that determine final accessibility to the patient (although of course the former does impact the latter).

On a technical level the study also has limitations. For example, the significance of country cultural block variables suggests that regulation, national payment structures, and other nationally-driven laws and processes could have a significant role in price determination. However these country characteristics were not closely examined. Finally, potential endogeneity and omitted variable bias could be problematic. Ideally the study would have instrumental variables to limit such problems however all those identified were weak. Greater analysis of this merits future exploration.

CONCLUSION

Results from this study confirm that the stages and evolution of country development are significantly associated with the pharmaceutical prices paid in middle- and high-income countries. On the whole, all else being equal, richer countries pay higher prices; more open and competitive markets pay lower prices; populations that were elderly pay higher prices; drugs that are newer to the global marketplace are more expensive. However, findings also point to important nuances in how these factors affect price and highlight important differences in the association of economic, demographic and social variables to pharmaceutical prices in middle- and high-income countries that lead to inherent differences in the ability to negotiate prices. Overall an older population and a higher death rate may dampen the ability to negotiate lower prices and thereby put relatively less healthy countries at a price disadvantage. The effect of having a significant proportion of the population 65 and over has a particularly strong bearing on prices in middle-income countries. Population growth, which is occurring much faster in MIC, also appears to disadvantage price negotiations. Middle-income countries also do not benefit from the effects of competition and globalization in the same way.

Looking to the future, one might predict that despite strong economic growth in several middle-income countries, prices may not follow suit. Indeed price trends detected in high-income countries will not necessarily be mirrored in richer middle-income countries given numerous price confounding effects of demographics and social development. As such, any response to the call for fairer pricing in medicines in middle-income countries should be nuanced. Whilst on the one hand countries should be expected to pay more than their lesser developed country counterparts as they themselves grow richer, their ability to adapt to the competitive global marketplace shouldn't be assumed to be on par with negotiators in the

richest countries. Conversely, lack of predictability and resorting to the threat of price regulation by new governments hinders normal market price movements and can hinder the ability of negotiators in MICs to gain access to the amount of drugs needed at a good price over the longer-term (indeed lurching movements towards price regulation may further reduce the ability to reap any advantages of competition and globalization). This can be disastrous in countries facing particularly difficult health challenges resulting from fast population growth or an aging population. Economies of scale are badly needed in negotiating price in such cases.

If the international community is committed to seeing fairer pricing of medicines, a nuanced approach is merited – based on finding ways to improve the negotiating power of middle-income countries in price discussions whilst also ensuring greater contribution relative to lesser developed country counterparts, where normal market functioning is rare due to poor resources and very limited infrastructure. Pooled funding mechanisms, for example, may be useful to improve leverage amongst MICs whilst maintaining control closer to country-level decisions-makers, payers, and relevant populations from which demand derives. Alternatively external, top-down mechanisms may be needed to circumvent the difficulties in achieving prices in-line with affordability and country development. Indeed internationally-supported institutions could be used to secure prices more in line with relative affordability and to improve the availability of drugs most needed in these populations.

In sum, the variation in relative and absolute influence of economic, social, and demographic variables detected in this study suggests some potentially important differences in how country drug prices are affected by these factors, giving MIC and HIC an overall different predisposition that deserves more explicit attention in global discussions surrounding fairer pricing and better access to medicines.

PAPER 4

PHARMACEUTICAL MARKETS ACROSS OECD COUNTRIES: HOW DO THE MARKETS DIFFER AND WHAT ROLE DO HEALTH SYSTEM STRUCTURES HAVE IN DETERMINING SUCH DIFFERENCES?

INTRODUCTION

Cross-national markets are increasingly of interest to politicians, civil society, and industry. This is particularly the case of goods like pharmaceuticals, access to which can be a matter of life and death, and which raise a number of normative issues. While countries sharing common key characteristics such as geographic situation and wealth might be expected to interact in a similar way with such markets—and thereby see similar prices and similar levels of consumption—country market trends are in fact more complex. The unique nature of each culture and market system leads to differences in the volume levels and prices at which similar goods are consumed. This study focusses on the ways in which the various countries within the wealthy group, the Organisation for Economic Co-operation and Development (OECD), have similarities and differences within their pharmaceutical markets. It uses the US market as the reference case, and explores whether similarities and differences amongst pharmaceutical markets can be explained by the characteristics of the health system that dominates in each country.

This study achieves this by building a picture of each national market, constructing price indices for individual markets for each the 10 years for which data were available. It then explores whether the type of health system or its main characteristics are related to pharmaceutical price levels or to other attributes of the various national markets. This study also examines how the relative prices of pharmaceuticals depend on what specific parts of the market (e.g. originators, generics) are compared and how the national markets differ in terms of key attributes such as levels of generic penetration, predominance of originator pharmaceuticals, predominance of over-the-counter pharmaceuticals, range in therapeutics, diversity in products available, therapeutic similarity to the US, and overall congruence with US market by volume (see Methods for further descriptions of these variables).

METHODS

COUNTRY SELECTION

As a group, OECD countries are of particular interest in that they have been relatively successful in fulfilling their mandate of maximizing economic growth and wealth creation--accounting for most of the world's wealth, trade and development aid. But their success in strengthening social objectives has been questioned (OECD 2002) and their stated mission of "improv[ing] economic and social well-being of people around the world (OECD 2015)" has not been proven. Indeed a key aim of the OECD is "to contribute to the expansion of world trade on a multilateral, non-discriminatory basis in accordance with international obligations" (Article 1 of its founding Convention) and this involves a "shared commitment to market economies backed by democratic institutions and focused on the wellbeing of all citizens" (OECD 2015). On a technical and practical front, OECD countries constitute an interesting group for this study for much is known about the economic and political structures that influence how an individual country adapts to globalizing forces within trade and the wider economy. Indeed the OECD classification of health systems is one of the best known typologies (the typology used in this work is an adaptation of the original OECD classification). While the OECD itself analyses and compares data (e.g. life expectancy at birth, number of doctor visits per capita per annum, pharmaceutical consumption and sales, etc.) to predict future trends and set international standards on a range of topics, including those in the health field, it does not examine pharmaceutical price relatives or market characteristics in detail. For example OECD publishes aggregate CPI data for all items, as well as individually for food, and energy. With regard to the pharmaceutical market the OECD looks at the share of generics in the market. However, it does not examine individual country pharmaceutical markets in much detail nor does it compare prices at which pharmaceuticals are available.

BUILDING A PICTURE OF THE PHARMACEUTICAL MARKET BY COUNTRY

Price indices were constructed for each country included in the extensively cited Böhm study (2013)[27] and for which price and volume data were available. Prices were calculated initially per standard unit, bilaterally-matched between the country in question and the United States in order to maximize sample size and seek overall market representativeness, and then

[27] Which builds on the original OECD health system classification.

aggregated upwards using the Fisher "Ideal" price index formula (see Introduction of this dissertation for a discussion on the merits of this index). To make comparisons possible, all price indices constructed represent prices relative to US prices, with the latter holding at the index value of one. Price indices were first constructed for the overall pharmaceutical market within each country and then restricted to only originator brand pharmaceuticals and only unbranded (here called "generic") pharmaceuticals.

Range in therapeutics was defined as the number of unique ATCMOLs (a variable combining anatomic therapeutic category and molecule) on the market[28]. Diversity in product availability was defined as the number of molecule presentations[29]. Therapeutic similarity to US market (how similar countries are to the US in terms of the drug choices they make for a given condition) was defined as the number of unique ATCMOLs matching with the US. Overall congruence with US market (how similar countries are to the US in terms of the volumes of each drug purchased) was defined as the proportion of total country market (by volume) matching with the US. Proportions of molecule presentations that were completely generic, originator brands, and OTC were also calculated for each national market.

HEALTH SYSTEM CLASSIFICATION

The oft-mentioned OECD classification of health systems (OECD 1987) in wealthy Western countries suggests three main health system types: the National Health Service (NHS), the social health insurance model (SHI), and the private health insurance model (PHI). The NHS model includes universal coverage, funding from general taxation, and public ownership of health infrastructure. The SHI model is a combination of universal coverage and funding primarily from employer/employee contributions, along with public or private delivery. Finally, in the PHI model, private insurance provides coverage and acts as the main funding source, while health care delivery is characterized by private ownership.

Böhm and colleagues (2013) have more recently refined this typology by proposing a hierarchy of actors and functions, which is much referenced classification of OECD health systems. The typology considers three core dimensions of health system: regulation, financing and provision of services and three types of actors including state, societal (private

[28] This aggregate identifier was first used by Danzon and Chao 2000. It allows for the same molecule to be counted separately for each of its respective uses.
[29] Molecules can differ along numerous lines such as therapeutic use, strength per dose, packaging, etc. All presentations are included in this measure.

non-profit) and private (for-profit) actors, reflecting the long-established trichotomy of state, society, and market that predominates in the social sciences.

Regulation refers largely to coordination or governance and includes numerous "objects" of regulation including coverage, administration of financing, provider remuneration, patient access to providers, and benefits packages (Böhm 2013). State-led or command-and-control systems constitute one of the main classes within regulation – here described as statist. Non-governmental dominance in regulation refers to networks, collegiality, or corporatism – here described as corporatist. Finally, the market itself can also be a mode of regulation – here described as private.

The financing dimension is characterized by general or earmarked tax revenues in the case of state financing. Böhm and colleagues highlight the lack of link between tax financing and direct entitlements to services. Social insurance involves parafiscal levies—often related to income--flowing to funds entirely separate from government and indeed to which government has no access. Social insurance contributions do lead to direct entitlement to services and are independent of individual health risks, thereby maintaining some redistributive elements. Private insurance and out-of-pocket payments take place in the private sector and are closely related to individual health risks.

The service provision dimension is measured using an index depending on the role of public, societal, or private providers.

Crucial to the classification of Böhm and coworkers is the idea of a hierarchy of dimensions (regulation > financing > provision) and amongst actors (state > society > private) with the dominant actor within the higher levels restricting the potential range of actors at the subordinate levels. The degree of collectivization (state being the highest, followed by society and then private) of superior dimensions is considered to limit the plausible attributes of the subordinate dimensions in that the subordinate ones can only have an equal or lower degree of collectivization. For example, state regulation is a prerequisite for tax funding, and tax funding is a prerequisite for public service provision (Böhm 2013). The authors suggest a trade-off between a public interest in health care and free market normativity in capitalist societies. This leads to democratic governments having to justify any state intervention using reasons of market failure or in the name of achieving distributive goals. Health care being both prone to market failures and a good example of a merit good, state involvement in it is easily justified – though it may occur at highly variable levels.

If state involvement is limited to the regulation dimension then systems can achieve "the highest potential for goal-attaining with lowest economic 'disturbance'. But access for high-risk and poor groups can only be guaranteed through the state (Böhm 2013). Therefore, to maintain high levels of coverage for all, the state either finances healthcare out of its own coffers or it grants privileges to societal actors to raise the necessary funds. While the result is not absolute state dominance, it still represents a high degree of state intervention in the economy since public money subsidizes market prices of providers or patients, thereby distorting demand. Yet provision can also be accessed by non-profit providers, which still represents heavy market intervention, although less intensive than state provision. Böhm and colleagues highlight the critical backdrop --the onus of legitimizing public involvement, which runs counter to the present norm of free enterprise and the interests of rent-seeking private actors. This onus increases at each stage of the process: during phases of welfare state expansion, regulation is the first area of public involvement in healthcare, followed by financing, and finally by service provision. Conversely during phases of retrenchment, service provision is most vulnerable to privatization (Böhm 2013).

Böhm and colleagues's framework allows for the number of plausible health system types to expand to five: National Health Service, National Health Insurance, Etatist Social Health Insurance, Social Health Insurance and the Private Health System (see Figure 1). National Health Service types give a dominant role to the state in all three dimensions. In National Health Insurance Systems the state also dominates regulatory powers but services are contracted out to for-profit providers. While the state also maintains regulatory power in the Etatist Social Health System, it grants privileges for financing and provision of health services to societal actors such as sickness funds with their own health facilities. In the Social Health System powers are decentralized in all dimensions, leaving corporatist actors dominating in regulation and financing and provision privatized to for-profit providers. Finally, the last plausible health system type, the Private Health System, is the only one to have financing devolved to private insurance or out-of-pocket payments.

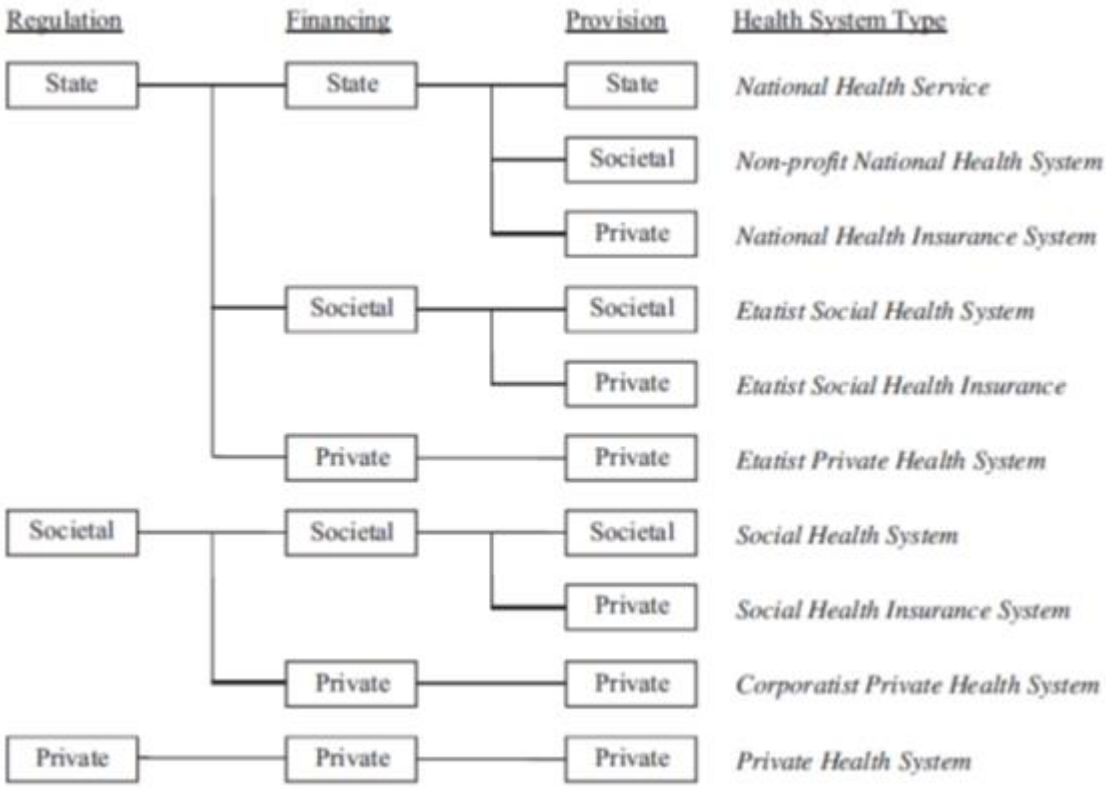
To classify the health systems of different countries, Böhm and co-workers (Böhm 2013), obtained information concerning the regulatory dimension from WHO HiT reviews. Classification of financing was based on 2008 OECD Health Data, which provides health expenditure, differentiating between agents (such as the state/government, society/social security funds, private insurers, and patients), with the largest share determining the classification. Classification of provision was based on the service provision index previously

developed by Rothgang H, Cacace M, Frisina L, Grimmeisen S, Schmid A, Wendt C. (2010), weighted in terms of relative share of health expenditure. Contrary to other studies, the Böhm classification was developed deductively, looking at all possible types, rather than inductively through observations of existing systems. Results of the classification are shown in Figure 2.

FIGURE 1. POSSIBLE HEALTH SYSTEM TYPOLOGIES BASED ON DEDUCTIVE METHOD. LIKELY COMBINATIONS PRESENTED IN BOLD (BÖHM 2013)

#	Healthcare system type	R	F	P	Cases
1	**National Health Service**	**St**	**St**	**St**	**Denmark, Finland, Iceland, Norway, Sweden, Portugal, Spain, UK**
2	Non-profit National Health System	St	St	So	
3	**National Health Insurance**	**St**	**St**	**Pr**	**Australia, Canada, Ireland, New Zealand, Italy**
4	State-based mixed-type	St	So	St	
5	State-based mixed-type	St	Pr	St	
6	State-based mixed-type	So	St	St	
7	State-based mixed-type	Pr	St	St	
8	Etatist Social Health System	St	So	So	
9	Social-based mixed-type	So	St	So	
10	**Social-based mixed-type**	**So**	**So**	**St**	**Slovenia**
11	Social Health System	So	So	So	
12	**Social Health Insurance**	**So**	**So**	**Pr**	**Austria*, Germany, Luxembourg, Switzerland***
13	Social-based mixed-type	So	Pr	So	
14	Social-based mixed-type	Pr	So	So	
15	Etatist Private Health System	St	Pr	Pr	
16	Private-based mixed-type	Pr	St	Pr	
17	Private-based mixed-type	Pr	Pr	St	
18	Corporatist Private Health System	So	Pr	Pr	
19	Private-based mixed-type	Pr	So	Pr	
20	Private-based mixed-type	Pr	Pr	So	
21	**Private Health System**	**Pr**	**Pr**	**Pr**	**USA**
22	Completely mixed-type	St	Pr	So	
23	**Etatist Social Health Insurance**	**St**	**So**	**Pr**	**Belgium, Estonia, France, Czech Republic, Hungary, Netherlands, Poland, Slovakia, Israel*†, Japan†, Korea***
24	Completely mixed-type	Pr	St	So	
25	Completelymixed-type	Pr	So	St	
26	Completelymixed-type	So	St	Pr	
27	Completelymixed-type	So	Pr	St	

FIGURE 2. RESULT OF BÖHM CLASSIFICATION, UTILIZED IN THIS STUDY



National Health Service: Denmark, Finland, Iceland, Norway, Sweden, Portugal, Spain, United Kingdom

National Health Insurance: Australia, Canada, Ireland, New Zealand, Italy

Private Health System: United States

Etatist Social Health Insurance: Belgium, Estonia, France, Czech Republic, Hungary, Netherlands, Poland, Slovakia, Israel, Japan, Korea

DETECTING RELATIONSHIPS BETWEEN HEALTH SYSTEM AND PHARMACEUTICAL MARKET ATTRIBUTES

In this study, the strength of association between variables (e.g.., price indices and characteristics of health care systems) was measured using simple, pairwise correlations. These were undertaken to examine the relationship between health system typologies (overall system and categorization of regulation, financing, and provision) and pharmaceutical price and market make-up (proportion of originator brand pharmaceuticals, proportion of generic pharmaceuticals, proportion of over-the-counter (OTC) pharmaceuticals). Strength of

association was then examined between each health system typology and broader characteristics of the pharmaceutical market—including range of therapeutics, diversity in product availability, therapeutic similarity to the US market, and overall congruence with the US market.

For inclusion in this study a country had to be a member of the Organisation for Economic Co-operation and Development (OECD), have been assigned a health system classification by Böhm and colleagues (2013), and have been included in the list of countries for which price data were available (in the IMS price database).

RESULTS

Price indices based on the entire pharmaceutical market suggested that prices in OECD were on average approximately half of US prices in the 10 years of the study period (see Figures 3-5), with an overall average of 0.49 amongst all comparator countries. The average price ratios compared to the US ranged from 0.32 for Poland to 0.83 for Canada. Switzerland had the second highest average ratio with 0.66 across the 10 years. The price ratios changed over time, with an average increase from 0.50 to 0.62 for all the countries over the 10 years of the study. An early dip in 2000 was followed by a steady rise, and then a sharp increase in the last year of the study due largely to a changes in relative prices from Austria, Germany, and Sweden. It should be noted that there were some unusual changes noted in prices of drugs that are widely used in Canada and Australia, presumably as a result of changes in price controls. Data error also cannot be excluded as a cause. These are discussed in a little more detail in Paper 2 but a detailed examination of the individual data sets is required to confidently pinpoint the underlying causes.

Price indices relative to the US were even lower when they were restricted to originator pharmaceuticals (Figures 6-7), with an overall average of 0.41, ranging from 0.31 for Greece and 0.32 for Portugal up to 0.60 for Japan. The relative trend amongst these price indices were similar to those for all pharmaceuticals but with a hump around 2003-2004 for most countries.

Strikingly, when the sample was restricted to generic pharmaceuticals only, prices in comparator countries were much higher (Figures 8-10), many of them surpassing US prices. This ranged from 0.56 for Korea and 0.64 for Poland up to 1.56 for Switzerland, 1.86 for

Australia, and 2.57 for Canada[30]. The overall average for this sample was 1.15, suggesting that prices for generic pharmaceuticals in other OECD countries were close to US prices in the years of the study. The predominance of these types of pharmaceuticals within each of the national markets is shown in Figure 11, the proportion being significantly higher amongst generic pharmaceuticals (average of 37%) than originator brands (average of 16%). Australia saw particularly high prices for generic pharmaceuticals in the early years of the study but these then joined the norm. Canada, began with generic prices marginally above US prices but then saw a sharp increase in 2003, a dip in 2006, and another sharp increase in 2007-2008.

Range in therapeutics (number of unique ATCMOLs available) across national markets as a whole averaged 1368, with a low value of 792 for Finland and a high value of 2532 for Germany (Figure 12). Diversity in products available (number of molecule presentations) across the national markets averaged 10,090, ranging from 4283 for Finland to 33,957 for Germany (Figure 13). Therapeutic similarity to the US (number of unique ATCMOLs matching with the US) averaged 1310 ATCMOLs, with again a low value for Finland (775) and a high value for Germany (2444; Figure 14). Overall congruence with US market by volume (proportion of total country market matching with the US by volume) averaged 84%, ranging from 65% for France to 99% for Australia (Figure 15).

Most correlation coefficients did not suggest notable relationships between pharmaceutical prices and health system typology and characteristics (Figure 16). However, the one coefficient that did stand out suggested a moderate relationship between the prices of pharmaceuticals across the markets and the regulatory system in place. Strength of association between market characteristics and health system typology and characteristics was fairly weak across the board (Figure 16), yet, again with some notable exceptions. Range of therapeutics and therapeutic similarity to the US both had a moderately strong association to regulation. Overall health system type had only weak associations to the market characteristics being measured.

[30] As noted earlier in this dissertation there were two years of price data from Canada that appeared conspicuously high and thus this 10-year average may be an overestimate.

Figure 3. Price indices, all pharmaceuticals

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
AUSTRALIA	0.54	0.44	0.38	0.36	0.43	0.49	0.63	0.56	0.60	0.60
AUSTRIA	0.72	0.47	0.50	0.50	0.49	0.53	0.48	0.48	0.54	0.67
BELGIUM	0.52	0.43	0.42	0.44	0.52	0.56	0.55	0.55	0.48	0.77
CANADA	0.42	0.43	0.42	0.64	1.58	1.49	0.88	0.92	0.79	0.79
FINLAND	0.35	0.32	0.35	0.37	0.44	0.48	0.48	0.46	0.54	0.65
FRANCE		0.29	0.33	0.33	0.38	0.43	0.44	0.43	0.46	0.49
GERMANY	0.59	0.45	0.51	0.49	0.58	0.63	0.63	0.61	0.65	0.91
GREECE	0.30	0.25	0.29	0.31	0.38	0.44	0.45	0.47	0.51	0.58
ITALY	0.52	0.46	0.43	0.43	0.49	0.50	0.48	0.48	0.54	0.65
JAPAN	0.86	0.90	0.57	0.54	0.54	0.55	0.55	0.51	0.53	0.65
KOREA	0.30	0.24	0.26	0.29	0.30	0.33	0.38	0.43	0.47	0.40
NETHERLANDS	0.53	0.42	0.43	0.44	0.51	0.53	0.51	0.50	0.56	0.57
POLAND	0.28	0.27	0.30	0.29	0.33	0.32	0.34	0.33	0.33	0.42
PORTUGAL	0.49	0.41	0.39	0.40	0.46	0.50	0.49	0.47	0.49	0.54
SPAIN	0.40	0.34	0.33	0.34	0.40	0.43	0.42	0.42	0.45	0.50
SWEDEN	0.40	0.35	0.36	0.38	0.44	0.48	0.48	0.49	0.46	0.69
SWITZERLAND	0.70	0.58	0.57	0.62	0.70	0.75	0.69	0.63	0.62	0.71
UNITED KINGDOM	0.52	0.46	0.44	0.45	0.47	0.51	0.47	0.46	0.51	0.47

Figure 4. Price index trends over 10-year study period, all pharmaceuticals[31]

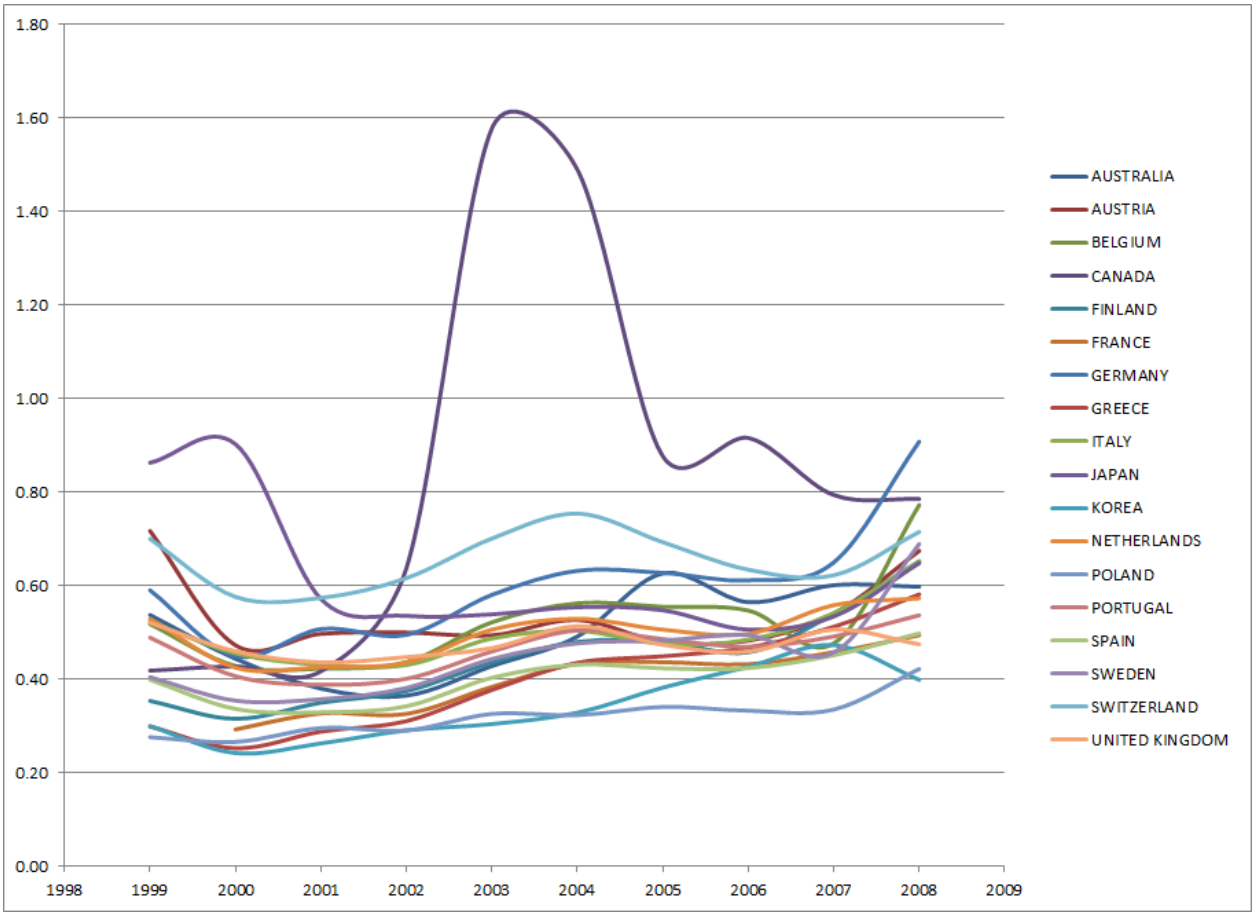


Figure 5. Price index trends over 10-year study period, all pharmaceuticals (note: graph excludes Canada in order to see price relatives in greater detail)

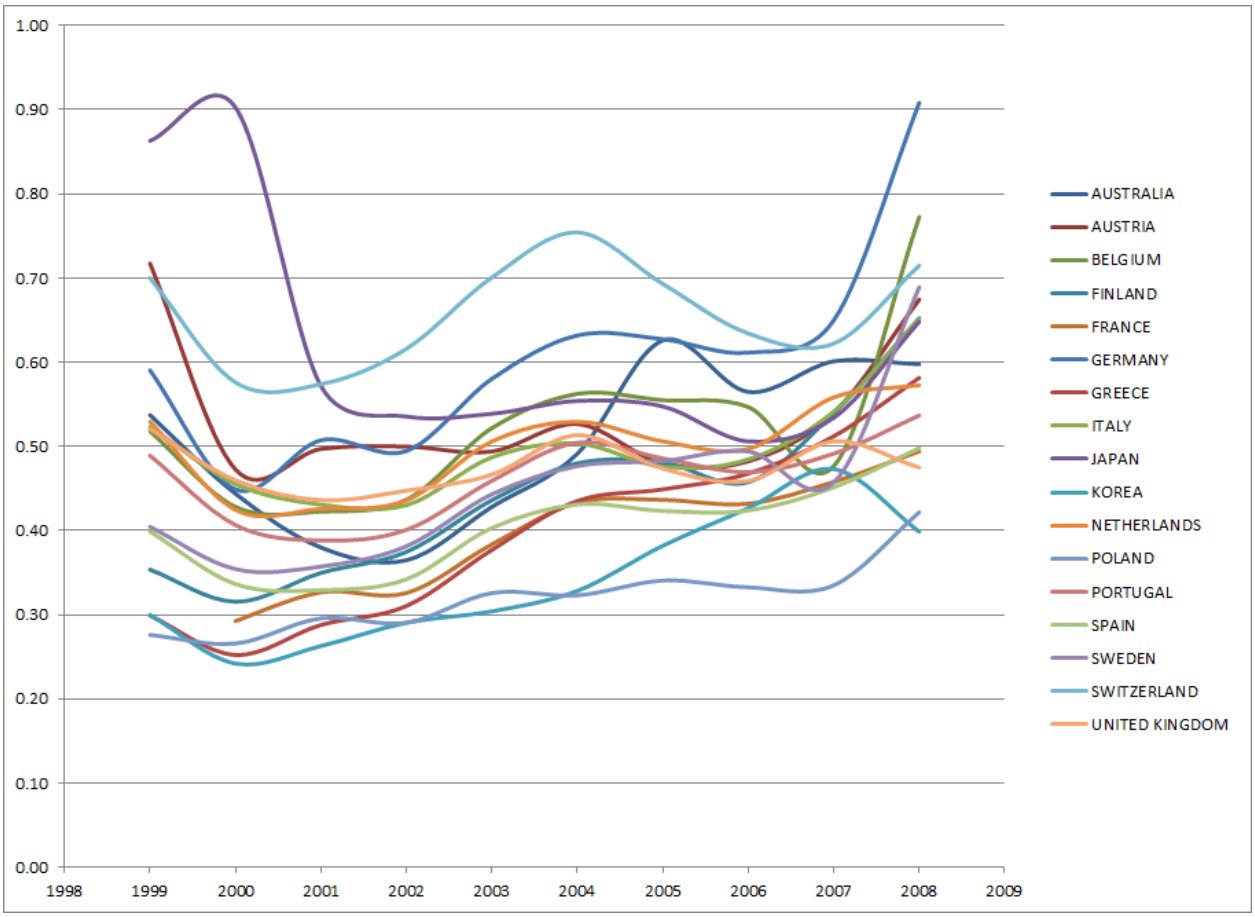


Figure 6. Price indices, originator brands only

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
AUSTRALIA	0.38	0.33	0.29	0.31	0.36	0.39	0.38	0.35	0.36	0.37
AUSTRIA	0.38	0.32	0.30	0.32	0.39	0.41	0.39	0.39	0.42	0.44
BELGIUM	0.44	0.37	0.35	0.36	0.44	0.45	0.42	0.41	0.45	0.47
FINLAND	0.47	0.39	0.35	0.35	0.41	0.43	0.40	0.38	0.41	0.43
FRANCE		0.29	0.27	0.27	0.33	0.37	0.36	0.37	0.38	0.42
GERMANY	0.43	0.38	0.36	0.37	0.45	0.50	0.49	0.50	0.53	0.58
ITALY	0.39	0.33	0.31	0.31	0.35	0.36	0.33	0.32	0.32	0.33
JAPAN	1.31	1.29	0.41	0.41	0.44	0.45	0.43	0.40	0.39	0.43
KOREA	0.38	0.38	0.31	0.32	0.33	0.32	0.36	0.38	0.39	0.34
NETHERLANDS	0.63	0.51	0.45	0.44	0.49	0.51	0.49	0.47	0.50	0.53
POLAND	0.39	0.36	0.34	0.33	0.36	0.34	0.34	0.34	0.34	0.39
PORTUGAL	0.34	0.29	0.27	0.29	0.34	0.36	0.33	0.31	0.32	0.32
SPAIN	0.38	0.32	0.29	0.31	0.36	0.38	0.36	0.35	0.36	0.37
SWEDEN	0.43	0.38	0.33	0.34	0.40	0.44	0.43	0.43	0.46	0.48
SWITZERLAND	0.49	0.42	0.42	0.46	0.54	0.56	0.53	0.51	0.52	0.55
UNITED KINGDOM	0.53	0.47	0.42	0.43	0.45	0.48	0.43	0.43	0.45	0.42
CANADA	0.49	0.48	0.45	0.44	0.47	0.51	0.52	0.54	0.55	0.55
GREECE	0.27	0.23	0.23	0.25	0.31	0.35	0.35	0.36	0.39	0.40

Figure 7. Price index trends, originator brands only (note: graph excludes two outlier index values for Japan 1999-2000 in order to see trends more clearly.)

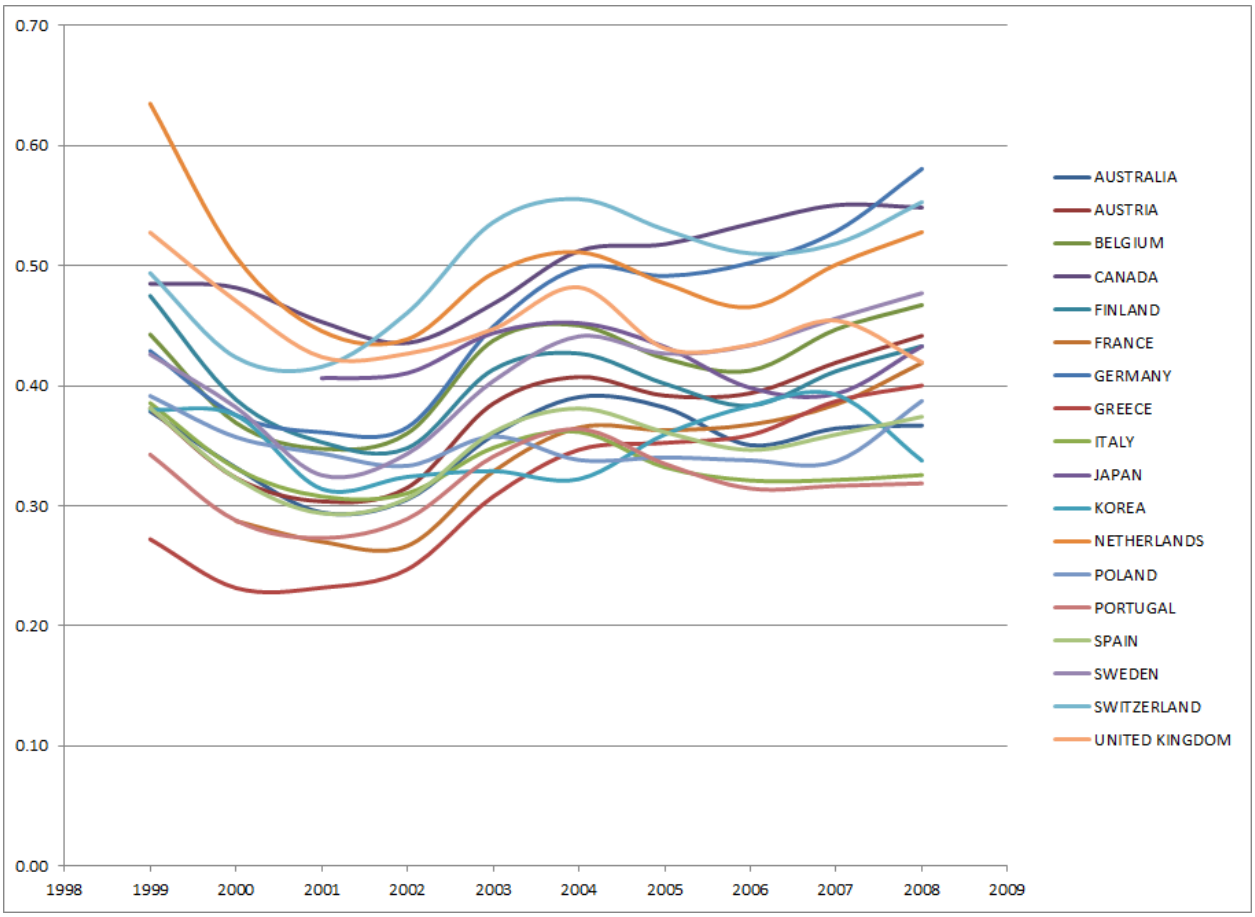
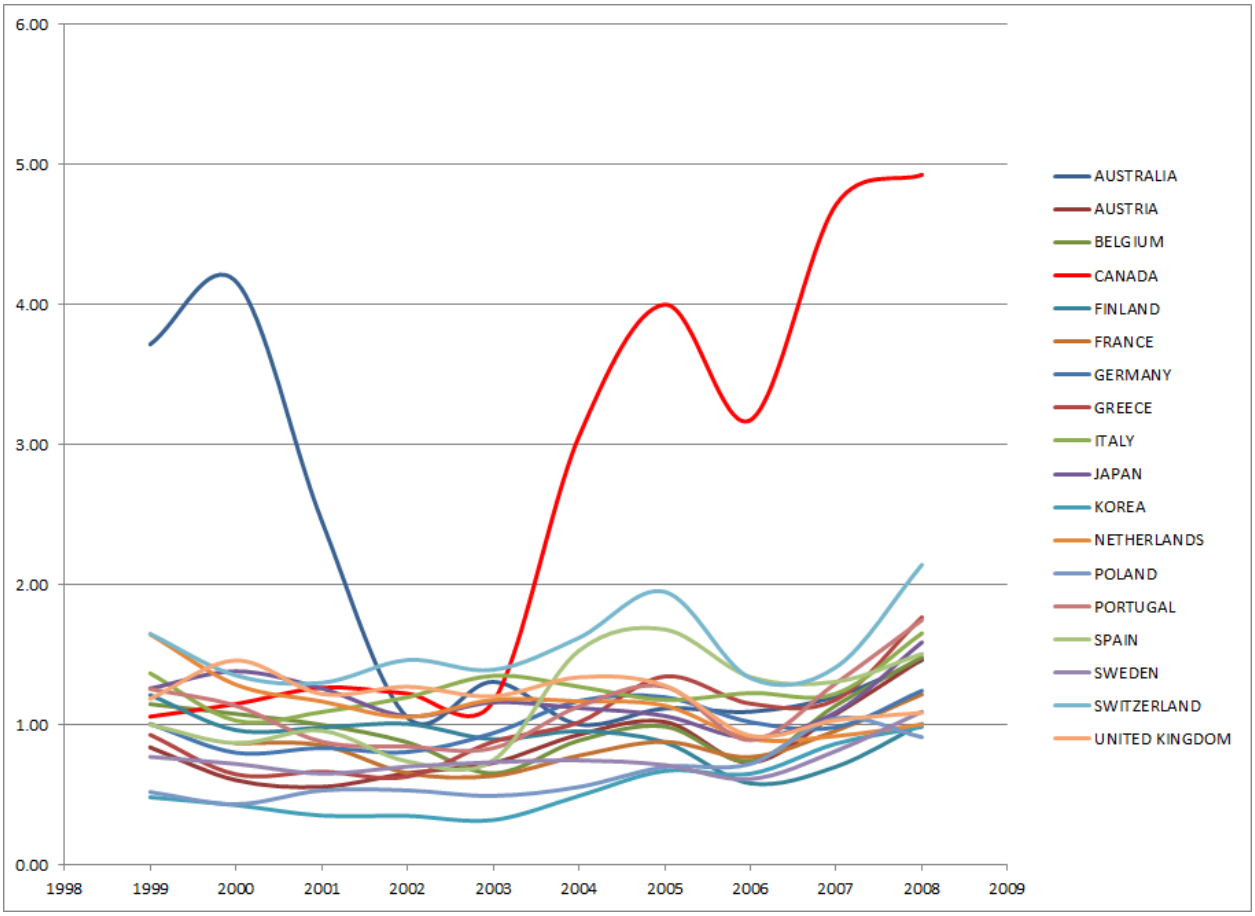


Figure 8. Price indices, generic pharmaceuticals only

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
AUSTRALIA	3.72	4.16	2.46	1.05	1.31	1.00	1.12	1.09	1.20	1.46
AUSTRIA	0.84	0.61	0.56	0.65	0.73	0.93	1.02	0.73	1.08	1.47
BELGIUM	1.15	1.08	1.00	0.88	0.65	0.89	0.99	0.74	1.14	1.48
CANADA	1.06	1.15	1.26	1.22	1.16	3.06	4.00	3.18	4.72	4.93
FINLAND	1.21	0.96	0.98	1.01	0.90	0.95	0.88	0.58	0.70	1.01
FRANCE		0.87	0.85	0.66	0.63	0.78	0.88	0.77	0.96	1.22
GERMANY	1.01	0.80	0.84	0.81	0.94	1.17	1.20	1.02	0.98	1.24
GREECE	0.93	0.65	0.67	0.63	0.88	1.02	1.35	1.15	1.18	1.77
ITALY	1.37	1.03	1.09	1.20	1.35	1.27	1.18	1.23	1.22	1.65
JAPAN	1.26	1.38	1.26	1.06	1.16	1.12	1.06	0.91	1.09	1.59
KOREA	0.48	0.43	0.35	0.35	0.32	0.49	0.67	0.65	0.87	0.99
NETHERLANDS	1.65	1.29	1.17	1.06	1.18	1.17	1.14	0.90	0.92	1.00
POLAND	0.52	0.43	0.53	0.53	0.49	0.56	0.70	0.72	1.05	0.91
PORTUGAL	1.26	1.14	0.88	0.84	0.83	1.13	1.27	0.89	1.30	1.75
SPAIN	1.00	0.87	0.96	0.74	0.75	1.53	1.68	1.34	1.31	1.51
SWEDEN	0.77	0.72	0.65	0.70	0.73	0.75	0.71	0.61	0.81	1.09
SWITZERLAND	1.65	1.35	1.30	1.46	1.39	1.62	1.95	1.33	1.41	2.14
UNITED KINGDOM	1.19	1.46	1.22	1.27	1.20	1.34	1.28	0.92	1.03	1.09

FIGURE 9. PRICE INDEX TRENDS, GENERIC PHARMACEUTICALS ONLY[32]



[32] Canada and Australia demonstrated conspicuous values for a few years presented here. It is unknown whether this is due to errors in the data (see Data description in introductory section for a brief description of such problems) or if indeed the values were a true reflection of price changes. After a brief investigation of price changes in these countries no obvious policy reason could be identified. However, more in-depth examination of the question would be needed to determine the cause. Whilst two values for Japan also appeared to be outliers, such price movements did seem to be potentially explained by the policy shifts (see Paper 2).

FIGURE 10. PRICE INDEX TRENDS OVER 10 YEARS OF STUDY, GENERICS ONLY (NOTE: EXCLUDES CANADA AND AUSTRALIA IN ORDER TO SEE TRENDS OF OTHER OUNTRIES MORE CLOSELY)

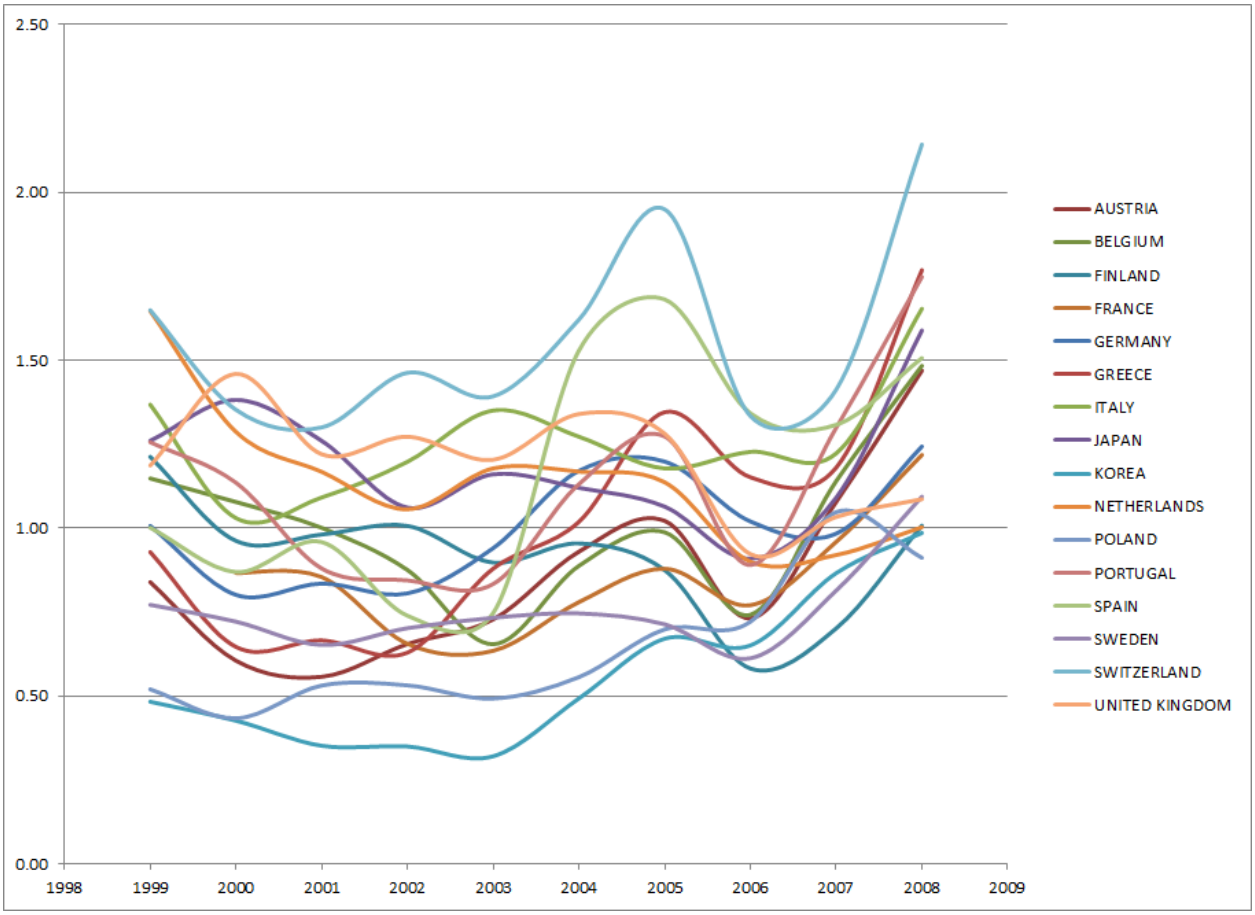


FIGURE 11. MARKET MAKE-UP BY COUNTRY

	generics	originator brands	OTC
AUSTRALIA	47%	15%	28%
AUSTRIA	29%	19%	7%
BELGIUM	28%	23%	14%
FINLAND	27%	21%	12%
GERMANY	41%	15%	12%
ITALY	34%	11%	8%
JAPAN	34%	8%	3%
KOREA	32%	4%	22%
NETHERLANDS	45%	26%	10%
POLAND	32%	11%	15%
PORTUGAL	42%	12%	3%
SPAIN	43%	9%	6%
SWEDEN	28%	31%	10%
SWITZERLAND	39%	19%	13%
UNITED KINGDOM	43%	17%	19%

FIGURE 12. RANGE IN THERAPEUTICS

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
AUSTRALIA	1430	1465	1494	1547	1569	1575	1536	1544	1564	1558
AUSTRIA	1205	1225	1216	1231	1244	1248	1242	1252	1252	1224
BELGIUM	1147	1156	1172	1182	1176	1173	1120	1129	1109	1067
FINLAND	784	784	784	790	795	795	800	803	799	792
FRANCE	1447	1436	1495	1458	1461	1457	1509	1608	1640	1618
GERMANY	2471	2516	2629	2630	2616	2509	2497	2481	2493	2486
ITALY	1348	1375	1367	1392	1369	1345	1330	1312	1304	1305
JAPAN	1735	1733	1742	1749	1738	1732	1720	1737	1735	1731
KOREA	1016	1333	1334	1492	1462	1501	1479	1496	1514	1482
NETHERLANDS	994	1006	1013	996	974	978	990	982	982	974
POLAND	1387	1411	1393	1416	1409	1371	1360	1350	1368	1342
PORTUGAL	924	943	953	960	973	990	937	935	929	918
SPAIN	1193	1219	1221	1220	1215	1208	1211	1181	1174	1171
SWEDEN	799	824	856	897	892	900	906	919	931	934
SWITZERLAND	1994	1990	1976	1966	1926	1858	1834	1794	1780	1739
UNITED KINGDOM	1354	1369	1388	1381	1391	1390	1387	1389	1382	1348

Figure 13. Diversity in product availability

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
AUSTRALIA	7911	8046	8138	8251	8289	8315	8268	8293	8328	8288
AUSTRIA	5726	5798	5815	5852	5870	5902	5898	5913	5904	5850
BELGIUM	4685	4716	4787	4844	4845	4845	4782	4794	4761	4677
FINLAND	4185	4222	4245	4258	4292	4319	4340	4330	4330	4310
FRANCE	10370	10438	10622	10596	10589	10616	10746	10926	11010	10937
GERMANY	33291	33634	33970	34105	34196	34146	34139	34128	34027	33936
ITALY	9061	9165	9203	9396	9379	9358	9322	9272	9254	9231
JAPAN	17371	17390	17478	17490	17504	17503	17482	17510	17510	17483
KOREA	11168	12506	12647	12882	12914	12994	12931	12996	13022	12929
NETHERLANDS	11772	11973	12168	12202	12278	12350	12388	12373	12394	12377
POLAND	6798	6915	6928	6988	6996	6961	6945	6922	6949	6881
PORTUGAL	5287	5359	5404	5450	5498	5533	5454	5455	5455	5412
SPAIN	7773	7849	7885	7912	7916	7926	7950	7879	7874	7840
SWEDEN	5553	5702	5791	5940	5971	6020	6029	6067	6084	6078
SWITZERLAND	8320	8342	8356	8367	8311	8236	8202	8139	8106	8021
UNITED KINGDOM	7504	7573	7627	7643	7666	7677	7655	7660	7655	7592

Figure 14. Therapeutic similarity to US market

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
AUSTRALIA	1382	1401	1427	1477	1482	1495	1452	1448	1477	1471
AUSTRIA	1171	1192	1187	1195	1204	1210	1207	1212	1217	1194
BELGIUM	1120	1133	1146	1149	1139	1138	1083	1090	1074	1038
CANADA	1395	1374	1430	1411	1406	1400	1460	1502	1526	1513
FINLAND	760	763	767	772	773	777	785	788	785	777
FRANCE		1395	1378	1373	1371	1378	1384	1374	1372	1359
GERMANY	2398	2438	2548	2541	2521	2420	2404	2384	2397	2390
GREECE	972	981	1006	1058	1049	1059	1074	1081	1079	1092
ITALY	1321	1348	1336	1354	1326	1313	1296	1272	1263	1263
JAPAN	1701	1697	1705	1709	1690	1681	1668	1681	1670	1669
KOREA	995	1313	1314	1464	1427	1464	1442	1446	1459	1427
NETHERLANDS	962	981	985	967	944	952	960	953	960	953
PORTUGAL	903	927	933	**937**	**942**	967	915	**913**	**906**	**899**
SPAIN	1165	1196	1190	1186	1170	1174	1170	1139	1133	1132
SWEDEN	769	796	827	867	867	876	885	899	909	910
SWITZERLAND	1923	1917	1902	1894	1846	1789	1769	1724	1718	1676
UNITED KINGDOM	1309	1323	1346	1335	1341	1343	1337	1331	1323	1294

FIGURE 15. OVERALL CONGRUENCE WITH US MARKET

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
AUSTRALIA	99%	99%	99%	99%	99%	99%	99%	99%	99%	99%
AUSTRIA	71%	72%	72%	72%	72%	72%	72%	72%	74%	74%
BELGIUM	80%	80%	80%	80%	81%	81%	81%	80%	82%	82%
CANADA	97%	97%	97%	97%	97%	98%	98%	95%	95%	95%
FINLAND	85%	85%	85%	85%	84%	85%	85%	86%	86%	87%
FRANCE		62%	63%	63%	62%	63%	65%	68%	70%	71%
GERMANY	79%	80%	80%	79%	79%	80%	80%	76%	79%	80%
ITALY	67%	68%	69%	70%	70%	72%	72%	73%	75%	77%
JAPAN	72%	72%	72%	72%	71%	70%	69%	67%	66%	65%
KOREA	99%	99%	98%	98%	98%	97%	97%	97%	97%	97%
NETHERLANDS	92%	93%	93%	93%	93%	93%	93%	92%	92%	92%
PORTUGAL	88%	88%	89%	90%	90%	91%	92%	92%	93%	94%
SPAIN	75%	76%	75%	75%	75%	77%	77%	76%	78%	78%
SWEDEN	94%	94%	94%	93%	93%	93%	93%	92%	92%	92%
SWITZERLAND	79%	79%	79%	78%	78%	78%	78%	75%	78%	78%
UNITED KINGDOM	86%	86%	86%	87%	87%	87%	87%	86%	85%	85%

FIGURE 16. STRENGTH OF ASSOCIATION BETWEEN MARKET CHARACTERISTICS AND HEALTH SYSTEMS

	Overall type	Regulation	Financing	Provision
Pharmaceutical price	0.067	0.614	0.203	0.266
Proportion generic	0.174	0.003	0.202	0.035
Proportion originator brands	0.170	0.120	0.073	0.198
Proportion OTC	0.106	0.100	0.101	0.22
Range in therapeutics	0.357	0.611	0.447	0.524
Diversity in product availability	0.321	0.407	0.400	0.372
Therapeutic similarity to US market	0.369	0.615	0.487	0.486
Overall congruence with US market	0.255	0.292	0.316	0.260

DISCUSSION

INFLUENCE OF HEALTH SYSTEMS

It seems generally intuitive that the pharmaceutical market of countries with similar types of market or planned economies should be generally similar. Countries with similar health systems often share important cultural, political or economic precursors. For example, countries with SHI systems share clear linguistico-cultural similarities. Alternatively, the establishment of NHSs require social democratic governments combined with negligible veto power on the part of providers (Toth 2010, Immergut 1992, Böhm 2013). Nonetheless, the quantitative analysis in this study suggests on the whole relatively weak relationships between pharmaceutical prices and the type of health system in place in wealthy Western countries.

Indeed the results shown in Figure 16 imply that there are only minor differences in the abilities of various types of health systems to negotiate favourable pharmaceutical prices. In other words, no sweeping generalization can be made regarding a given health system's ability to apply more or less leverage on pharmaceutical prices, an informative and somewhat counterintuitive conclusion. In short, the type of health system by itself doesn't seem to be a first order determinant of prices.

A more detailed analysis of the data focussing on the structural components of health systems does suggest, however, that the level of state intervention at the highest levels of the system may affect pharmaceutical prices. The moderately strong relationship between prices and regulation dominance (coefficients larger than 0.6 in Figure 16) suggests that the primary regulation-driving actor is more important than who is in charge of financing or provision in determining prices. The ability of the state to contain prices in its role as primary regulator follows from its role in governance. This result suggests in particular that the privatization of provision (an effective transition from an NHS to an NHI) in the name of budget constraints or efficiencies does not necessarily translate into more competitive prices in the pharmaceutical market. The closer relationship between pharmaceutical prices and regulation than between pharmaceutical prices and provision is striking, all the more so as the total expenditure was one of the parameters included to characterize provision. A larger total expenditure on pharmaceuticals does not necessarily translate into higher prices.

The results of this study also suggest that allowing the devolvement of financing to sick funds (a transition from an NHS to an ESHI) does not necessarily translate into a loss of ability to contain prices. According to the data, such a transition would have little effect on pharmaceutical prices. In contrast, decentralization of regulation, finance, and provision (e.g. in a transition from an NHS or ESHI to an SHI) would generally be expected to limit the ability to contain prices. Interestingly, this would not result from a loss of monopsonistic (sole payer) leverage, as there would be no change in financing dominance from ESHI to SHI, but rather from the transition away from state governance. In the case of pharmaceuticals, prices seem to be more effectively controlled by regulation than by market forces.

Interestingly a non-negligible relationship was detected between the availability of pharmaceuticals and regulation. In this case the direction of influence is as one might predict: state dominance in regulation leads to more limited availability of pharmaceuticals—but this comes more from state dominance in regulation than in financing or provision. The relative

strength of the relationship also suggests that the governance role appears to be a more important determinant of the number of therapeutics available than who finances them or who prescribes them. This may mean that when financing is devolved to corporatist groups, these groups do not compete on the ground of greater availability—at least in a way that would noticeably impact the overall measures of availability used in this study. Similarly, when provision is devolved to private providers, competition based on greater pharmaceutical availability is not significant. Simply stated, maintaining state dominance of regulation is sufficient to marginally restrain product availability, regardless of financing or provision arrangements.

The US is the only country left with a private health system (Switzerland switched to SHI in 1996), so the analysis of this particular system is limited to only the American situation. As it was compared to each of the other OECD countries directly, this limitation is actually an opportunity to look closely at how the US market differs from others and, in particular, to examine common beliefs about the implications of high US prices. Findings from this study show that over the 10 years in question (1999 through 2008) the average across all countries went from 50% to only 62% of US prices (Figures 3-5). This could suggest some increasing convergence with US prices over time but also demonstrates that, for the most part, other rich countries pay far less for pharmaceuticals than in the US. When focussing only on originator pharmaceuticals this difference is even greater, with other countries having an overall average of 41% of US prices over the study period (Figures 6 and 7). However, the results are strikingly different for generic pharmaceuticals, the prices of generic pharmaceuticals in comparator countries relative to the US being much higher than those of originator brands (Figures 8-10), many of them even surpassing US prices. The 10-year average ranged from 0.56 for Korea and 0.64 for Poland up to 1.56 for Switzerland, 1.86 for Australia, and 2.57 for Canada[33]. The overall average for this sample was 1.15, suggesting that prices for generic pharmaceuticals in other OECD countries were close to US prices in the years of the study. By the end of the study period, almost all countries had generic prices surpassing US prices. This is a highly significant result given the importance of generics which account on average for a higher proportion of pharmaceuticals (average of 37%) than originator brands (average of 16%) in the OECD markets (Figure 11).

[33] As noted earlier in this dissertation there were two years of price data from Canada that appeared conspicuously high and thus this 10-year average may be an overestimate.

The finding that US prices are actually lower than many other countries when looking at the generics market is of particular interest given the often made claim that other wealthy countries free-ride on high US prices. This is indeed one of the most common critiques of the global pricing of pharmaceuticals, although the debate is rarely supported by concrete data. Market evidence suggests that US consumers (here a complex combination of prescribers, patients, and third-party payers) value newer, cutting-edge and generally more expensive pharmaceuticals (albeit not always of proven better quality). The evidence here also suggest, however, that the US system also allows for rapid and deep generic penetration. The price of generics in the US appears to face much downward pressure from free market competition – which is actively supported through legislation (e.g. general Wax-Hatchman provisions[34]). Conversely, the price of originator products are somewhat protected through related legislation (e.g. reverse payments or "pay-for-delay" permissions[35]). The approach to pharmaceutical pricing in European countries has been quite different from the laissez-faire or free market approach of the US (although one could argue that the aforementioned US legislation makes it a somewhat false free market). Most other OECD countries use either monopsonistic leverage or other explicit tools --including external reference pricing, internal reference pricing, health technology assessments, profit-limiting pricing-- to control prices and/or to bring price in line with expert-assessed therapeutic value (as opposed to purely market-assessed). The evidence suggests that these price controls result in lower pharmaceutical prices overall. However, these measure also restrict the normal price-limiting effects of competition which are particularly effective for generic pharmaceuticals.

So in answer to the question of whether other countries are free-riding on high US prices – yes, US prices for originator pharmaceuticals and for the overall basket of pharmaceuticals consumed according to US preferences are higher than anywhere else. This means that the US consumers are arguably paying more for innovation as they contribute out of proportion to the bottom lines of drug companies that carry out pharmaceutical research. However, as the US has no formal cost-effectiveness assessment processes (and indeed the main public payer, the CMS, as well as private insurance companies, officially do not utilize such studies in

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[34] The Hatch-Waxman Act streamlines the market approval process for generic drug products, allowing them to file an abbreviated New Drug Application (ANDA) that incorporates the safety/effectiveness data submitted by original pioneer drug manufacturer, adding only bioequivalence studies. As a result, generic manufacturers can get their products onto the market more quickly and with less fear of pursuit for infringement by the originator company.

[35] Such permissions allow for payment by the originator patent holder to the generic manufacturer to delay entry.

their coverage decisions), the innovation Americans are paying for may not represent the real innovation from which the rest of the world benefits. It is very difficult here to argue that high US prices motivate much more than incremental innovation or that the American patient is seeing true value-for-money in the newer pharmaceuticals they consume.

Looked at another way, the higher prices paid for generics in Europe may actually be subsidizing US generics manufacturers whose profit margin is constrained by competition. Overall, while the US may be subsidizing innovation to some extent, constraints on competition in other OECD countries arguably buoy generic manufacturers of the older products. For companies that operate on both sides of the Atlantic this may translate into some balancing of the books. Certainly the bigger companies, who are well aware of the different pricing structures, position themselves accordingly.

One difficulty in analysing the relative prices of pharmaceuticals is to know when high prices result from the payer's weak ability to negotiate them down, or from the payer's willingness to pay higher prices (or at least not drive them down to marginal cost) with the aim of supporting long-term investment in pharmaceutical R&D. In rich countries, governments use negotiation with industry to establish prices for pharmaceuticals that will continue to incentivize R&D while achieving a fair price for consumers—in many cases the latter being the government itself. The US, UK, and Germany have generally claimed to encourage R&D in their pharmaceutical pricing policies. However, for the UK and Germany this is not completely borne out by the data in that their respective overall 10-year averages for originator brands were still very far below US prices, at 45% and 46% of US prices, only slightly higher than the average for the OECD countries (average of 41% across all countries over the 10 years (range of average by country of 31 to 60%). In the case of Germany, there is a very clear trend towards higher prices of originator pharmaceuticals over time, reaching 58% of US prices in 2008, the highest value amongst all comparator countries, yet far below parity with the US.

The policy- and price-setting environment may also in some cases work against the competitive nature of companies. For example, through their national or regional industry associations such as Pharmaceutical Research and Manufacturers of America, the Association of the British Pharmaceutical Industry, and European Federation of Pharmaceutical Industries and Associations, pharmaceutical companies (primarily large ones) are able to exert considerable pressure on regulators (in this case mainly Congressional leaders in the US and public payers in Europe) to support conditions favouring originator market share and/or to

refrain from using monopsonistic or oligopsonistic leverage to drive down prices for newer products. So both as a direct result of regulation and the indirect result of hampered competition, prices can be higher than would result from a true free market. Such effects are difficult to detect with the available aggregated price data.

Characteristics of the respective pharmaceutical markets

An additional finding of interest is the major difference in market structure found amongst some European countries. For example, in terms of the range of therapeutics (which is the number of unique molecule-indications) and the diversity of available products (which includes all versions of all molecules, counting variety across strengths, formulations, packaging, etc), Finland and Germany represent opposing extremes, from smallest to largest, respectively (Figure 12 and 13). This relationship holds also for their respective level of similarity to the US market – similarity in *what* is consumed (Figure 14). Interestingly this disparity does not relate to the congruence with the US market (Figure 15 - i.e. it does not hold for the amount of the goods bought) as Finland is actually closer to the US in this respect than Germany. This suggests that while Finland may not have as many individual therapeutics matching with the US, the ones that do match make up a large portion of what they consume (by volume). Interestingly, these two countries also represent different approaches in terms of health system structures (no similarity in approach in regulation, financing, or provision).

The similarity of the Australian market with the US market is also of interest (Figure 14). This similarity could result in part from private provision and commonality of language, which would favour the importation of pharmaceuticals already packaged and labelled in English, overall easing registration processes. The lack of similarity between the French and the US markets (Figures 14 and 15) is to be expected given the strong support for in-country production of pharmaceuticals, especially generics, in France.

Limitations

In order to examine potential relationships between the characteristics of various health systems and the pharmaceutical prices attained within those systems, it is necessary to use price indices that aggregate prices in each pharmaceutical market, such that price differences between two countries are quantified by a single number. This is not a simple or controversy-free task in that pharmaceuticals vary immensely in their branding, formulation, strength, etc. across countries and there is no single, accepted way to combine their prices to create a single

measure of their price differences. It is thus with many trade-offs that this is done here. For example, the more one imposes a comparison of like-for-like pharmaceuticals (e.g. imposing that the sample include only identical brands, strengths, dosing, etc.), the more the sample size of products diminishes. Samples based on bilaterally-matched products matched with the US were used as the basis of the price indices in order to maximize the number, and thus representativeness, of products. Fisher indices were constructed because they depend the least on the choice of base country (the country whose consumption patterns determine the how each drug in the sample is weighted in the index calculation). Rather than using only the consumption patterns of the base country (as in Laspeyres indices) or only the consumption patterns of the comparator country (as in Paasche indices), Fisher indices combine the two in what can be described as a fairer, more country-invariant measure of price relatives.

In terms of their interpretation Fisher indices do not provide a completely straightforward answer. For example Paasche and Laspeyres indices can be more readily interpreted for national-level policy-making – indeed the level at which most health and pharmaceutical policies are made in OECD countries. However, for making international comparisons, conducted in an effort to clarify globally-relevant (rather than nationally-relevant) questions—Fisher indices are both mathematically as well as economically optimal (See section on Index Number Theory in Introduction for more detailed discussion of Fisher indices).

CONCLUSION

Health systems in industrialized OECD countries are complex institutional constructs and there are significant variations across countries. Nonetheless it seems possible that commonalities across health system types could have a similar influence on national pharmaceutical markets. Findings from this study suggest that what seems to matter most for both the price and the availability of pharmaceuticals is not the type of health system overall or its mechanisms for financing or provision, but rather its governance, i.e., the regulation of the relationship between payers, providers, and patients. Of most interest is the apparent lack of relationship between financing mechanisms and drug prices and availability given the seemingly strong leverage of single payers and their ability to influence the market. Also of interest is the finding that competition amongst non-state payers or providers does not translate into greater availability of therapeutics compared to state provision. Such findings are of particular relevance for state dominated health systems in view of the tendency to

decentralize and move towards a plurality in financing and lesser state involvement in the provision of health services in the name of greater efficiencies and/or budget constraints.

Findings also suggest that a Private Health System such as that of the US may lack the ability or the motivation to contain prices, resulting in much higher pharmaceutical prices than elsewhere. Looked at very bluntly (and disregarding the disconnection between prices and R&D) this finding supports the claim that US prices subsidize R&D for the rest of the world – or that the rest of the world free-rides on high US prices. However, the picture of very high relative US prices does not hold for all sections of the pharmaceutical market. Indeed the price of generic pharmaceuticals in comparator countries are quite close to those in the US, many of them even surpassing US prices. The aforementioned claim of the quasi-unique role of the US in financing pharmaceutical R&D thus needs to be nuanced. National pharmaceutical policies should clearly take into account the differences between the different sectors of the market.

CONCLUSION

The various parts of this dissertation explore the differences in pharmaceutical prices across countries, rich and poor, the likely determinants of these price differences, and their consequences in terms of fairness and efficiency. This concluding chapter brings together the key findings of the individual papers to provide a synoptic and coherent view of the topic. The first section highlights the principal results from the quantitative analyses of price differences amongst countries and their evolution over time, focusing primarily on high-income countries. The second section synthesizes the key results from the papers analysing the determinants of pharmaceutical prices, including the development characteristics of countries (economic, social and demographic), external factors (competition and globalization) and the characteristics of the health system. The issue of fairness in pharmaceutical pricing is addressed in the next two sections, first from the perspective of relative affordability and access to pharmaceuticals and then from the perspective of relative contribution to global R&D.

The methodological advances that undergird the quantitative analyses presented in this dissertation are then presented and followed by a discussion of the limitations of the work. Both are related in large part to the intrinsic difficulty in measuring price differences, a classic and long-standing problem in economics, which is further complicated by the dizzying variety of presentation, dosage and composition of pharmaceutical products that vary from country to country. The final section discusses the possible policy implications of this thesis focusing on the question of fairness in the pricing of pharmaceuticals amongst countries in different stages of economic development.

TRENDS IN PHARMACEUTICAL PRICING ACROSS COUNTRIES

The work presented in this dissertation shows that, with few exceptions, prices in the United States are higher than in any other country in the world. This result, which has been previously published for a more limited number of countries and time periods, was consistently borne out in each of the papers presented, Papers 1, 2, 3 and 4. However, although pharmaceutical prices in comparator countries were lower than in the US, they became more similar over the 10 years of the study. In addition, as discussed in the next section, the results from these chapters confirm intuitive notions that, *ceteris paribus*, richer countries generally pay higher prices than poorer ones, more open and competitive markets

pay lower prices, and pharmaceuticals that are newer to the global marketplace are more expensive.

The magnitude of the difference in prices amongst countries was found to depend on the methods used in sampling pharmaceuticals across markets, in particular on the consumption pattern used to weight individual pharmaceutical prices and on the number of products included in the sample. As explained below, when the comparator country's consumption pattern was used to weight pharmaceutical prices (Paasche index, P) the overall difference with the US was larger than when the prices were weighted according to the US's consumption pattern (Laspeyres index, L), as demonstrated by the systematic difference between the indices: $L > P$. This difference was further increased when the sample contained a larger number of products matched bilaterally between the US and the comparator country (P_B and L_B based on a mean sample size of 1250 products) instead of a smaller number matched across all of the countries multilaterally (P_M and L_M based on a mean sample size of about 150 products) and thereby limited to only globally-available products: $L_B > L_M > P_M > P_B$. This study exploited the range of values calculated by these various price indices to obtain a more thorough understanding of price differences in pharmaceuticals between countries than is possible with a single index. A mean value of the various indices provided a dependable quantifier of price differences when the indices were close to each other. Vice-versa, large differences amongst indices indicated unusual features of particular pharmaceutical markets that could often be determined by a detailed analysis of the various indices and the underlying data.

For eight countries, the range of values for the Laspeyres and Fisher indices was found to be relatively narrow ($L_B - P_B < 0.25$). In this situation, the bilateral Fisher index, F_B, which is the geometric mean of L_B and P_B, provided a useful single number approximation of relative prices of pharmaceuticals between these countries and the US. According to the results, over the ten years of the study, the manufacturer-level prices of pharmaceuticals were on average between 40% and 50% of US prices in Finland, France, Italy, Spain, Portugal, Greece and the Netherlands and somewhat lower in Korea (34%). This result applied to a large fraction of the pharmaceutical markets in these countries, on average 85% of the products in a given country in any given year (ranging from 65% for France to 99% for Australia).

When limiting the comparison to "global molecules" included in the multilaterally matched sample, the results showed a similar difference (a factor of 2 to 2.5) in average pharmaceutical prices between the US and a much larger number of countries: Australia, Austria, Belgium,

Canada, Finland, France, Germany, Greece, Italy, Korea, Netherlands, Philippines, Poland, Portugal, South Africa, Saudi Arabia, Spain, Sweden, and the United Kingdom. This result was based on the Fisher index F_M, when the average difference between L_M and P_M was small ($L_M - P_M < 0.15$). In the case of Taiwan, the difference in the price of these common pharmaceuticals compared to the US was somewhat larger (a factor of 2.7). Because these price differences for global molecules are nearly independent (within a few percent) of whether they are weighted by US or domestic consumption patterns, they are useful to guide policy decisions.

In contrast, for Japan, Singapore and Switzerland the relatively large difference observed between price indices calculated with US or domestic consumption patterns made it impossible to robustly quantify price differences with a single number (although that difference was undoubtedly best approximated by the Fischer index). This was particularly true of Japan for which pharmaceutical prices showed a very large mean difference between L_M and P_M (L_M-P_M = 0.49). This is most likely due to large differences in the patterns of pharmaceutical consumption between Japan and the US. This explanation is consistent with the very low fraction (16%) of the Japanese pharmaceutical market that was included in the multilaterally-matched samples, likely reflecting geographical barriers and the predominantly domestic nature of the Japanese market. Dissimilarities in the pattern of pharmaceutical usage between comparator countries and the US resulting from cultural differences is also likely responsible for large numerical differences between the Paasche price indices calculated for multilaterally and bilaterally matched pharmaceutical samples for Korea, Japan, Saudi Arabia and Taiwan.

The narrowing of differences in pharmaceutical prices between comparator countries and the US over time was quantified by the evolution of both the Laspeyres and Paasche indices. For example, in most high income countries these indices increased between 2001 and 2008 with a mean increase of about 50% for the Laspeyres indices and of 30% for the Paasche indices. The two exceptions were Saudi Arabia for which all the indices decreased systematically and the United Kingdom for which all the indices remained approximately constant. In other words, whilst pharmaceutical prices in most wealthy countries increased compared to the US between 2001 and 2008, they decreased in Saudi Arabia and remained relatively constant in the UK. In the case of the UK this result suggests a containment of pharmaceutical prices resulting from specific policy tools (e.g., health technology assessments and the

Pharmaceutical Price Regulation Scheme[36]), as well as policies to promote the use of generic pharmaceuticals.

As explained below, the generally larger relative increase over time in the Laspeyres indices compared to the Paasche indices is expected as a result of the negative relationship between price and consumption. In some countries, however, the relative increases in L and P, based either on bilaterally or multilaterally matched samples, were similar. For these countries, the increases in the corresponding Fisher indices provide good measures of the changes in pharmaceutical prices relative to the US: a range from zero increase (Taiwan) to a near doubling for the bilaterally matched samples (F_B going from 0.36 to 0.69 in Sweden), and a narrower range for the multilaterally matched sample, going from 23% in Taiwan (F_M = 0.35 to 0.43) to 46% in Sweden (F_M = 0.39 to 0.57).

DETERMINANTS OF PHARMACEUTICAL PRICES

Once the differences in pharmaceutical prices amongst countries have been quantified, the obvious question becomes that of the main drivers responsible for these price differences. This question is addressed in detail in the dissertation, focusing first on social, demographic, economic and product-related factors (Paper 3) and then on the effect of the characteristics of the health systems (Paper 4).

The results suggest that the prices of pharmaceuticals in middle-income countries are particularly dependent on several socio-demographic variables rather than purely economic ones. The percentage of old people living in middle-income countries was found to be the strongest determinant of pharmaceutical prices, most probably reflecting a rapid increase in demand. The length of time since launch of a pharmaceutical was also strongly positively related with its price, likely a result of product recognition, associated marketing strategy and ensuing purchaser behaviour. Notably, pharmaceutical prices in middle-income countries were found to be more sensitive to certain demographic trends such as population growth and death rate than they were in high-income countries. Overall, the results suggest that prices offered to purchasers in middle-income and high-income countries are affected differently by globalization and competition. Social and demographic particularities in middle-income countries give them a notably different negotiation predisposition that may

[36] The PPRS in its previous form is referred to here.

deserve attention in global discussions surrounding fairer pricing and better access to pharmaceuticals (see below).

A potentially important determinant of differences in pharmaceutical prices is the type of the health system in use in a particular country. Variations amongst health systems that may affect pharmaceutical prices include the extent of coverage, the mode of financing and delivery of care and the public or private actors that control these: state, corporatist (private non-profit), or private (for-profit). The quantitative tests performed in this thesis suggest, perhaps surprisingly, that health system type is not in itself a clear determinant of prices. However, a fairly strong relationship was detected between the type of actor who maintains the greatest role in regulation and pharmaceutical prices. Interestingly it was the control over regulation, not financing or provision, that had the greater impact on the pharmaceutical price levels ultimately negotiated within the market. Indeed state dominance of governance structures (i.e., the regulation of the relationship between payers, providers, and patients) was found to help reduce overall pharmaceutical prices. Of particular interest was the apparent lack of relationship between financing mechanisms and pharmaceutical prices despite the seemingly strong leverage of single payers and their ability to influence the market. Perhaps more intuitively, state dominance over regulation was also found to lead to a slightly reduced scope in pharmaceuticals available within the system. State regulation appears to in some way inhibit the variety of therapeutics coming onto the country market. This may be a reflection of the more discriminatory approach to market entrees when the state is heavily invested in regulation—in particular when it takes a stance on what is "appropriate" or "inappropriate" for the national market on cost-effectiveness grounds. Indeed state activity in establishing, adhering to, and standardizing norms of quality may exist under any system structure but when the state controls the relationship between payers, providers, and patients it may have greater opportunity to push the market towards products it deems to offer greater value-for-money (the obvious example here is NICE in the UK). Also of interest is the finding that competition amongst non-state payers or providers does not translate into greater availability of therapeutics compared to state provision. Such findings may be of particular relevance to state dominated health systems given the tendency to decentralize and move towards a plurality in financing and lesser state involvement in the provision of health services in the name of greater efficiencies and/or budget constraints.

Overall the findings from this dissertation are interesting in view of the increasing pressure to legitimize public involvement in health care, which is being perceived to run counter to the present norm of free enterprise and the interests of rent-seeking private actors. This leads to democratic governments having to justify any state intervention using reasons of market failure or in the name of achieving distributive goals (Bohm 2013). The result is that state dominance in any sector is increasingly hard to justify—although it is arguably less difficult to justify in health care as a result of the numerous market failures that exist and the emotive nature of redistribution (or rather lack thereof) when it concerns health. Yet even in health care there is increasing political pressure to devolve power in each of these areas—regulation, financing, and provision—as soon as budget concerns or perceived inefficiency arise (these being, of course, easily manipulated according to the ideological orientations of those in power and in the media). The findings of the work presented help debunk some of the underlying assumptions used to argue for or against devolvement and privatization. First, contrary to arguments made in phases of retrenchment, the privatization of health services does not necessarily lead to overall greater opportunity for competition amongst health commodities that will drive down prices. According to the study results, the type of actor in control of provision had little or no influence on pharmaceutical prices. Second, contrary to arguments made in defence of state controlled financing (i.e. state as single payer) towards more pluralistic arrangements in the name of greater choice, efficiency, etc., such a move does not translate into a loss of monopsonistic leverage. Indeed the findings suggest that very little changes in the pricing of pharmaceuticals occur when control over financing is less concentrated.

FAIRNESS IN PRICING FROM THE PERSPECTIVE OF RELATIVE AFFORDABILITY AND ACCESS TO PHARMACEUTICALS GLOBALLY

An important aspect of price relatives calculated on the basis of indices lays in how they are or are not perceived to be "fair". Fairness here pertains for the most part to notions of vertical equity—the idea that people of different means should pay amounts based on their respective means. In the case of pharmaceuticals the basic idea of vertical equity is that patients should be able to access the products they need at prices they can afford. The normative economic perspective of this argument is effectively based on a value judgement: this is the direction that public policy *ought* to favour. However, the differential pricing of pharmaceuticals according to means is also supported from the point of view of positive (or quasi-positive) economics. It can, for example, be argued for on the grounds of static efficiency according to which social surplus—the sum of consumer surplus and producer

surplus—is maximized at a given point in time as a result of the greater number of consumers who are able to afford the product and the greater number of sales that ensue. In theory differential pricing allows for the expansion of sales to the full extent that the market can bear; in other words, demand can be fully exploited out to the equilibrium point, shown in traditional economics as the crossing of the supply and demand curve assuming no other changes. Differential pricing also helps achieve dynamic efficiency where sufficient earnings flow back into R&D to sustain innovation and improve production over the longer term, thereby helping to bring down average costs over the long-run. Of great importance to traditional IP-driven firms (which continues to characterize most large pharmaceutical companies), differential pricing can also potentially help enforce patents by lowering the chances of involuntary licensing. If indeed the product is available in less wealthy areas at a price more suited to affordability then manufacturers will be less likely to want to manufacturer the product legally or illegally[37].

Despite the many arguments in favour of differential pricing of pharmaceuticals, it is unclear whether differential pricing strategies are what actually drive pharmaceutical prices across the world. In reality very little is known about what drives pharmaceutical prices in either their absolute or relative measure. Indeed one economist is reported to have recently dryly remarked in a closed-door session of pricing experts in the US that she could find no economic theory to explain how pharmaceutical companies price their products (Economist 2015). This dissertation has sought to help fill this critical gap in the health economic and policy literature.

Overall the work suggests that national income does not have consistent influence on prices across countries. Paper 1 first highlighted this inconsistency, showing that the prices of pharmaceuticals from 1999 through 2008 were not systematically related to per capita income or gross domestic product. Indeed it also pointed to a few major perversions in relative pricing across income categories: some middle-income countries pay more for pharmaceuticals than high-income countries and some pay less than low-income countries. For example prices in Mexico were high compared to the United States, prices in Morocco were high compared to France, and prices in Egypt and India (two middle-income countries) were found to be very low, even compared to prices in western Africa. When this inconsistent relationship between price and per capita national income is examined in greater

[37] The notion of illegality of such practices is of course debatable here given flexibilities provided under agreements such as TRIPS and TRIPS Plus. This is consciously ignored by the Candidate here.

depth in Paper 3 it becomes clear that it is really in middle-income countries that the relationship is very weak. The relationship is stronger in high-income countries, although even there the influence of national income is trumped by other factors as discussed above.

FAIRNESS IN PRICING FROM THE PERSPECTIVE OF RELATIVE CONTRIBUTION TO GLOBAL R&D

The topic of relative pharmaceutical prices also brings with it the issue of fairness from the perspective of relative contribution to global R&D, the latter being considered a public good. This issue is largely unavoidable as soon as one compares prices across more than a few high-income countries. The basic notion is that of horizontal equity, interpreted in this context as the idea that populations with similar means should pay their "fair share" towards global public goods. This issue is often brought up in a provocative manner to stress the disproportionate burden of R&D costs falling on the American consumer (patients or payers) through the high prices of pharmaceuticals charged in the US compared to other countries. It is used in contexts such as political races where the vote of older, poorly covered, populations is sought, discussions over potential price controls in the US Congress (these are of course very "light touch" versions debated in the US compared to their European counterparts), and lobbying efforts by pharmaceutical companies attempting to achieve higher prices for their products in Europe. The international price comparisons conducted in the past have indeed been motivated by this question of "free riding" more than any other. However, with the studies by Danzon and colleagues in 1999-2000 much light was shed on important technical limitations of the earlier comparisons and thus also brought into question their policy implications. The Danzon studies demonstrated the bias in limiting the sample to originator pharmaceuticals, prescription pharmaceuticals, those defined according only to US preferences, etc. The authors emphasized that the perception of price differences depends to a great extent on the framing of the comparison, in particular the choice of country used to determine consumption patterns to weight prices and appropriate sampling methods. The Danzon studies are however limited by the number of countries and the time frame they covered cross-sectionally (1992 and 1999 individually), precluding any insight into price evolution; they are also now relatively out-dated. The studies presented in this doctoral work bring the price comparison closer to modern times, include many more countries, and delve into greater depth into the question of whether the cost of pharmaceutical R&D really falls disproportionally on US consumers. For example, the work presented in Paper 2 goes into depth on the effect of using different price indices on the overall interpretation of price relatives—so on the extent to which US pharmaceutical prices are really higher than those of

other high-income countries. The detected difference between US prices and those of the comparator high-income country are relatively small when looking at Laspeyres indices, which use the consumption pattern of the US to weight prices. But the political relevance of this is questionable in that the calculations are biased toward pharmaceuticals that are important for US consumers not for those of the comparator country. Importantly Paper 2 introduces the use of Fisher indices in such comparisons (the geometric average of the Laspeyres and Paasche indices) which helps to remove this dependence on single country preferences and, in so doing, allows for greater policy relevance of the price comparison at the global level.

On the whole, the price comparisons presented in Paper 2 do confirm that prices in the US tend to be higher than other countries when looking across the entire pharmaceutical markets. However, the results of Paper 4, which uses Fisher indices constructed for OECD countries, show that this result does not apply for all pharmaceutical products. Paper 4 shows that prices of pharmaceuticals for which patents have expired are not higher in the US than in other wealthy countries. Indeed prices of such products are higher in several other countries than in the US. By 2008 all OECD countries included in the analysis had prices higher than US prices except for Korea and Poland. In many ways this finding highlights the success of the US approach to price control through competition (here the support for faster and multiple market entry by competitors post patent expiry on the originator) rather than through more direct price controls as applied in, for example, many European countries.

Regarding the question of unfairness in relative contribution to global R&D the cumulative findings of this work suggest that the answer must be nuanced. US prices for new products are higher than in other countries but as soon as the main patent protection is removed US prices fall below almost all wealthy countries. The critical question of course then becomes to what extent R&D resources come from different sectors within the market or derive exclusively from sales on originator products. This is a more complex issue than it may appear at first glance or what the industry lobbyists would lead one to believe. Firstly, the connection between price and R&D investment is at best tenuous and certainly indirect. As Scherer and colleagues stress, pharmaceutical prices are a function of demand, not how much has been invested in producing the product. Also, much of the revenues from pharmaceutical sales go into other activities such as marketing or are (rather notoriously) passed on as profits rather than being absorbed back into novel research and development. So, in practice, the high prices of pharmaceuticals in the US do not necessarily translate to greater American contribution to global R&D. Stronger arguments for how the US may be contributing more

than other countries lie in the generally industry-friendly environment, tax breaks, public funding of basic and translational research, good universities preparing skilled personnel for industry, etc. These factors are likely to contribute as much or more to the success of global R&D efforts than high US pharmaceutical prices by themselves.

METHODOLOGICAL CONTRIBUTIONS IN CALCULATING AND COMPARING PRICE DIFFERENCES

Previous studies of differences in the prices of pharmaceuticals amongst countries encountered two major obstacles: the available data were limited in scope and the data analysis faced the fundamental (and irresolvable) problem of quantifying the price differences with a single number despite heterogeneity in preferences amongst countries --the classic and long-standing problem of Index Number Theory.

The most comprehensive previous cross-national comparisons of pharmaceutical prices, that of Danzon and colleagues, were limited to only a few countries (seven in Danzon and Chao 2000 and eight in Danzon and Furukawa 2004) with only one study comparing prices over time (between 1992 and 1999 in Danzon and Furukawa). Danzon and Furukawa also demonstrated the need for a large, representative sample, one not limited to molecules matched by form, strength or usage, to obtain accurate measures of relative prices. The first major methodological contribution of the work presented in this dissertation is very simply the scale and scope of the data utilized in constructing a representative picture of national pharmaceutical markets for use in Papers 1, 2, 3, and 4. The work builds on previous cross-national price analyses but includes a much more comprehensive set of data both in terms of the number of countries and the time frame covered. Together the papers in this dissertation explore pharmaceutical prices in over 30 countries over a period of 10 years. Two different types of comparisons were made, one based on about 150 samples matched each year for all countries, and another based on a many more samples (~ 1000 to 2500) matched each year for any two countries being compared. This dual approach allows for a rich description of the price differences amongst countries. The sample of 150 "global" pharmaceuticals allowed comparison of prices amongst all countries simultaneously, but the conclusions that could be reached were necessarily limited by the small fraction of individual markets that were represented. In contrast, the much larger bilaterally matched samples provided a much more complete representation of individual pharmaceutical markets, albeit at the cost of generality. Pharmaceuticals were defined by molecule name and indication, according to the third Anatomic Therapeutic Category (ATC 3) with all other characteristics allowed to vary (e.g.

brand name, pack-size, strength, form, etc.). The pharmaceutical prices analysed represented deflated manufacturer prices for pharmaceuticals sold in the retail market, except in the case of a few countries for which distribution pathways were not delineated between retail and other outlets. Such an extensive data set made possible a high level of comprehensiveness and a lack of bias that was not achieved in previous studies.

Comparing prices of similar goods in different places or at different times is a fundamental activity in economics and there is an extensive literature dealing with this question. To make such comparisons, economists rely on indices that summarize into one number a vast amount of price and sales volume information. The difficulty is that different indices can give widely diverging estimations of price differences, a much-discussed problem in economic theory that can be shown to have no absolute, objective solution. The fundamental problem of quantifying price differences is particularly acute in the case of pharmaceuticals, the presentation, dosage, composition, availability and consumption of which vary widely amongst countries. The second methodological contribution of the work presented in this dissertation is to use simultaneously several indices that respond differently to consumption patterns and to the variations in the prices of individual products. A total of six indices were used, the Laspeyres and Paasche indices (L and P, calculated respectively by weighting prices according to the consumption patterns of the US and the comparator country) and their geometric mean, known as the Fisher index (F), all calculated for both the multilaterally and bilaterally matched samples: L_M, L_B, P_M, P_B, F_M and F_B.

This pragmatic approach obviates many of the fundamental difficulties inherent with the use of a single index and provides a much deeper quantitative understanding of cross-national differences in pharmaceutical prices and their causes. Using multiple indices provides useful information not only from the numerical values of these indices and their evolution over time, but also from their differences. As a result of the inverse relationship between usage and price, the Laspeyres indices (which use weights based on consumption in the base country) are always larger than the Paasche indices (which use own-weights based on consumption in the comparator country) and this effect is magnified when the sample size is larger such that $L_B > L_M > P_M > P_B$. When the differences between the Laspeyres and Paasche indices are small, the corresponding Fisher indices (which are the geometric means of L and P) provide a robust quantification of price differences between countries and of the evolution of these differences over time.

In a number of cases, however, the data showed large differences between the values of Laspeyres and Paasche indices based on the same sample, or between the same index based on multilaterally or bilaterally matched samples, or in the relative evolution of these four indices over time. In such cases, price differences amongst pharmaceuticals cannot be well captured by a single number, although the Fisher index still provides the best rough estimation of these differences. Importantly, large differences between indices served as flags indicating unusual features of the pharmaceutical market in individual countries during the period of the study. In several instances, a detailed examination of the indices led to a likely explanation in terms of differences or changes in pricing or consumption patterns between the comparator country and the US. Of particular interest in this context is the sensitivity of the respective indices to preferences in different countries (base country or comparator country), and how this helps explain the reasons for difference or relative differences between the index values. As Laspeyres indices weight prices according to US preferences, the increase from L_M to L_B must be particularly sensitive to the negative relation between price and volume in the US. Vice-versa because Paasche indices use own-weighting for the comparative country, the decrease from P_M to P_B must depend chiefly on the negative relationship between price and volume in that country. The by and large greater difference that was observed between L_M and L_B than between P_M and P_B therefore reflected in part the greater level of price elasticity in the free pricing US than in other countries. This result was apparently falsified in countries where price regulations are particularly effective at controlling the prices of highly used pharmaceuticals.

Overall the methodological exploration performed in the context of Paper 2 helped provide a richer interpretation of the findings of Papers 1, 3 and 4.

LIMITATIONS OF THE WORK

Measuring price relatives across thousands of different products is not simple and requires making a number of trade-offs. To meaningfully compare prices amongst goods requires that the comparison be made on like-for-like products. In this sense price comparisons of pharmaceuticals should utilize samples that are defined according to clear criteria for matching products across countries and common units for measuring both price and volume. In reality however, the immense diversity in available pharmaceuticals makes defining a sample for comparison very challenging.

Pharmaceutical products sold throughout the world come in a plethora of different names, product type, levels of patent protection and license status, therapeutic purpose, packaging, formulations/combinations, and strengths. The level of intellectual property protection accorded to a pharmaceutical also varies from country to country as does time-on-market (which depends on launching time) both of which have important implications for price. In addition, variation in societal preferences has led to different products and strengths being dispensed as well as to different approaches to dispensing (e.g. pack-splitting) which also impact unit price and makes standardization difficult. Currency conversion poses further challenges for international price comparison. Whilst exchange rates are a common method of converting from one currency to another, as they are affected by often volatile financial market conditions, they too can fluctuate significantly. Purchasing power parities are meant to smooth out fluctuations in exchange rates since they are independent of financial market conditions, however, they are not actual transaction prices.

Even within a single country, a given pharmaceutical can be available with a variety of names reflecting significant variation in licensing status and marketing strategies. For example, it may have a known brand name, a generic brand name, or just a generic international non-proprietary name. Also, the same molecule may be used in many different products and be sold in a variety of different forms. For example, a given molecule may come as a traditional tablet, a slow-release tablet, a capsule, a suppository, an injection, etc. Often the different forms are launched by the same manufacturer, but this is not always the case. In addition, different technologies used to produce the different forms as well as the marketing strategies behind their sales can create significant variations in price amongst products with the same molecule. Within a single country pharmaceutical prices can also vary by batch, and thus be affected by the scale of purchasing, pharmaceutical policies, and sales sector (e.g. retail, hospital, prescription, over-the-counter).

Given this immense diversity in product mix both within and across countries, standardization across samples imposes poses significant challenges. Whilst standard physical units such as grams, kilograms, litres, tablets, etc. as well as packs and prescriptions are common ways to measure volume of pharmaceuticals, these units are only useful if the pharmaceuticals being studied are uniform. Comparison involving pharmaceuticals with even slightly different characteristics requires other units for standardization. If volume is standardized in terms of grams of active ingredient, pharmaceuticals with low potency will comprise a larger fraction of the total than pharmaceuticals with higher potency. The use of

tablets as the unit of standardized measurement also presents problems due to their differing strengths. The price per pill or "standard unit" is often used but leads to bias if the relation between unit price and volume is non-linear because of economies of scale in packaging or high-volume discounts.

To allow meaningful comparisons despite these complications, the studies presented in this dissertation define pharmaceuticals using an aggregate measure of molecule and therapeutic category. This attempts to capture price differences amongst pharmaceuticals used for the same purpose. However, it also may capture differences in products that are actually used somewhat differently within their therapeutic category and that are therefore not real treatment alternatives. Use of the aggregate measure also means that there can exist much variation across other characteristics of the product such as strength, branding, packaging, time-on-local market, etc. So whilst there is the desire to compare like-for-like products, the more narrowly the sample is defined to ensure similarity of products, the more the sample is restricted and thus less representative of the country's pharmaceutical market as a whole. This can be seen as a significant limitation of the product definition used throughout this work.

The inability to make exact like-for-like comparison across products is also worsened as the number of countries included in the comparison increases. Identifying products that match across country markets becomes increasingly difficult as more countries (especially those with very different underlying cultures and related preferences) are included in the comparison. As a result, the number of products included in the comparison decreases, thereby reducing the representativeness of the sample relative to the markets of the individual countries. The studies presented here made all possible attempts to capture representative samples of pharmaceuticals in calculating relative prices. The sample size of the pharmaceutical products matched multilaterally across several markets is relatively small, however, weakening the conclusions that can be drawn from the simultaneous comparisons of several countries. Whilst efforts were made to put the sample sizes into perspective by mentioning the corresponding relative market volume sizes where appropriate, the limited number of pharmaceuticals captured in the comparisons is certainly a limitation.

The aggregation of price also relies on the use of indices and, as discussed above, index number theory does not provide a single, straightforward formula for how to aggregate prices. Due to variation in preferences across spatial entities (here in terms of countries) that are used to weight prices there is no one perfect index. This is one of the obvious and

unavoidable weaknesses of previous studies. This work presented here has strived to improve on this fundamental limitation by taking a practical approach and using simultaneously several price indices. Depending on the policy context, different indices are more appropriate (e.g. in terms of population preferences for weighting, time-frame, etc.). Using an index weighted according to country preferences allows for the index to help draw findings for policy-making within that country context. This attribute of indices such as the Laspeyres index—which uses preferences of the base country--and Paasche index—which uses preferences of the comparator country—explains why these are the two most commonly used indices within countries, Laspeyres being by far the most popular (see Intro section for other useful attributes of these indices). However, the predominance of one country in the calculation of these indices also limits them in terms of their ability to answer policy questions posed specifically at the global level. Averaging these two indices offers one way around this problem. As the geometric average of the Laspeyres and Paasche indices, Fisher indices allow for a more neutral calculation of price relatives. This is the general approach taken in this work. However, in being a mix of two indices that use different consumption patterns to weight prices make Fisher indices also less easy to interpret.

In sum, given the inherent differences in and between pharmaceutical markets, there is no single ideal measure of price differences. However, whilst none are perfect, certain methods are more appropriate than others. The methods chosen for the studies presented here purposefully tackle pharmaceutical price comparison from multiple angles in order to mitigate these problems and provide robust estimates for relative differences across as many products and countries as possible. Perhaps the most significant advantage of the multi-index approach taken in this work is that the differences in the values of the individual indices make particularly obvious the inherent limitation of the price comparisons, and they provide in some way a measure of that limitation.

WHERE TO FROM HERE?

One of the primary policy implications of this dissertation comes out of its findings on pharmaceutical pricing and the inability of current strategies to achieve acceptable levels of vertical equity. The international pharmaceutical industry can in principle choose either to be constrained by national or private payer price negotiations, or simply to refrain from entering national markets completely. This industry could in principle be maximizing sales and improving efficiency by pricing their products differentially in different countries in line with affordability yet it doesn't appear to be doing so. The findings presented in Papers 1 and 3

suggest that this is a particular concern for middle-income countries, some of which appear to pay higher prices than those offered in high-income countries and some of which seem to pay extremely low prices, even when compared to very poor countries. Looking to the future, one might predict that despite strong economic growth in several middle-income countries, prices may not follow suit. Indeed pharmaceutical prices in richer middle-income countries may not evolve like those of high-income countries as a consequence of the numerous price-confounding effects of demographics and social development identified in Paper 3. The call for fairer pricing in pharmaceuticals in middle-income countries requires a nuanced response. These countries should be expected to pay more as they grow richer, in line with notions of vertical equity, but their ability to adapt to the competitive global marketplace shouldn't be assumed to be on par with that of high-income countries. Conversely, normal market price movements are hindered by unpredictability, including the possibility of price regulation by new governments, thus decreasing the ability of middle-income countries to negotiate prices for pharmaceuticals over the longer-term. This can be disastrous in countries facing particularly difficult health challenges resulting from fast population growth, an aging population, or some particular epidemic or environment-related disease. Economies of scale are badly needed in negotiating price in such situations.

Findings of this dissertation suggest that there are other attributes, particularly social and demographic, that harm the ability of countries to negotiate prices and to obtain the needed volumes of pharmaceuticals for the most disadvantaged and least healthy populations. As a consequence, a discriminate approach is necessary if the international community is committed to fairer pricing of pharmaceuticals. The difficulty is to simultaneously improve the negotiating power of middle-income countries in price discussions whilst also ensuring their greater contribution relative to lesser developed countries, where normal market functioning is rare due to limited resources and insufficient infrastructure. Further, as stressed in Paper 1, to make any real headway on this issue the question of differential access to pharmaceuticals *within* countries must also be addressed. Indeed levels of financial inequality and related inequity of access are sometimes worse in some regions of middle-income countries than anywhere in the world. If a uniform price existed for each country based on national income, some poorer populations would simply fall out of the market. This is now occurring in some middle-income countries where pharmaceuticals tend to be sold at uniform prices aimed at the richer parts of the population. Even when existing natural barriers between markets (e.g., the separation of rich urban classes from poor rural areas utilizing different dispensing outlets) make them potentially feasible, local pricing strategies in line with

affordability for the benefit of the poor are rarely enacted. This results partly from a number of perceived difficulties on the part of pharmaceutical companies and political expediency on the part of governments.

Ultimately the difficulty is to incentivize pharmaceutical companies to sell their products into less certain, less familiar, or simply poorer markets. One possibility is to use external, pooled price negotiations through international tendering. This is being done, for example, to improve access to malaria, TB, and HIV pharmaceuticals in poor countries. Such external price negotiation can help pool resources to improve monopsonistic leverage and achieve prices more in line with affordability. As has been demonstrated in the case of HIV pharmaceuticals, the use of even broad classification of countries by income category can do much to alleviate notions of unfairness amongst company negotiators. Crucially, pooled procurement initiatives have not tried to push prices down to levels of marginal costs. This balanced approach is a necessary condition to build a constructive dialogue that ultimately helps smooth the way for badly needed pharmaceuticals to be sold at reasonable prices in developing markets. From the viewpoint of pharmaceutical companies, external, pooled price negotiation can also help streamline registration processes, for example through WHO prequalification. The resulting knock-on effects improve the perceived quality of the product and thereby increase uptake (Danzon, Mulcahy, Towse 2011) towards more statically efficient levels. It can also help lower the financial risk to pharmaceutical companies by increasing the certainty of present and future sale volumes—an important factor for pharmaceuticals and a critical one for vaccines. The benefits of external, pooled price negotiation are numerous and, in addition to facilitating access in low-income countries, they may be an important option for overcoming the inherently poor negotiating position of countries with particular social or demographic weaknesses such as those identified in Paper 3. For these countries, internationally-supported institutions could be used to help improve the availability of the most needed pharmaceuticals at affordable prices.

Even when countries do not want to relinquish price negotiations to external parties, more can be done to encourage pharmaceutical companies to sell into under-served or negotiation-disadvantaged markets. The key is to convince them that, if they sell at different price points—either across countries or within countries—they will be able to adequately segment the different markets and thereby maintain differential prices according to means (for example so that richer middle-income countries will not end up paying prices offered for "compassionate" purposes to poorer populations). In other words pharmaceutical companies

need to receive greater assurances that their efforts to improve access on the grounds of vertical equity will not erode what they perceive as horizontal equity. This is a difficult proposition for several reasons. A common worry is that, if companies make their products available to poorer countries at low prices in line with national affordability, richer countries that can afford to pay more may simply demand similar low prices. This is particularly the case if procurement is sufficiently centralized as in the case of a sole public payer or powerful large private payers which have strong bargaining power. Such "external price referencing" pushes prices down toward marginal costs, a very unattractive situation for companies which may, as a result, choose to simply exit some markets or refrain from registering their product in some countries. The use of external price referencing, which has expanded considerably over the past two decades as a means of price control (Espin et al., 2010), hinders differential pricing that could simultaneously improve efficiencies for companies and increase access for poorer populations. Nonetheless it is widely practiced amongst countries claiming to be supportive of industry and of better global access to pharmaceuticals. Some countries are becoming increasingly aware of the negative implications that their own prices are being used as references (Ruggeri and Nolte 2013). But the situation is unlikely to change unless there is more transparency in terms of which countries use external price referencing and its consequences in terms of shortages or disproportionate prices in lower income countries. An approach of more publicized country stratification and an explicit process of naming-and-shaming could be a starting point.

More could also be done to address the physical hindrances to segmenting markets. For example, pharmaceutical companies could be helped in marketing their products to different populations in a way that would prevent leakage between poorer and richer markets. This could be achieved through packaging differences to demarcate specific sales streams, coupled with quality stamps (e.g. WHO pre-approval stamps) to help uptake and prevent stigmatization of products intended for sales in poorer markets. In addition steps could be taken to alleviate the fears of parallel importing—the re-importation of lower priced products from poorer into richer markets. Whilst experts have found little evidence that this practice is very common across income categories, there does seem to be a stronger possible role for the international community in preventing such practice, particularly through better use of border controls. Finally, and perhaps most difficult to tackle, is the problem of mark-ups. Companies fear that if they are to make their products available at lower cost to under-served and poorer populations, the lack of infrastructure and regulation will allow middlemen to exploit price differences and effectively undermine the intended increase in availability and

affordability. This is a problem that needs to be solved by national agencies, possibly with support from the international community.

In sum, improving universal access to pharmaceuticals by pricing them in line with national or regional affordability is an endeavour in which pharmaceutical companies, national governments and, in some instances, the international community should all play a role. Critically, there needs to be a more constructive two-way exchange between companies and governments. Companies can offer pharmaceuticals at an affordable price in exchange for a better understanding on how they can optimally segment markets across and within-countries. In turn, governments are well placed to provide information regarding local income patterns and ensure that markets remain segmented.

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APPENDIX 1
SUPPORT MATERIAL FOR PAPER 1

CONTENTS

- Additional technical specifications
- Additional study limitations
- Description of sample representativeness
- Additional results (30 additional sets of indices)

Additional indices were constructed based on the following samples:

1. Prices relative to United States based on bilaterally-matched sample, Paasche price indices, price per standard unit standard unit
2. Prices relative to United States based on bilaterally-matched sample, Laspeyres price indices, price per standard unit
3. Prices relative to United States based on bilaterally-matched sample, Paasche price indices, price per standard unit standard unit (graph)
4. Prices relative to United States based on bilaterally-matched sample, Laspeyres price indices, price per standard unit (graph)
5. Prices relative to United States based on bilaterally-matched sample, Paasche price indices, price per kilogram
6. Prices relative to United States based on bilaterally-matched sample, Laspeyres price indices, price per kilogram
7. Prices relative to discounted US prices based on bilaterally-matched sample, Paasche price indices, price per standard unit
8. Prices relative to discounted US based on bilaterally-matched sample, Laspeyres price indices, price per standard unit
9. Prices relative to discounted US prices based on bilaterally-matched sample, Paasche price indices, price per kilogram
10. Prices relative to discounted US based on bilaterally-matched sample, Laspeyres price indices, price per kilogram
11. Prices relative to United States based on multilaterally-matched sample, Paasche price indices, price per standard unit
12. Prices relative to United States based on multilaterally-matched sample, Laspeyres price indices, price per standard unit

13. Prices relative to United States based on multilaterally-matched sample, Paasche price indices, price per kilogram
14. Prices relative to United States based on multilaterally-matched sample, Laspeyres price indices, price per kilograms
15. Prices relative to United Kingdom based on bilaterally-matched sample, Paasche price indices, price per standard unit
16. Prices relative to UK based on bilaterally-matched sample, Laspeyres price indices, price per standard unit
17. Prices relative to United Kingdom based on multilaterally-matched sample, Paasche price indices, price per standard unit
18. Prices relative to United Kingdom based on multilaterally-matched sample, Laspeyres price indices, price per standard unit
19. Prices relative to United Kingdom based on multilaterally-matched sample, Paasche price indices, price per kilogram
20. Prices relative to United Kingdom based on multilaterally-matched sample, Laspeyres price indices, price per kilogram
21. Prices relative to France based on bilaterally-matched sample, Paasche price indices, price per standard unit
22. Prices relative to France based on bilaterally-matched sample, Laspeyres price indices, price per standard unit
23. Prices relative to France based on multilaterally-matched sample, Paasche price indices, price per standard unit
24. Prices relative to France based on multilaterally-matched sample, Laspeyres price indices, price per standard unit
25. Prices relative to France based on bilaterally-matched sample, Paasche price indices, price per kilogram
26. Prices relative to France based on bilaterally-matched sample, Laspeyres price indices, price per kilogram
27. Prices relative to France based on multilaterally-matched sample, Paasche price indices, price per kilogram
28. Prices relative to France based on multilaterally-matched sample, Laspeyres price indices, price per kilogram
29. Prices relative to western Africa based on bilaterally-matched sample, Paasche price indices, price per standard unit
30. Prices relative to western Africa based on bilaterally-matched sample, Laspeyres price indices, price per standard unit (table)
31. Prices relative to western Africa based on bilaterally-matched sample, Paasche price indices, price per standard unit (graph)
32. Prices relative to western Africa based on bilaterally-matched sample, Laspeyres price indices, price per standard unit (graph)

33. Prices relative to western Africa based on bilaterally-matched sample, Paasche price indices, price per kilogram

    Prices relative to western Africa based on bilaterally-matched sample, Laspeyres price indices, price per kilogram

- ❖ Brief summary of findings from Additional results

ADDITIONAL TECHNICAL SPECIFICATIONS

As stated in the text, prices generally correspond to those placed on a product as it leaves the manufacturer, headed for the retail pharmacy. Exceptions were: 1. Indonesia and Malaysia, which included aggregate prices for medicines destined for retail, hospitals, and dispensing doctors and 2. The United States where prices were based on drugstore, food store and mail service distribution channels, excluding discounts. As stated in the text prices were based on year-on-year comparison. Multi-molecule products as well as those with very small sales volumes (the lowest 3 percent of sales) were excluded to avoid double counting, small number and entry (negative numbers) errors.

The hypothesis behind Exhibit 5 was that drug prices could vary in line with other medical-related costs, even those that tend to be largely affected by within-country non-tradeables. Drug costs are not part of these hospital costs. Indeed the cost per beddday estimates "represent only the hotel component of hospital costs, i.e., excluding the cost of drugs and diagnostic tests but including costs such as personnel, capital and food costs." (WHO Choice database, Unit cost estimates)

ADDITIONAL STUDY LIMITATIONS

We recognise that relative prices may be very sensitive to other elements of study design. For example, although we do not present prices per kilogram, it is known that the unit of measurement will affect results[7]. Formulations with smaller amounts of active ingredient may require more doses to achieve the same therapeutic levels.

We also recognise that the prices used in the estimation may not reflect those faced by the patient and related levels of access or issues surrounding parallel trade. Indeed, as has been suggested in previous studies, post-landing mark-ups can have a significant impact on eventual sale prices, especially in countries where there is poor infrastructure and governance. In an examination of prices of 14 medicines for chronic diseases in 36 country settings, Gelders et al. found that taxes and

duties levied on medicines, as well as the mark-ups applied, frequently contributed more to pharmaceutical end price than manufacturer price. If fairer prices are ever to become a reality for patients these issues must be addressed on a national/regional level. Finally, this study also ignores the issues of parallel trade and external referencing, which could in theory cause differential pricing policies to fail. The risk that low prices granted in low-income countries will lead richer countries to demand similar prices or acquire them through imports from low-price countries is sometimes argued to be the most important obstacle to attaining lower prices in lower-income countries.

DESCRIPTION OF SAMPLE REPRESENTATIVENESS

Market description by country (average across years)						
	% OB in sample	**% OB in overall database**	**% any brand in sample**	**% in overall database**	**% OTC in sample**	**% OTC in overall database**
BRAZIL	9%	9%	76%	74%	23%	26%
EGYPT	9%	10%	78%	76%		
INDIA						
INDONESIA	9%	10%	81%	79%	12%	13%
MALAYSIA	13%	14%	73%	71%	23%	25%
MEXICO	12%	13%	76%	76%	12%	14%
MOROCCO	16%	17%	85%	82%		
PHILIPPINES	10%	11%	70%	69%	10%	12%
POLAND	14%	15%	69%	68%	23%	24%
SOUTH AFRICA	17%	17%	70%	68%	35%	38%
THAILAND	6%	6%	79%	75%		
TUNISIA	20%	22%	79%	77%		
TURKEY	13%	14%	85%	82%		
WESTERN AFRICA	14%	14%	65%	63%		

The table above describes the data sample described in Paper 1. Missing values in tables represent non-availability in the database. For countries for which full market structure data were available and products prices were available in all years, the average deviation of the sample composition from the

overall market (here the database as a whole) was -1[38], +2, and - 2 percentage points for capturing all branded products, original brands, and over the counter medications respectively. In other words, the make-up of our sample matched the broader market very closely. For products available in only 5 out of 10 years the deviation was –9, 0, and 8 percentage points respectively.

ADDITIONAL RESULTS

Note that Exhibit 2 in Paper 1 in the text presents the price comparison based on samples bilaterally matched with the United States and weighted according to that country's consumption patterns using Laspeyres indices. Exhibit 3 presents the price comparison based on samples bilaterally matched with the United States and weighted according to the foreign country's consumption pattern using Paasche index calculation methods. In order to see how results differed by country sample, by base country, by unit of physical measurement, by type of index used, by matched sample, and by the effects of discounting, several additional analyses to those in Paper 1 were undertaken.

[38] (+) signifies that the number of products in the sample that had this characteristic was greater than the number within the overall database with that characteristic. (-) signifies that there were fewer in the sample.

1. PRICES RELATIVE TO UNITED STATES BASED ON BILATERALLY-MATCHED SAMPLE, PAASCHE PRICE INDICES, PRICE PER STANDARD UNIT

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
ALGERIA				0.19	0.15	0.14	0.14	0.13	0.13	0.13
BRAZIL	0.51	0.49	0.37	0.30	0.28	0.29	0.34	0.35	0.34	0.39
EGYPT	0.13	0.12	0.16	0.12	0.10	0.10	0.11	0.11	0.10	0.09
INDIA	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04
INDONESIA	0.19	0.15	0.12	0.14	0.16	0.15	0.11	0.05	0.05	0.04
MALAYSIA	0.17	0.17	0.18	0.19	0.19	0.17	0.17	0.20	0.19	0.18
MEXICO	0.26	0.26	0.74	0.71	0.64	0.62	0.70	0.68	0.67	0.65
MOROCCO	0.26	0.24	0.23	0.22	0.23	0.27	0.27	0.27	0.28	0.30
PHILIPPINES	0.36	0.27	0.25	0.24	0.20	0.19	0.20	0.22	0.16	0.16
POLAND	0.18	0.18	0.21	0.20	0.23	0.23	0.24	0.22	0.21	0.27
SOUTH AFRICA	0.48	0.40	0.30	0.25	0.34	0.34	0.32	0.27	0.24	0.20
THAILAND	0.06	0.05	0.04	0.04	0.05	0.04	0.04	0.05	0.07	0.05
TUNISIA	0.21	0.16	0.15	0.15	0.16	0.17	0.16	0.15	0.15	0.16
TURKEY	1.09	0.69	0.44	0.37	0.35	0.33	0.31	0.27	0.27	0.25
WESTERN AFRICA	0.14	0.10	0.11	0.09	0.10	0.13	0.12	0.12	0.13	0.13

2. PRICES RELATIVE TO UNITED STATES BASED ON BILATERALLY-MATCHED SAMPLE, LASPEYRES PRICE INDICES, PRICE PER STANDARD UNIT

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
ALGERIA				0.44	0.42	0.42	0.41	0.39	0.42	0.41
BRAZIL	0.91	0.88	0.61	0.46	0.46	0.47	0.56	0.62	0.71	0.82
EGYPT	0.63	0.55	0.46	0.38	0.30	0.25	0.27	0.27	0.27	0.27
INDIA	0.18	0.14	0.12	0.11	0.12	0.11	0.10	0.10	0.11	0.13
INDONESIA	0.63	0.56	0.47	0.57	0.61	0.53	0.46	0.46	0.48	0.53
MALAYSIA	0.52	0.50	0.51	0.47	0.48	0.41	0.39	0.40	0.43	0.47
MEXICO	1.07	1.05	1.08	1.06	0.96	0.93	0.95	0.97	1.01	1.08
MOROCCO	0.52	0.45	0.41	0.41	0.45	0.48	0.46	0.45	0.49	0.54
PHILIPPINES	1.06	0.84	0.72	0.68	0.68	0.60	0.60	0.65	0.76	0.82
POLAND	0.42	0.40	0.41	0.42	0.46	0.45	0.48	0.49	0.53	0.65
SOUTH AFRICA	0.80	0.62	0.48	0.39	0.55	0.59	0.53	0.48	0.47	0.42
THAILAND	0.45	0.38	0.34	0.37	0.36	0.36	0.35	0.38	0.46	0.48
TUNISIA	0.47	0.37	0.34	0.34	0.36	0.38	0.36	0.35	0.40	0.46
TURKEY	2.12	1.27	0.69	0.58	0.54	0.46	0.43	0.38	0.44	0.45
WESTERN AFRICA	0.55	0.43	0.40	0.39	0.41	0.52	0.49	0.46	0.51	0.55

3. PRICES RELATIVE TO UNITED STATES BASED ON BILATERALLY-MATCHED SAMPLE, PAASCHE PRICE INDICES, PRICE PER KILOGRAM

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
ALGERIA				0.12	0.09	0.11	0.07	0.06	0.01	0.05
BRAZIL	0.53	0.50	0.37	0.29	0.14	0.00	0.00	0.31	0.39	0.30
EGYPT	0.12	0.12	0.12	0.10	0.07	0.02	0.00	0.11	0.03	0.05
INDIA	0.05	0.03	0.05	0.05	0.04	0.01	0.00	0.04	0.04	0.04
INDONESIA	0.23	0.17	0.14	0.18	0.21	0.12	0.02	0.11	0.09	0.07
MALAYSIA	0.15	0.17	0.19	0.18	0.11	0.00	0.00	0.03	0.04	0.03
MEXICO	0.66	0.61	0.69	0.64	0.11	0.00	0.00	0.59	0.49	0.27
MOROCCO	0.22	0.16	0.16	0.15	0.14	0.01	0.00	0.07	0.01	0.04
PHILIPPINES	0.47	0.31	0.33	0.30	0.23	0.02	0.00	0.21	0.23	0.17
POLAND	0.18	0.18	0.21	0.20	0.09	0.00	0.00	0.08	0.28	0.02
SOUTH AFRICA	0.15	0.15	0.12	0.07	0.10	0.00	0.00	0.13	0.20	0.08
THAILAND	0.08	0.06	0.06	0.06	0.06	0.00	0.00	0.04	0.08	0.06
TUNISIA	0.20	0.09	0.10	0.09	0.09	0.12	0.12	0.09	0.15	0.10
TURKEY	1.08	0.18	0.05	0.03	0.00	0.00	0.00	0.27	0.27	0.09
WESTERN AFRICA	0.20	0.06	0.06	0.04	0.04	0.06	0.01	0.05	0.02	0.05

4. PRICES RELATIVE TO UNITED STATES BASED ON BILATERALLY-MATCHED SAMPLE, LASPEYRES PRICE INDICES, PRICE PER KILOGRAM

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
ALGERIA				0.50	0.54	0.54	0.80	0.74	0.48	0.50
BRAZIL	1.39	1.48	0.63	0.51	0.52	0.53	1.37	0.84	2.95	1.43
EGYPT	0.48	0.45	0.43	0.72	0.29	0.25	0.27	0.27	0.27	0.28
INDIA	0.16	0.14	0.13	0.12	0.12	0.12	0.12	0.12	0.16	0.37
INDONESIA	0.74	0.69	0.52	0.63	0.72	0.68	0.53	0.61	0.86	2.69
MALAYSIA	0.48	0.46	0.48	0.46	0.45	0.44	0.45	0.46	0.49	0.60
MEXICO	4.04	4.25	4.34	8.48	7.13	6.54	21.1	1.06	1.15	1.22
MOROCCO	0.87	0.47	0.45	0.46	0.53	0.56	0.55	0.54	0.56	0.63
PHILIPPINES	1.65	1.31	1.05	1.04	0.97	0.66	0.73	0.75	0.92	0.96
POLAND	0.96	0.80	0.99	1.20	2.78	0.47	0.50	19.2	6.12	0.71
SOUTH AFRICA	0.83	0.69	1.38	2.98	1.87	1.42	0.69	0.55	0.52	0.46
THAILAND	0.46	0.44	0.48	0.58	0.64	0.55	0.53	0.66	3.50	0.86
TUNISIA	0.54	0.43	2.95	0.44	0.49	0.52	0.44	0.43	0.63	5.32
TURKEY	1.93	1.26	0.69	0.61	0.59	3.58	0.51	0.41	0.50	0.59
WESTERN AFRICA	0.73	0.56	0.52	0.55	0.58	0.57	0.53	0.53	0.57	0.62

5. PRICES RELATIVE TO DISCOUNTED US PRICES BASED ON BILATERALLY-MATCHED SAMPLE, PAASCHE PRICE INDICES, PRICE PER STANDARD UNIT

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
ALGERIA				0.21	0.16	0.15	0.15	0.14	0.14	0.14
BRAZIL	0.56	0.54	0.41	0.33	0.31	0.32	0.37	0.38	0.37	0.42
EGYPT	0.14	0.13	0.17	0.13	0.11	0.11	0.12	0.12	0.11	0.10
INDIA	0.05	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04
INDONESIA	0.21	0.16	0.13	0.15	0.18	0.16	0.12	0.06	0.05	0.04
MALAYSIA	0.18	0.18	0.20	0.20	0.21	0.18	0.18	0.22	0.21	0.19
MEXICO	0.29	0.28	0.81	0.77	0.70	0.67	0.76	0.74	0.73	0.70
MOROCCO	0.28	0.26	0.25	0.24	0.25	0.29	0.29	0.29	0.30	0.33
PHILIPPINES	0.39	0.30	0.28	0.26	0.22	0.20	0.22	0.24	0.17	0.17
POLAND	0.20	0.19	0.23	0.22	0.25	0.25	0.26	0.24	0.23	0.30
SOUTH AFRICA	0.52	0.43	0.33	0.27	0.37	0.37	0.35	0.30	0.26	0.22
THAILAND	0.07	0.05	0.04	0.05	0.05	0.05	0.05	0.05	0.08	0.06
TUNISIA	0.22	0.17	0.17	0.16	0.17	0.19	0.17	0.16	0.16	0.17
TURKEY	1.19	0.75	0.48	0.41	0.38	0.36	0.34	0.29	0.29	0.28
WESTERN AFRICA	0.16	0.11	0.12	0.10	0.11	0.14	0.13	0.13	0.14	0.14

6. PRICES RELATIVE TO DISCOUNTED US BASED ON BILATERALLY-MATCHED SAMPLE, LASPEYRES PRICE INDICES, PRICE PER STANDARD UNIT

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
ALGERIA				0.47	0.46	0.46	0.45	0.42	0.45	0.45
BRAZIL	0.99	0.96	0.66	0.50	0.50	0.51	0.60	0.68	0.78	0.89
EGYPT	0.69	0.59	0.49	0.41	0.33	0.28	0.30	0.30	0.30	0.30
INDIA	0.20	0.15	0.13	0.12	0.13	0.12	0.11	0.11	0.12	0.14
INDONESIA	0.68	0.61	0.52	0.62	0.67	0.58	0.50	0.51	0.52	0.57
MALAYSIA	0.56	0.54	0.55	0.51	0.52	0.45	0.43	0.44	0.47	0.51
MEXICO	1.17	1.14	1.17	1.15	1.04	1.01	1.04	1.06	1.10	1.18
MOROCCO	0.56	0.49	0.44	0.44	0.49	0.52	0.50	0.49	0.53	0.59
PHILIPPINES	1.15	0.91	0.79	0.74	0.74	0.65	0.65	0.70	0.82	0.89
POLAND	0.46	0.43	0.44	0.45	0.50	0.49	0.52	0.54	0.58	0.70
SOUTH AFRICA	0.87	0.68	0.53	0.42	0.60	0.64	0.58	0.52	0.51	0.46
THAILAND	0.49	0.42	0.37	0.40	0.39	0.39	0.39	0.41	0.49	0.52
TUNISIA	0.51	0.41	0.37	0.37	0.39	0.41	0.39	0.39	0.43	0.50
TURKEY	2.31	1.39	0.75	0.64	0.59	0.50	0.47	0.41	0.48	0.49
WESTERN AFRICA	0.60	0.46	0.44	0.43	0.45	0.57	0.53	0.50	0.55	0.60

7. PRICES RELATIVE TO DISCOUNTED US PRICES BASED ON BILATERALLY-MATCHED SAMPLE, PAASCHE PRICE INDICES, PRICE PER KILOGRAM

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
ALGERIA				0.13	0.10	0.12	0.07	0.06	0.01	0.05
BRAZIL	0.57	0.55	0.40	0.31	0.15	0.00	0.00	0.33	0.42	0.33
EGYPT	0.13	0.13	0.13	0.11	0.07	0.02	0.00	0.12	0.03	0.05
INDIA	0.06	0.04	0.05	0.05	0.05	0.01	0.00	0.05	0.05	0.04
INDONESIA	0.25	0.18	0.15	0.20	0.22	0.13	0.02	0.12	0.10	0.08
MALAYSIA	0.17	0.18	0.20	0.20	0.12	0.00	0.00	0.03	0.04	0.03
MEXICO	0.72	0.67	0.76	0.70	0.12	0.00	0.00	0.64	0.53	0.29
MOROCCO	0.24	0.18	0.17	0.16	0.15	0.01	0.00	0.08	0.01	0.04
PHILIPPINES	0.51	0.34	0.36	0.32	0.25	0.02	0.00	0.23	0.25	0.19
POLAND	0.20	0.20	0.23	0.21	0.09	0.00	0.00	0.08	0.31	0.02
SOUTH AFRICA	0.16	0.17	0.13	0.08	0.11	0.00	0.00	0.14	0.22	0.08
THAILAND	0.09	0.07	0.06	0.07	0.06	0.00	0.00	0.04	0.09	0.07
TUNISIA	0.22	0.09	0.11	0.10	0.10	0.13	0.14	0.10	0.16	0.10
TURKEY	1.17	0.19	0.06	0.03	0.00	0.00	0.00	0.29	0.30	0.10
WESTERN AFRICA	0.21	0.06	0.06	0.05	0.04	0.07	0.01	0.05	0.02	0.05

8. PRICES RELATIVE TO DISCOUNTED US BASED ON BILATERALLY-MATCHED SAMPLE, LASPEYRES PRICE INDICES, PRICE PER KILOGRAM

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
ALGERIA				0.54	0.59	0.59	0.87	0.81	0.52	0.55
BRAZIL	1.51	1.61	0.69	0.55	0.56	0.58	1.49	0.91	3.21	1.56
EGYPT	0.52	0.49	0.47	0.78	0.32	0.28	0.29	0.29	0.30	0.31
INDIA	0.17	0.15	0.14	0.13	0.13	0.13	0.13	0.13	0.18	0.40
INDONESIA	0.80	0.75	0.56	0.68	0.78	0.74	0.58	0.66	0.93	2.92
MALAYSIA	0.53	0.50	0.52	0.50	0.48	0.48	0.49	0.50	0.53	0.65
MEXICO	4.39	4.62	4.72	9.22	7.75	7.10	22.94	1.15	1.25	1.33
MOROCCO	0.95	0.51	0.49	0.50	0.58	0.61	0.60	0.59	0.61	0.68
PHILIPPINES	1.79	1.42	1.14	1.13	1.06	0.72	0.79	0.81	1.00	1.05
POLAND	1.05	0.87	1.08	1.31	3.02	0.51	0.55	20.87	6.65	0.77
SOUTH AFRICA	0.90	0.75	1.50	3.24	2.03	1.54	0.75	0.60	0.57	0.50
THAILAND	0.50	0.48	0.52	0.63	0.70	0.60	0.58	0.72	3.80	0.94
TUNISIA	0.59	0.47	3.21	0.47	0.54	0.56	0.48	0.47	0.68	5.78
TURKEY	2.09	1.37	0.75	0.66	0.64	3.89	0.56	0.45	0.54	0.64
WESTERN AFRICA	0.79	0.61	0.56	0.59	0.63	0.62	0.58	0.58	0.62	0.67

9. PRICES RELATIVE TO UNITED STATES BASED ON MULTILATERALLY-MATCHED SAMPLE, PAASCHE PRICE INDICES, PRICE PER STANDARD UNIT

	2002	2003	2004	2005	2006	2007	2008
ALGERIA	0.34	0.32	0.33	0.33	0.30	0.26	0.27
BRAZIL	0.38	0.36	0.37	0.44	0.48	0.44	0.47
EGYPT	0.18	0.13	0.13	0.16	0.17	0.14	0.15
FRANCE	0.32	0.38	0.43	0.42	0.40	0.39	0.46
INDIA	0.05	0.04	0.04	0.04	0.05	0.05	0.05
INDONESIA	0.29	0.31	0.28	0.27	0.15	0.12	0.05
MALAYSIA	0.19	0.21	0.20	0.21	0.16	0.15	0.13
MEXICO	1.04	0.92	0.90	0.97	0.95	0.79	0.73
MOROCCO	0.33	0.37	0.43	0.46	0.44	0.41	0.47
PHILIPPINES	0.21	0.18	0.16	0.19	0.21	0.22	0.13
POLAND	0.19	0.21	0.20	0.21	0.21	0.21	0.26
SOUTH AFRICA	0.33	0.44	0.42	0.36	0.30	0.24	0.20
THAILAND	0.04	0.04	0.04	0.03	0.04	0.06	0.04
TUNISIA	0.28	0.30	0.32	0.34	0.25	0.23	0.23
TURKEY	0.40	0.35	0.34	0.31	0.27	0.24	0.27
UNITED KINGDOM	0.40	0.42	0.45	0.38	0.37	0.41	0.40
WESTERN AFRICA	0.31	0.33	0.39	0.39	0.37	0.33	0.30

10. PRICES RELATIVE TO UNITED STATES BASED ON MULTILATERALLY-MATCHED SAMPLE, LASPEYRES PRICE INDICES, PRICE PER STANDARD UNIT

	2002	2003	2004	2005	2006	2007	2008
ALGERIA	0.41	0.40	0.40	0.37	0.34	0.35	0.37
BRAZIL	0.40	0.37	0.38	0.46	0.55	0.61	0.78
EGYPT	0.41	0.32	0.29	0.34	0.34	0.33	0.35
FRANCE	0.39	0.45	0.50	0.50	0.49	0.54	0.66
INDIA	0.08	0.08	0.07	0.08	0.08	0.09	0.10
INDONESIA	0.37	0.46	0.41	0.42	0.40	0.39	0.41
MALAYSIA	0.41	0.42	0.31	0.31	0.36	0.39	0.46
MEXICO	1.06	0.98	0.93	1.01	1.06	1.14	1.33
MOROCCO	0.40	0.44	0.47	0.48	0.49	0.52	0.59
PHILIPPINES	0.60	0.58	0.53	0.53	0.62	0.74	0.83
POLAND	0.27	0.30	0.27	0.28	0.30	0.31	0.40
SOUTH AFRICA	0.37	0.49	0.51	0.46	0.45	0.43	0.41
THAILAND	0.29	0.32	0.34	0.35	0.38	0.46	0.52
TUNISIA	0.33	0.35	0.37	0.36	0.36	0.41	0.49
TURKEY	0.44	0.39	0.36	0.32	0.28	0.32	0.36
UNITED KINGDOM	0.44	0.48	0.52	0.45	0.48	0.53	0.52
WESTERN AFRICA	0.38	0.37	0.45	0.42	0.43	0.48	0.55

11. PRICES RELATIVE TO UNITED STATES BASED ON MULTILATERALLY-MATCHED SAMPLE, PAASCHE PRICE INDICES, PRICE PER KILOGRAM

	2002	2003	2004	2005	2006	2007	2008
ALGERIA	0.37	0.35	0.36	0.42	0.38	0.39	0.36
BRAZIL	0.38	0.36	0.37	0.46	0.49	0.35	0.22
EGYPT	0.21	0.14	0.13	0.16	0.16	0.14	0.06
FRANCE	0.27	0.34	0.46	0.48	0.46	0.48	0.06
INDIA	0.06	0.06	0.06	0.07	0.07	0.07	0.05
INDONESIA	0.33	0.34	0.31	0.32	0.12	0.09	0.07
MALAYSIA	0.22	0.26	0.26	0.26	0.15	0.13	0.06
MEXICO	1.15	0.90	0.82	0.87	0.74	0.47	0.16
MOROCCO	0.29	0.34	0.40	0.48	0.46	0.46	0.07
PHILIPPINES	0.47	0.46	0.45	0.46	0.33	0.35	0.23
POLAND	0.21	0.24	0.24	0.25	0.25	0.24	0.01
SOUTH AFRICA	0.12	0.19	0.27	0.26	0.25	0.24	0.04
THAILAND	0.06	0.07	0.07	0.07	0.07	0.08	0.08
TUNISIA	0.28	0.31	0.33	0.39	0.33	0.32	0.12
TURKEY	0.41	0.37	0.36	0.34	0.28	0.27	0.04
WESTERN AFRICA	0.28	0.28	0.35	0.37	0.36	0.35	0.09

12. PRICES RELATIVE TO UNITED STATES BASED ON MULTILATERALLY-MATCHED SAMPLE, LASPEYRES PRICE INDICES, PRICE PER KILOGRAM

	2002	2003	2004	2005	2006	2007	2008
ALGERIA	0.45	0.51	0.52	0.48	0.43	0.46	0.48
BRAZIL	0.42	0.42	0.43	0.53	0.64	0.69	0.87
EGYPT	0.27	0.25	0.23	0.25	0.25	0.24	0.26
FRANCE	0.42	0.51	0.58	0.58	0.56	0.64	0.77
INDIA	0.10	0.11	0.11	0.11	0.11	0.13	0.14
INDONESIA	0.46	0.58	0.54	0.53	0.51	0.49	0.51
MALAYSIA	0.35	0.39	0.37	0.37	0.39	0.42	0.65
MEXICO	1.10	1.07	1.02	1.09	1.17	1.28	1.48
MOROCCO	0.43	0.53	0.57	0.58	0.60	0.60	0.67
PHILIPPINES	0.71	0.69	0.63	0.63	0.70	0.91	0.99
POLAND	0.31	0.33	0.32	0.32	0.32	0.34	0.45
SOUTH AFRICA	7.59	2.42	0.57	0.51	0.47	0.47	0.45
THAILAND	0.30	0.40	0.42	0.41	0.45	0.53	0.58
TUNISIA	0.36	0.45	0.47	0.46	0.45	0.50	0.59
TURKEY	0.48	0.46	7.62	0.39	0.34	0.37	0.39
WESTERN AFRICA	0.43	0.44	0.56	0.54	0.57	0.61	0.70

13. PRICES RELATIVE TO UNITED KINGDOM BASED ON BILATERALLY-MATCHED SAMPLE, PAASCHE PRICE INDICES, PRICE PER STANDARD UNIT

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
ALGERIA				0.41	0.40	0.37	0.37	0.36	0.35	0.37
BRAZIL	0.70	0.74	0.60	0.47	0.46	0.41	0.58	0.66	0.66	0.81
EGYPT	0.26	0.27	0.27	0.20	0.17	0.13	0.19	0.16	0.14	0.15
INDIA	0.10	0.10	0.10	0.10	0.09	0.08	0.09	0.09	0.09	0.09
INDONESIA	0.33	0.33	0.30	0.32	0.39	0.32	0.26	0.24	0.20	0.21
MALAYSIA	0.37	0.40	0.47	0.44	0.40	0.36	0.40	0.43	0.39	0.46
MEXICO	0.94	1.08	1.37	1.34	1.17	0.98	1.09	1.10	1.03	1.14
MOROCCO	0.47	0.47	0.47	0.50	0.53	0.53	0.63	0.62	0.63	0.74
PHILIPPINES	1.02	0.95	0.94	0.90	0.81	0.67	0.71	0.71	0.74	0.87
POLAND	0.17	0.17	0.23	0.26	0.31	0.29	0.38	0.42	0.43	0.56
SOUTH AFRICA	0.84	0.80	0.66	0.47	0.60	0.52	0.52	0.47	0.41	0.38
THAILAND	0.17	0.18	0.17	0.18	0.19	0.17	0.17	0.17	0.20	0.22
TUNISIA	0.40	0.40	0.44	0.46	0.46	0.44	0.45	0.43	0.42	0.46
TURKEY	1.76	1.32	0.79	0.65	0.59	0.49	0.51	0.45	0.46	0.48
WESTERN AFRICA	0.38	0.32	0.34	0.36	0.37	0.37	0.40	0.34	0.36	0.39

14. PRICES RELATIVE TO UK BASED ON BILATERALLY-MATCHED SAMPLE, LASPEYRES PRICE INDICES, PRICE PER STANDARD UNIT

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
ALGERIA				0.91	0.83	0.85	0.92	0.90	0.87	0.92
BRAZIL	1.77	1.76	1.33	1.02	0.95	0.89	1.20	1.40	1.52	1.92
EGYPT	1.09	1.03	0.93	0.76	0.55	0.41	0.55	0.59	0.55	0.60
INDIA	0.31	0.32	0.28	0.21	0.23	0.19	0.22	0.23	0.25	0.28
INDONESIA	0.97	0.95	0.85	1.20	1.10	0.96	1.12	1.00	1.05	1.16
MALAYSIA	0.76	0.82	0.94	0.86	0.77	0.77	0.88	0.89	0.90	1.05
MEXICO	2.06	2.19	2.52	2.44	2.20	2.17	2.70	2.86	2.35	2.73
MOROCCO	0.91	0.94	0.95	0.92	0.98	1.01	1.11	1.11	1.11	1.31
PHILIPPINES	1.66	1.54	1.48	1.43	1.28	1.14	1.28	1.43	1.61	1.90
POLAND	0.59	0.60	0.68	0.67	0.68	0.63	0.76	0.82	0.82	1.08
SOUTH AFRICA	1.57	1.41	1.19	0.91	1.16	1.14	1.07	0.97	0.86	0.84
THAILAND	0.71	0.78	0.76	0.76	0.77	0.68	0.77	0.87	1.00	1.16
TUNISIA	0.79	0.75	0.76	0.75	0.76	0.74	0.85	0.89	0.94	1.15
TURKEY	3.22	2.23	1.29	1.08	0.93	0.76	0.82	0.73	0.75	0.80
WESTERN AFRICA	0.93	0.82	0.87	0.85	0.83	0.93	1.02	1.04	1.07	1.21

15. PRICES RELATIVE TO UNITED KINGDOM BASED ON MULTILATERALLY-MATCHED SAMPLE, PAASCHE PRICE INDICES, PRICE PER STANDARD UNIT

	2002	2003	2004	2005	2006	2007	2008
ALGERIA	0.71	0.64	0.60	0.60	0.56	0.57	0.62
BRAZIL	0.82	0.70	0.69	0.90	0.96	0.99	1.32
EGYPT	0.35	0.24	0.21	0.25	0.25	0.26	0.30
FRANCE	0.77	0.85	0.89	1.02	0.97	0.95	1.13
INDIA	0.12	0.11	0.10	0.12	0.12	0.12	0.14
INDONESIA	0.40	0.41	0.34	0.29	0.24	0.21	0.25
MALAYSIA	0.45	0.44	0.41	0.45	0.48	0.44	0.56
MEXICO	2.21	1.79	1.56	1.77	1.70	1.60	1.77
MOROCCO	0.76	0.79	0.78	0.82	0.79	0.85	1.09
PHILIPPINES	0.97	0.86	0.73	0.76	0.75	0.79	1.00
POLAND	0.35	0.35	0.34	0.46	0.50	0.53	0.72
SOUTH AFRICA	0.79	0.96	0.87	0.86	0.77	0.67	0.67
THAILAND	0.18	0.19	0.17	0.16	0.16	0.20	0.23
TUNISIA	0.61	0.61	0.57	0.62	0.60	0.58	0.68
TURKEY	0.92	0.72	0.64	0.65	0.56	0.59	0.60
WESTERN AFRICA	0.70	0.74	0.76	0.73	0.63	0.64	0.78

16. PRICES RELATIVE TO UNITED KINGDOM BASED ON MULTILATERALLY-MATCHED SAMPLE, LASPEYRES PRICE INDICES, PRICE PER STANDARD UNIT

	2002	2003	2004	2005	2006	2007	2008
ALGERIA	0.91	0.84	0.85	0.98	0.88	0.86	0.95
BRAZIL	1.06	0.96	0.92	1.32	1.50	1.57	2.18
EGYPT	0.76	0.57	0.48	0.71	0.72	0.68	0.77
FRANCE	1.00	1.06	1.10	1.30	1.23	1.28	1.64
INDIA	0.19	0.18	0.17	0.21	0.20	0.22	0.29
INDONESIA	0.88	1.01	0.85	1.32	0.95	0.82	0.90
MALAYSIA	0.69	0.67	0.60	0.73	0.77	0.76	0.92
MEXICO	2.70	2.31	2.07	2.70	2.80	2.80	3.55
MOROCCO	0.88	0.92	0.92	1.12	1.13	1.12	1.38
PHILIPPINES	1.53	1.35	1.14	1.39	1.54	1.69	2.07
POLAND	0.56	0.59	0.52	0.64	0.66	0.68	0.97
SOUTH AFRICA	0.82	0.99	0.96	1.00	0.93	0.84	0.87
THAILAND	0.54	0.62	0.61	0.78	0.86	0.98	1.15
TUNISIA	0.72	0.75	0.74	0.87	0.88	0.95	1.23
TURKEY	1.11	0.88	0.75	0.87	0.71	0.74	0.86
WESTERN AFRICA	0.89	0.83	0.92	1.05	1.09	1.12	1.33

17. PRICES RELATIVE TO UNITED KINGDOM BASED ON MULTILATERALLY-MATCHED SAMPLE, PAASCHE PRICE INDICES, PRICE PER KILOGRAM

	2002	2003	2004	2005	2006	2007	2008
ALGERIA	0.76	0.69	0.65	0.67	0.61	0.61	0.70
BRAZIL	0.80	0.69	0.68	0.87	0.94	0.68	0.93
EGYPT	0.39	0.23	0.20	0.23	0.24	0.24	0.27
FRANCE	0.55	0.64	0.87	1.00	0.95	0.95	1.11
INDIA	0.13	0.12	0.10	0.13	0.12	0.13	0.14
INDONESIA	0.46	0.48	0.39	0.36	0.29	0.26	0.33
MALAYSIA	0.44	0.43	0.40	0.44	0.47	0.39	0.42
MEXICO	2.05	1.36	1.04	1.11	1.00	0.82	0.86
MOROCCO	0.66	0.69	0.69	0.72	0.71	0.73	0.93
PHILIPPINES	1.03	0.88	0.77	0.79	0.80	0.84	1.08
POLAND	0.38	0.38	0.36	0.48	0.52	0.56	0.77
SOUTH AFRICA	0.40	0.51	0.57	0.55	0.49	0.45	0.48
THAILAND	0.21	0.20	0.18	0.18	0.18	0.19	0.21
TUNISIA	0.58	0.60	0.58	0.62	0.62	0.62	0.75
TURKEY	0.78	0.62	0.55	0.56	0.48	0.51	0.54
WESTERN AFRICA	0.65	0.68	0.68	0.67	0.60	0.61	0.76

18. PRICES RELATIVE TO UNITED KINGDOM BASED ON MULTILATERALLY-MATCHED SAMPLE, LASPEYRES PRICE INDICES, PRICE PER KILOGRAM

	2002	2003	2004	2005	2006	2007	2008
ALGERIA	0.85	0.89	0.91	1.09	0.99	0.98	1.08
BRAZIL	0.86	0.80	0.81	1.22	1.42	1.51	2.08
EGYPT	0.54	0.46	0.41	0.60	0.62	0.59	0.65
FRANCE	0.90	0.99	1.07	1.29	1.22	1.32	1.67
INDIA	0.22	0.23	0.21	0.27	0.27	0.30	0.37
INDONESIA	0.95	1.09	0.98	1.12	1.09	0.93	1.03
MALAYSIA	0.75	0.70	0.63	0.78	0.81	0.81	1.22
MEXICO	2.41	2.09	1.91	2.56	2.80	2.93	3.70
MOROCCO	0.86	0.95	0.99	1.27	1.29	1.24	1.52
PHILIPPINES	1.48	1.34	1.14	1.34	1.46	1.62	1.99
POLAND	0.62	0.63	0.56	0.68	0.70	0.71	1.00
SOUTH AFRICA	30.48	8.50	1.02	1.08	1.00	0.92	0.93
THAILAND	0.61	0.70	0.69	0.85	0.94	1.03	1.22
TUNISIA	0.70	0.81	0.82	1.02	1.01	1.08	1.35
TURKEY	1.00	0.87	6.88	0.77	0.68	0.71	0.80
WESTERN AFRICA	0.89	0.88	1.02	1.23	1.33	1.35	1.55

19. PRICES RELATIVE TO FRANCE BASED ON BILATERALLY-MATCHED SAMPLE, PAASCHE PRICE INDICES, PRICE PER STANDARD UNIT

	2000	2001	2002	2003	2004	2005	2006	2007	2008
ALGERIA			0.77	0.63	0.58	0.53	0.50	0.50	0.47
BRAZIL	0.61	0.52	0.42	0.36	0.36	0.45	0.51	0.54	0.58
EGYPT	0.34	0.31	0.26	0.17	0.15	0.19	0.18	0.16	0.15
INDIA	0.13	0.14	0.13	0.11	0.10	0.10	0.10	0.11	0.10
INDONESIA	0.39	0.36	0.43	0.41	0.35	0.28	0.27	0.23	0.22
MALAYSIA	0.45	0.52	0.50	0.41	0.37	0.35	0.38	0.34	0.35
MEXICO	1.83	2.09	2.03	1.56	1.40	1.48	1.56	1.46	1.39
MOROCCO	0.75	0.76	0.75	0.71	0.71	0.70	0.65	0.71	0.70
PHILIPPINES	1.04	1.04	1.01	0.80	0.68	0.67	0.72	0.75	0.75
POLAND	0.35	0.41	0.43	0.42	0.39	0.45	0.41	0.41	0.46
SOUTH AFRICA	1.11	0.90	0.64	0.73	0.65	0.60	0.53	0.45	0.36
THAILAND	0.19	0.19	0.19	0.17	0.16	0.15	0.18	0.23	0.22
TUNISIA	0.58	0.57	0.56	0.49	0.36	0.34	0.35	0.35	0.37
TURKEY	1.95	1.15	0.97	0.79	0.68	0.62	0.56	0.57	0.53
WESTERN AFRICA	0.70	0.72	0.70	0.66	0.63	0.58	0.57	0.57	0.52

20. PRICES RELATIVE TO FRANCE BASED ON BILATERALLY-MATCHED SAMPLE, LASPEYRES PRICE INDICES, PRICE PER STANDARD UNIT

	2000	2001	2002	2003	2004	2005	2006	2007	2008
ALGERIA			1.03	0.88	0.83	0.76	0.81	0.78	0.68
BRAZIL	2.78	2.04	1.39	1.12	1.06	1.21	1.39	1.43	1.50
EGYPT	1.30	1.08	0.87	0.57	0.43	0.47	0.49	0.45	0.41
INDIA	0.58	0.48	0.42	0.34	0.31	0.31	0.29	0.29	0.27
INDONESIA	1.53	1.46	1.48	1.60	1.26	1.16	1.13	0.97	1.06
MALAYSIA	1.59	1.75	1.65	1.33	1.16	1.03	0.99	0.88	0.87
MEXICO	3.05	3.29	3.16	2.39	2.29	2.18	2.23	2.05	1.97
MOROCCO	1.12	1.06	1.04	1.01	0.97	0.97	1.01	0.98	0.98
PHILIPPINES	4.13	3.65	3.25	2.62	2.17	2.02	1.80	1.80	1.84
POLAND	1.01	1.02	1.01	0.93	0.87	0.93	1.02	0.99	1.08
SOUTH AFRICA	1.94	1.58	1.20	1.43	1.40	1.17	1.04	0.87	0.70
THAILAND	0.93	0.89	0.93	0.83	0.79	0.80	0.90	1.00	0.96
TUNISIA	0.86	0.88	0.86	0.82	0.77	0.76	0.80	0.83	0.83
TURKEY	6.02	3.14	2.47	1.82	1.33	1.11	0.93	0.86	0.81
WESTERN AFRICA	0.93	0.96	0.96	0.89	1.13	1.10	1.10	1.10	1.02

21. PRICES RELATIVE TO FRANCE BASED ON MULTILATERALLY-MATCHED SAMPLE, PAASCHE PRICE INDICES, PRICE PER STANDARD UNIT

	2002	2003	2004	2005	2006	2007	2008
ALGERIA	0.77	0.65	0.59	0.55	0.56	0.55	0.49
BRAZIL	0.86	0.70	0.65	0.76	0.91	0.91	0.94
EGYPT	0.40	0.27	0.23	0.25	0.27	0.26	0.24
FRANCE	1.00	1.00	1.00	1.00	1.00	1.00	1.00
INDIA	0.12	0.10	0.09	0.10	0.11	0.11	0.11
INDONESIA	0.41	0.40	0.33	0.28	0.26	0.21	0.20
MALAYSIA	0.42	0.39	0.35	0.35	0.39	0.35	0.36
MEXICO	2.07	1.59	1.41	1.47	1.59	1.50	1.41
MOROCCO	0.87	0.82	0.79	0.78	0.82	0.83	0.82
PHILIPPINES	0.88	0.72	0.61	0.65	0.75	0.79	0.80
POLAND	0.38	0.37	0.34	0.39	0.44	0.44	0.49
SOUTH AFRICA	0.82	0.94	0.81	0.70	0.69	0.59	0.47
THAILAND	0.16	0.15	0.14	0.13	0.16	0.20	0.19
TUNISIA	0.70	0.65	0.61	0.61	0.63	0.63	0.62
TURKEY	1.06	0.79	0.68	0.62	0.56	0.58	0.52
WESTERN AFRICA	0.78	0.73	0.70	0.65	0.63	0.62	0.58

22. PRICES RELATIVE TO FRANCE BASED ON MULTILATERALLY-MATCHED SAMPLE, LASPEYRES PRICE INDICES, PRICE PER STANDARD UNIT

	2002	2003	2004	2005	2006	2007	2008
ALGERIA	0.94	0.81	0.78	0.75	0.72	0.70	0.59
BRAZIL	1.12	0.89	0.86	1.04	1.26	1.31	1.36
EGYPT	0.66	0.48	0.41	0.47	0.49	0.44	0.35
FRANCE	1.00	1.00	1.00	1.00	1.00	1.00	1.00
INDIA	0.26	0.21	0.20	0.21	0.22	0.23	0.19
INDONESIA	0.97	1.23	0.88	0.98	0.89	0.85	0.71
MALAYSIA	1.02	0.83	0.62	0.65	0.73	0.72	0.69
MEXICO	2.88	2.26	1.91	2.07	2.23	2.14	2.03
MOROCCO	0.93	0.90	0.89	0.92	0.99	0.94	0.85
PHILIPPINES	1.65	1.34	1.14	1.15	1.32	1.56	1.39
POLAND	0.71	0.67	0.60	0.64	0.68	0.66	0.71
SOUTH AFRICA	1.03	1.15	1.09	0.98	0.92	0.78	0.61
THAILAND	0.71	0.66	0.66	0.71	0.82	0.98	0.83
TUNISIA	0.79	0.75	0.72	0.72	0.76	0.76	0.72
TURKEY	1.14	0.89	0.77	0.74	0.64	0.65	0.56
WESTERN AFRICA	0.89	0.79	0.90	0.84	0.87	0.88	0.79

23. PRICES RELATIVE TO FRANCE BASED ON BILATERALLY-MATCHED SAMPLE, PAASCHE PRICE INDICES, PRICE PER KILOGRAM

	2000	2001	2002	2003	2004	2005	2006	2007	2008
ALGERIA			0.93	0.78	0.71	0.64	0.63	0.62	0.56
BRAZIL	1.65	1.24	0.89	0.70	0.64	0.74	0.74	0.83	0.84
EGYPT	0.52	0.35	0.29	0.18	0.18	0.22	0.23	0.19	0.17
INDIA	0.16	0.15	0.14	0.12	0.11	0.11	0.11	0.12	0.10
INDONESIA	0.49	0.42	0.49	0.46	0.39	0.31	0.30	0.26	0.24
MALAYSIA	0.54	0.61	0.57	0.48	0.19	0.21	0.04	0.05	0.04
MEXICO	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
MOROCCO	0.81	0.79	0.78	0.74	0.72	0.72	0.74	0.74	0.73
PHILIPPINES	1.40	1.25	1.19	0.92	0.77	0.69	0.64	0.73	0.66
POLAND	0.01	0.02	0.02	0.03	0.03	0.05	0.06	0.07	0.07
SOUTH AFRICA	0.86	0.75	0.59	0.65	0.65	0.58	0.48	0.41	0.33
THAILAND	0.28	0.25	0.26	0.22	0.20	0.21	0.22	0.20	0.16
TUNISIA	0.71	0.71	0.71	0.63	0.58	0.58	0.65	0.64	0.64
TURKEY	0.93	0.47	0.48	0.43	0.41	0.42	0.39	0.41	0.40
WESTERN AFRICA	0.75	0.80	0.81	0.75	0.68	0.58	0.20	0.53	0.40

24. PRICES RELATIVE TO FRANCE BASED ON BILATERALLY-MATCHED SAMPLE, LASPEYRES PRICE INDICES, PRICE PER KILOGRAM

	2000	2001	2002	2003	2004	2005	2006	2007	2008
ALGERIA			1.27	1.10	1.01	1.55	0.90	0.85	0.74
BRAZIL	11.26	2.14	1.61	1.93	1.27	92.35	1.65	12.55	2.62
EGYPT	1.19	1.08	0.89	0.61	0.49	0.53	0.56	0.51	0.46
INDIA	0.68	0.62	1.41	0.47	0.44	0.44	1.11	1.31	2.97
INDONESIA	3.83	2.58	2.74	3.29	2.64	2.25	2.10	1.66	1.83
MALAYSIA	2.87	3.05	2.68	2.06	2.58	2.22	2.36	1.83	1.92
MEXICO	5.65	5.66	5.04	3.50	5.08	4.06	3.48	2.60	2.71
MOROCCO	1.43	1.37	1.27	1.17	1.12	1.13	1.15	1.10	1.07
PHILIPPINES	7.36	6.59	6.16	4.52	3.79	4.19	5.22	4.16	5.20
POLAND	1.62	1.33	1.26	1.13	1.00	1.08	47.89	220.5	1.23
SOUTH AFRICA	3.62	3.90	8.40	3.75	2.19	1.66	1.39	1.30	1.10
THAILAND	1.53	1.48	1.53	1.18	1.11	1.14	1.19	1.73	1.19
TUNISIA	1.05	26.38	1.02	0.97	0.94	0.92	0.93	1.25	23.74
TURKEY	24.91	11.89	9.44	6.62	9.75	3.74	2.44	1.89	2.14
WESTERN AFRICA	1.14	1.11	1.10	1.01	1.10	1.07	1.06	1.04	0.96

25. PRICES RELATIVE TO FRANCE BASED ON MULTILATERALLY-MATCHED SAMPLE, PAASCHE PRICE INDICES, PRICE PER KILOGRAM

	2002	2003	2004	2005	2006	2007	2008
ALGERIA	0.87	0.72	0.65	0.62	0.63	0.62	0.56
BRAZIL	0.91	0.74	0.68	0.79	0.93	0.66	0.71
EGYPT	0.49	0.25	0.21	0.21	0.25	0.23	0.20
FRANCE	1.00	1.00	1.00	1.00	1.00	1.00	1.00
INDIA	0.13	0.11	0.10	0.10	0.11	0.11	0.10
INDONESIA	0.50	0.46	0.38	0.32	0.30	0.24	0.24
MALAYSIA	0.48	0.44	0.37	0.37	0.40	0.35	0.34
MEXICO	2.31	1.33	0.96	0.92	0.86	0.68	0.60
MOROCCO	0.80	0.75	0.69	0.68	0.72	0.72	0.73
PHILIPPINES	1.23	0.98	0.85	0.85	0.94	0.99	0.97
POLAND	0.46	0.43	0.37	0.42	0.45	0.44	0.50
SOUTH AFRICA	0.59	0.69	0.68	0.59	0.57	0.51	0.42
THAILAND	0.23	0.21	0.19	0.18	0.18	0.15	0.12
TUNISIA	0.74	0.68	0.62	0.62	0.66	0.67	0.66
TURKEY	0.92	0.70	0.58	0.52	0.47	0.48	0.44
WESTERN AFRICA	0.81	0.74	0.70	0.64	0.62	0.62	0.58

26. PRICES RELATIVE TO FRANCE BASED ON MULTILATERALLY-MATCHED SAMPLE, LASPEYRES PRICE INDICES, PRICE PER KILOGRAM

	2002	2003	2004	2005	2006	2007	2008
ALGERIA	1.19	1.04	0.91	0.84	0.81	0.81	0.68
BRAZIL	1.32	1.07	0.90	1.10	1.37	1.38	1.50
EGYPT	0.67	0.51	0.42	0.47	0.49	0.43	0.36
FRANCE	1.00	1.00	1.00	1.00	1.00	1.00	1.00
INDIA	0.32	0.29	0.24	0.25	0.27	0.27	0.23
INDONESIA	1.27	1.31	1.03	1.14	1.01	0.86	0.74
MALAYSIA	0.98	0.84	0.69	0.69	0.76	0.73	0.75
MEXICO	3.05	2.44	2.01	2.18	2.43	2.38	2.25
MOROCCO	1.06	1.05	0.98	1.02	1.09	1.01	0.92
PHILIPPINES	1.90	1.60	1.28	1.28	1.45	1.72	1.53
POLAND	1.13	0.97	0.66	0.69	0.73	0.72	0.78
SOUTH AFRICA	17.91	5.11	1.10	0.97	0.92	0.81	0.65
THAILAND	0.79	0.84	0.82	0.81	0.91	0.91	0.83
TUNISIA	0.90	0.89	0.80	0.81	0.84	0.83	0.78
TURKEY	1.27	1.04	12.42	0.77	0.68	0.68	0.59
WESTERN AFRICA	1.09	0.96	1.01	1.00	1.07	1.04	0.93

27. PRICES RELATIVE TO WESTERN AFRICA BASED ON BILATERALLY-MATCHED SAMPLE, PAASCHE PRICE INDICES, PRICE PER STANDARD UNIT

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
ALGERIA				0.88	0.10	0.07	0.15	0.43	0.41	0.44
BRAZIL	1.12	1.19	0.89	0.72	0.67	0.56	0.70	0.87	0.94	1.08
EGYPT	0.46	0.55	0.47	0.39	0.27	0.23	0.28	0.29	0.27	0.27
INDIA	0.14	0.16	0.15	0.14	0.12	0.11	0.13	0.14	0.15	0.15
INDONESIA	0.37	0.44	0.41	0.48	0.44	0.38	0.37	0.36	0.31	0.33
MALAYSIA	0.44	0.50	0.57	0.54	0.49	0.39	0.43	0.50	0.47	0.51
MEXICO	1.71	2.07	2.20	2.18	1.78	1.48	1.69	1.88	1.83	1.91
MOROCCO	0.74	0.90	0.90	0.89	0.87	0.79	0.86	0.93	0.95	1.03
PHILIPPINES	1.14	1.26	1.19	1.15	0.94	0.79	0.88	0.99	1.04	1.11
POLAND	0.31	0.34	0.40	0.44	0.44	0.39	0.46	0.51	0.47	0.57
SOUTH AFRICA	1.36	1.24	0.97	0.71	0.89	0.72	0.68	0.64	0.52	0.45
THAILAND	0.21	0.26	0.25	0.27	0.23	0.21	0.23	0.28	0.33	0.33
TUNISIA	0.76	0.83	0.81	0.80	0.78	0.66	0.70	0.76	0.76	0.81
TURKEY	2.30	1.97	1.13	0.96	0.81	0.62	0.62	0.56	0.60	0.60
UNITED STATES	1.80	2.35	2.50	2.55	2.41	1.92	2.05	2.15	1.97	1.81

28. PRICES RELATIVE TO WESTERN AFRICA BASED ON BILATERALLY-MATCHED SAMPLE, LASPEYRES PRICE INDICES, PRICE PER STANDARD UNIT

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
ALGERIA				1.23	1.07	0.93	0.88	0.92	0.89	0.84
BRAZIL	3.64	4.47	3.34	2.10	1.71	1.71	2.09	2.48	2.57	2.97
EGYPT	0.82	1.20	1.17	0.72	0.50	0.39	0.47	0.51	0.48	0.48
INDIA	0.58	0.86	0.90	0.93	0.62	0.71	0.79	0.79	0.74	0.83
INDONESIA	2.01	2.34	2.07	2.48	2.47	2.08	1.90	2.38	1.86	1.83
MALAYSIA	2.19	2.83	3.44	3.46	2.72	3.36	3.13	3.26	2.42	2.44
MEXICO	3.99	5.01	5.63	5.66	4.19	6.33	4.80	5.32	4.17	4.61
MOROCCO	1.00	1.93	1.15	1.12	1.15	1.18	1.29	1.36	1.39	1.49
PHILIPPINES	5.78	8.30	8.30	8.94	6.91	6.48	5.81	6.91	6.88	7.71
POLAND	1.03	1.63	1.52	2.06	1.95	2.01	1.96	2.17	2.11	2.53
SOUTH AFRICA	2.80	3.26	2.94	2.51	3.03	2.71	2.27	1.90	1.61	1.40
THAILAND	1.29	1.97	1.88	1.95	1.72	2.13	2.23	2.31	2.40	1.98
TUNISIA	0.84	0.92	0.95	0.90	0.90	0.86	0.92	0.98	1.02	1.10
TURKEY	22.45	21.6	13.9	13.5	10.0	6.45	5.11	4.18	3.31	3.41
UNITED STATES	6.92	9.62	9.40	10.8	10.0	7.92	8.44	8.66	7.82	7.52

29. PRICES RELATIVE TO WESTERN AFRICA BASED ON BILATERALLY-MATCHED SAMPLE, PAASCHE PRICE INDICES, PRICE PER KILOGRAM

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
ALGERIA				0.99	0.83	0.72	0.69	0.68	0.66	0.64
BRAZIL	1.51	1.77	1.32	1.01	0.79	0.69	0.83	0.94	0.98	1.07
EGYPT	0.29	0.34	0.25	0.21	0.14	0.20	0.29	0.30	0.23	0.24
UNITED STATES	1.37	1.79	1.93	1.83	1.73	1.75	1.88	1.89	1.75	1.62
INDIA	0.13	0.15	0.14	0.14	0.12	0.12	0.14	0.14	0.15	0.15
INDONESIA	0.54	0.59	0.48	0.46	0.48	0.43	0.41	0.40	0.27	0.24
MALAYSIA	0.35	0.48	0.51	0.49	0.51	0.27	0.24	0.03	0.04	0.05
MEXICO	1.71	2.16	2.32	2.25	1.83	1.49	1.63	1.81	1.11	1.66
MOROCCO	0.81	0.95	0.92	0.91	0.90	0.86	0.91	0.97	0.99	1.06
PHILIPPINES	1.57	1.73	1.52	1.14	0.97	0.78	0.83	0.91	0.91	0.86
POLAND	0.23	0.29	0.33	0.35	0.36	0.43	0.50	0.52	0.56	0.68
SOUTH AFRICA	1.05	1.19	0.95	0.75	0.93	0.85	0.75	0.67	0.48	0.40
THAILAND	0.27	0.32	0.27	0.27	0.24	0.25	0.26	0.29	0.29	0.26
TUNISIA	0.72	0.77	0.76	0.76	0.72	0.66	0.66	0.75	0.76	0.82
TURKEY	2.06	1.76	1.10	0.84	0.59	0.40	0.44	0.42	0.47	0.47

30. PRICES RELATIVE TO WESTERN AFRICA BASED ON BILATERALLY-MATCHED SAMPLE, LASPEYRES PRICE INDICES, PRICE PER KILOGRAM

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
ALGERIA				1.40	3.79	1.03	3.28	1.24	1.01	16.8
BRAZIL	4.37	60.6	4.01	3.36	2.51	2.49	31.3	3.62	8.68	8.19
EGYPT	3.82	1.72	1.44	0.82	1.16	0.50	0.58	0.63	0.58	0.53
UNITED STATES	5.10	16.7	16.7	22.3	25.0	15.6	131.	19.8	53.8	21.5
INDIA	1.26	1.64	1.78	2.53	1.82	1.63	1.74	1.72	1.58	2.51
INDONESIA	7.27	8.70	7.73	10.3	10.4	8.39	7.38	7.02	4.11	4.69
MALAYSIA	6.28	9.55	12.2	13.4	10.6	16.2	14.7	17.6	11.5	10.5
MEXICO	13.28	16.69	18.79	19.55	13.01	30.39	19.83	16.80	7.81	9.35
MOROCCO	1.07	1.44	1.34	1.14	1.15	1.17	1.31	1.34	1.41	1.48
PHILIPPINES	31.92	37.54	39.73	45.19	35.83	31.17	29.40	36.89	23.20	30.34
POLAND	4.00	6.80	4.94	4.72	16.34	5.32	2.95	2.16	4.84	1.95
SOUTH AFRICA	6.26	7.65	14.13	68.20	23.29	7.33	4.32	2.61	2.05	1.74
THAILAND	3.05	3.17	4.29	7.34	2.78	2.54	2.53	2.65	2.02	2.27
TUNISIA	0.88	0.96	3.87	0.87	0.86	0.84	0.91	0.95	1.04	7.32
TURKEY	130.0	115.4	68.19	70.31	52.84	34.18	24.59	20.76	12.73	13.43

BRIEF SUMMARY OF FINDINGS FROM THE ADDITIONAL RESULTS

The publication of Paper 1 limited the number of countries that could be presented together in the price comparison. In these additional comparisons presented here all MICs for which data was available were included.

In order to make the MIC price comparisons fairer, numerous additional indices were constructed using alternative pharmaceutical sampling methods, base countries, and a greater number of MIC. On the whole, expanding the selection of countries to include all of the middle-income countries (14 countries) for which data was available did not substantially alter findings (the Health Affairs papers shows results for only a short selection of countries). Overall the findings suggest that many MIC have prices below those attained in LIC. Beyond Egypt and India which were mentioned the published version of Paper 1, US-based results suggest that Algeria and Tunisia were consistently far below those in western Africa over several years of the study, irrespective of the consumption patterns or sample used. This is further highlighted in the additional indices using western Africa as the base country and maximizing the sample size through bilaterally-matched sampling. Indeed when using consumption patterns from western Africa itself, Egypt, India, and Tunisia have prices below western Africa in over half of the study period. When focussing on a sample weighted according to the comparator MIC, results estimate that in many of the MIC countries had prices inferior to those in western Africa over the decade. Overall these findings reinforce the message that the relative price of pharmaceuticals in lesser developed parts of the world is not consistently related to relative income.

When comparing US to MIC, generally (when matching molecule-indications across all MIC--rather than bilaterally with the US as in Paper 1) results did not change significantly. Except for the case of Mexico (and Turkey during the banking and currency crisis of 1999-2000) all MICs had prices less than half of US prices throughout the study period.

Irrespective of the sample of comparison prices in MIC were consistently below UK prices when using UK as the base country (although much closer to UK prices than US prices), with the exceptions of Mexico and Philippines. When looking exclusively at prices calculated using UK-specific consumption patterns, a number of MIC had prices higher than UK prices in several years. These included South Africa, Tunisia, Brazil, Indonesia, and even western Africa in some years. Broadly speaking, pharmaceuticals the UK had prices similar to several lesser (relative to the UK) developed countries.

When focussing on MIC prices relative to France findings were similar, with a few more MIC, such as Poland and Morocco, having prices above French prices over several years when basing prices on French consumption patterns.

Overall the effect of discounting US prices has a minor effect on price relatives. The overall average effect on individual index values across Paasche indices was 0.02 whilst for the Laspeyres indices it was 0.04.

Technical notes: Paper 1 referred to western Africa using IMS categorization of "French West Africa", a 10-country aggregation made by IMS Health -- covering the formal pharmaceutical market in Benin, Burkina Faso, Cameroon, Côte d'Ivoire, Gabon, Guinea, Mali, Republic of the Congo, Senegal, and Togo. This is the sole source of pharmaceutical prices in low-income countries available and, as such, was used here to represent low-income countries generally.

By definition index calculations based on multilaterally-matched samples were limited to the years for which data were available from all of the countries included in the comparison. In the case the multilateral comparisons the years were limited by France (missing data for 1999) and Algeria (missing data for 1999-2001). As a result the MIC multilateral comparisons were limited to 2002 through 2008.

It should be noted that—when it came to analysis of findings--more weight was given to calculations based on prices per standard unit than prices per kilogram. Comparison to price indices based on price per kilogram unit unfortunately did not provide a meaningful comparison due to data errors across many countries in the years 2003-2005. Outliers were also estimated for several countries in 2007. After many discussions with IMS about data entries in this form, it was made clear that indeed they had some errors within their database. Results from samples based on price per kilogram are therefore reflected upon very little in this appendix and not at all in Paper 1.

ASSUMED PRICE EVOLUTION THROUGH PRODUCT DISTRIBUTION

IMS collects pharmaceutical price data a different points in the distribution chain, depending on practicalities within each country. Prices are then brought into line (converted to manufacturer, wholesaler, or retail level) using a set of assumptions. These assumptions are outlined for each country here-below.

	Manufacturer	Wholesaler	Retailer
Algeria	100	122	146
Australia	100	108	134
Austria	100	118	251
Belgium	100	115	177
Brazil	100	118	160
Canada	100	105	139
Egypt	100	116	142
Finland	100	104	154
France	100	111	168
Germany	100	109	163
Greece	100	108	146
India	100	109	130
Indonesia*	100	120	154
Italy	100	110	167
Japan	100	109	121
Korea	100	104	113
Malaysia*	100	115	153
Mexico	100	118	142
Morocco	100	111	159
Netherlands	100	115	160
Philippines	100	110	119
Poland	100	110	137
Portugal	100	109	140
South Africa	100	111	140
Saudi Arabia	100	112	129

Singapore*	100	115	153
Spain	100	108	156
Sweden	100	103	123
Switzerland	100	123	186
Taiwan	100	105	124
Thailand	100	116	134
Tunisia	100	109	149
Turkey	100	108	144
United Kingdom	100	114	152
United States	100	105	139
western Africa	100	139	184

APPENDIX 2
SUPPORT MATERIAL FOR PAPER 2

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❖ **Rebased indices for analysis of trend over time**

7. $L_M^{2001base}$: Prices relative to discounted United States prices based on multilaterally-matched sample, Laspeyres price indices, price per standard unit (US=1)
8. $P_M^{2001base}$: Prices relative to discounted United States prices based on multilaterally-matched sample, Paasche price indices, price per standard unit (US=1)
9. $L_B^{2001base}$: Prices relative to discounted US based on bilaterally-matched sample, Laspeyres price indices, price per standard unit (US=1)
10. $P_B^{2001base}$: Prices relative to discounted US prices based on bilaterally-matched sample, Paasche price indices, price per standard unit (US=1)

❖ **Sensitivity analysis**

11. L_M^{DISC}: Prices relative to discounted United States prices based on multilaterally-matched sample, Laspeyres price indices, price per standard unit (US=1)
12. P_M^{DISC}: Prices relative to discounted United States prices based on multilaterally-matched sample, Paasche price indices, price per standard unit (US=1)
13. L_B^{DISC}: Prices relative to discounted US based on bilaterally-matched sample, Laspeyres price indices, price per standard unit (US=1)
14. P_B^{DISC}: Prices relative to discounted US prices based on bilaterally-matched sample, Paasche price indices, price per standard unit (US=1)
15. L_M^{UK}: Prices relative to United Kingdom based on multilaterally-matched sample, Laspeyres price indices, price per standard unit
16. P_M^{UK}: Prices relative to United Kingdom based on multilaterally-matched sample, Paasche price indices, price per standard unit

17. L_B^{UK}: Prices relative to United Kingdom based on bilaterally-matched sample, Laspeyres price indices, price per standard unit
18. P_B^{UK}: Prices relative to United Kingdom based on bilaterally-matched sample, Paasche price indices, price per standard unit
19. L_M^{FR}: Prices relative to France based on multilaterally-matched sample, Laspeyres price indices, price per standard unit
20. P_M^{FR}: Prices relative to France based on multilaterally-matched sample, Paasche price indices, price per standard unit
21. L_B^{FR}: Prices relative to France based on bilaterally-matched sample, Laspeyres price indices, price per standard unit
22. P_B^{FR}: Prices relative to France based on bilaterally-matched sample, Paasche price indices, price per standard unit

SAMPLE DESCRIPTIONS

1. UNIQUE ATCMOLS PER BILATERALLY-MATCHED (WITH US) SAMPLE PER YEAR

	1999	**2000**	**2001**	**2002**	**2003**	**2004**	**2005**	**2006**	**2007**	**2008**
AUSTRALIA	1382	1401	1427	1477	1482	1495	1452	1448	1477	1471
AUSTRIA	1171	1192	1187	1195	1204	1210	1207	1212	1217	1194
BELGIUM	1120	1133	1146	1149	1139	1138	1083	1090	1074	1038
CANADA	1395	1374	1430	1411	1406	1400	1460	1502	1526	1513
FINLAND	760	763	767	772	773	777	785	788	785	777
FRANCE		1395	1378	1373	1371	1378	1384	1374	1372	1359
GERMANY	2398	2438	2548	2541	2521	2420	2404	2384	2397	2390
GREECE	972	981	1006	1058	1049	1059	1074	1081	1079	1092
ITALY	1321	1348	1336	1354	1326	1313	1296	1272	1263	1263
JAPAN	1701	1697	1705	1709	1690	1681	1668	1681	1670	1669
KOREA	995	1313	1314	1464	1427	1464	1442	1446	1459	1427
NETHERLANDS	962	981	985	967	944	952	960	953	960	953
PORTUGAL	903	927	933	937	942	967	915	913	906	899
SAUDI ARABIA	792	802	825	822	804	791	750	747	751	745
SINGAPORE	1101	1102	1064	1058	1029	1077	1085	1094	1057	1030
SPAIN	1165	1196	1190	1186	1170	1174	1170	1139	1133	1132
SWEDEN	769	796	827	867	867	876	885	899	909	910
SWITZERLAND	1923	1917	1902	1894	1846	1789	1769	1724	1718	1676
TAIWAN	846	863	880	882	896	912	921	918	918	891
UNITED KINGDOM	1309	1323	1346	1335	1341	1343	1337	1331	1323	1294

2. PROPORTION OF TOTAL COUNTRY MARKET CAPTURED (BY SU VOLUME) IN MULTILATERALLY-MATCHED SAMPLE

	2000	**2001**	**2002**	**2003**	**2004**	**2005**	**2006**	**2007**	**2008**
AUSTRALIA	36	36	36	36	35	35	33	35	34
AUSTRIA	28	27	29	30	30	30	31	34	34
BELGIUM	31	31	33	33	33	33	34	37	37
CANADA	39	38	38	38	38	37	38	38	37
FINLAND	43	44	45	45	45	44	44	45	44
FRANCE	26	25	26	27	26	27	29	31	32
GERMANY	27	27	29	30	31	30	31	35	36
GREECE	28	27	28	28	28	27	28	31	33
ITALY	31	30	30	30	29	30	31	34	35
JAPAN	18	16	15	16	17	16	16	17	16
KOREA	22	23	21	20	21	20	20	21	21
NETHERLANDS	37	38	40	40	41	40	41	43	42
PORTUGAL	33	32	33	34	33	34	35	37	38
SAUDI ARABIA	32	31	34	34	32	33	33	38	38
SINGAPORE	34	33	34	35	36	34	36	36	36
SPAIN	31	30	32	33	32	33	34	37	38
SWEDEN	43	39	39	39	39	39	39	42	41
SWITZERLAND	23	23	25	25	25	26	27	31	31
TAIWAN	51	50	47	42	43	41	40	42	40
UNITED KINGDOM	33	33	34	34	35	35	36	39	38
UNITED STATES	34	34	34	34	34	36	38	39	39

3. DESCRIPTION OF SAMPLE BILATERALLY-MATCHED WITH US (AVERAGES ACROSS ALL YEARS)

	% originator brand	**% any brand**	**% OTC**
AUSTRALIA	13	54	47
AUSTRIA	25	71	15
BELGIUM	27	72	22
CANADA	11	53	11
FINLAND	29	73	11
FRANCE	14	50	25
GERMANY	19	60	28
GREECE	20	87	0
ITALY	14	66	15
JAPAN	8	66	7
KOREA	5	68	28
NETHERLANDS	33	55	9
PORTUGAL	18	58	6
SAUDI ARABIA	23	86	0
SINGAPORE	19	71	24
SPAIN	15	57	11
SWEDEN	37	72	8
SWITZERLAND	18	62	39
TAIWAN	8	73	0
UNITED KINGDOM	19	57	25
UNITED STATES	10	47	34

4. UNIQUE ATCMOLS IN SAMPLE MULTILATERALLY-MATCHED ACROSS ALL HIC

2000	2001	2002	2003	2004	2005	2006	2007	2008
140	142	148	147	146	141	144	158	151

5. PROPORTION OF TOTAL COUNTRY MARKET (BY SU VOLUME) CAPTURED IN BILATERALLY-MATCHED SAMPLES

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
AUSTRALIA	99	99	99	99	99	99	99	99	99	99
AUSTRIA	71	72	72	72	72	72	72	72	74	74
BELGIUM	80	80	80	80	81	81	81	80	82	82
CANADA	97	97	97	97	97	98	98	95	95	95
FINLAND	85	85	85	85	84	85	85	86	86	87
FRANCE		62	63	63	62	63	65	68	70	71
GERMANY	79	80	80	79	79	80	80	76	79	80
GREECE	98	98	98	98	98	98	97	97	98	98
ITALY	67	68	69	70	70	72	72	73	75	77
JAPAN	72	72	72	72	71	70	69	67	66	65
KOREA	99	99	98	98	98	97	97	97	97	97
NETHERLANDS	92	93	93	93	93	93	93	92	92	92
PORTUGAL	88	88	89	90	90	91	92	92	93	94
SAUDI ARABIA	92	92	91	90	87	86	86	80	82	81
SINGAPORE	81	81	85	85	82	82	81	83	83	84
SPAIN	75	76	75	75	75	77	77	76	78	78
SWEDEN	94	94	94	93	93	93	93	92	92	92
SWITZERLAND	79	79	79	78	78	78	78	75	78	78
TAIWAN	80	81	83	82	82	81	82	81	82	82
UNITED KINGDOM	86	86	86	87	87	87	87	86	85	85

6. PROPORTION OF BILATERALLY-MATCHED SAMPLE (BY SU VOLUME) THAT IS CAPTURED IN MULTILATERALLY-MATCHED SAMPLE

	2000	**2001**	**2002**	**2003**	**2004**	**2005**	**2006**	**2007**	**2008**
AUSTRALIA	62	61	62	61	61	62	62	63	63
AUSTRIA	47	46	49	49	48	48	57	56	56
BELGIUM	61	58	61	61	60	60	63	63	60
CANADA	29	27	23	22	21	21	22	22	20
FINLAND	57	58	61	61	61	62	67	68	68
FRANCE	50	48	50	49	46	46	51	51	51
GERMANY	57	57	57	55	50	47	52	50	48
GREECE	42	41	43	44	45	45	50	49	52
ITALY	45	43	43	42	40	41	52	52	52
JAPAN	14	12	12	13	14	14	16	17	18
KOREA	2	2	2	2	2	2	2	2	2
NETHERLANDS	80	80	81	80	80	79	80	76	74
PORTUGAL	82	82	82	81	82	81	83	83	84
SAUDI ARABIA	22	25	30	30	28	28	34	37	39
SINGAPORE	50	48	50	53	52	50	50	49	50
SPAIN	41	40	43	43	42	43	48	50	51
SWEDEN	37	37	40	42	43	44	48	50	51
SWITZERLAND	54	52	52	45	45	45	53	53	52
TAIWAN	60	58	54	48	50	46	47	47	44
UNITED KINGDOM	37	37	38	38	39	39	43	46	45

7. $L_M^{2001BASE}$: PRICES RELATIVE TO UNITED STATES PRICES BASED ON MULTILATERALLY-MATCHED SAMPLE, LASPEYRES PRICE INDICES (US=1)

	2000	**2001**	**2002**	**2003**	**2004**	**2005**	**2006**	**2007**	**2008**
AUSTRALIA	1.16	1.00	1.01	1.23	1.36	1.42	1.40	1.71	1.94
AUSTRIA	1.09	1.00	1.02	1.16	1.23	1.20	1.26	1.49	1.72
BELGIUM	1.14	1.00	1.07	1.23	1.31	1.22	1.20	1.40	1.61
CANADA	1.08	1.00	0.97	1.07	1.18	1.26	1.38	1.64	1.80
FINLAND	1.08	1.00	1.03	1.18	1.24	1.18	1.16	1.45	1.67
FRANCE	1.08	1.00	1.00	1.21	1.34	1.30	1.29	1.52	1.72
GERMANY	1.06	1.00	1.01	1.18	1.30	1.27	1.30	1.50	1.70
GREECE	1.07	1.00	1.03	1.28	1.48	1.40	1.52	1.91	2.27
ITALY	1.07	1.00	1.01	1.14	1.20	1.13	1.14	1.33	1.47
JAPAN	5.11	1.00	0.98	1.06	1.13	1.13	1.07	1.24	1.54
KOREA	1.19	1.00	0.99	1.02	1.05	1.19	1.41	1.65	1.63
NETHERLANDS	1.11	1.00	0.99	1.13	1.13	1.06	1.08	1.29	1.37
PORTUGAL	1.10	1.00	0.99	1.13	1.22	1.19	1.21	1.39	1.61
SAUDI ARABIA	1.04	1.00	0.91	0.82	0.77	0.78	0.82	0.83	0.76
SINGAPORE	1.27	1.00	0.97	1.02	0.99	0.98	1.08	1.28	1.46
SPAIN	1.09	1.00	1.02	1.22	1.27	1.23	1.31	1.66	1.90
SWEDEN	1.19	1.00	1.03	1.12	1.16	1.14	1.12	1.37	1.53
SWITZERLAND	1.05	1.00	1.05	1.19	1.27	1.21	1.11	1.18	1.40
TAIWAN	1.10	1.00	0.90	0.90	0.94	0.96	1.04	1.11	1.20
UNITED KINGDOM	1.11	1.00	0.98	1.05	1.12	0.97	1.01	1.17	1.14

8. P_M [2001BASE]: PRICES RELATIVE TO UNITED STATES PRICES BASED ON MULTILATERALLY-MATCHED SAMPLE, PAASCHE PRICE INDICES (US=1)

	2000	**2001**	**2002**	**2003**	**2004**	**2005**	**2006**	**2007**	**2008**
AUSTRALIA	1.15	1.00	1.02	1.27	1.42	1.44	1.38	1.57	1.65
AUSTRIA	1.10	1.00	1.01	1.20	1.25	1.19	1.23	1.09	1.46
BELGIUM	1.16	1.00	1.04	1.21	1.31	1.22	1.21	1.43	1.75
CANADA	2.04	1.00	1.62	2.01	2.21	2.27	2.55	2.78	2.47
FINLAND	1.07	1.00	1.03	1.18	1.23	1.15	1.07	1.26	1.37
FRANCE	1.06	1.00	0.99	1.20	1.34	1.33	1.33	1.36	1.55
GERMANY	1.01	1.00	1.00	1.17	1.27	1.18	1.28	1.02	1.47
GREECE	1.02	1.00	1.05	1.25	1.43	1.48	1.57	1.48	2.07
ITALY	1.09	1.00	1.02	1.14	1.21	1.15	1.17	1.01	1.15
JAPAN	1.06	1.00	1.04	1.11	1.09	1.07	1.05	1.15	1.55
KOREA	1.03	1.00	1.16	1.16	1.17	1.44	1.71	2.05	1.41
NETHERLANDS	1.09	1.00	0.99	1.13	1.10	1.03	1.05	1.28	1.30
PORTUGAL	1.07	1.00	0.96	1.10	1.20	1.17	1.17	1.20	1.52
SAUDI ARABIA	0.97	1.00	0.93	0.83	0.77	0.80	0.90	0.50	0.58
SINGAPORE	1.01	1.00	0.91	0.86	0.69	0.82	0.84	1.22	1.14
SPAIN	1.10	1.00	0.98	1.17	1.28	1.25	1.31	1.25	1.53
SWEDEN	1.21	1.00	1.01	1.09	1.10	1.09	1.11	1.29	1.43
SWITZERLAND	1.00	1.00	1.08	1.23	1.33	1.25	1.13	0.87	1.27
TAIWAN	0.98	1.00	1.05	1.05	1.11	1.30	1.22	1.14	1.26
UNITED KINGDOM	1.11	1.00	1.02	1.11	1.17	1.00	0.97	1.10	1.02

9. $L_B^{2001BASE}$: PRICES RELATIVE TO UNITED STATES PRICES BASED ON BILATERALLY-MATCHED SAMPLE, LASPEYRES PRICE INDICES (US=1)

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
AUSTRALIA	1.55	1.26	1.00	1.00	1.17	1.33	2.15	1.88	2.04	2.06
AUSTRIA	1.86	1.18	1.00	0.99	0.81	0.85	0.74	0.77	1.03	1.40
BELGIUM	1.39	1.09	1.00	1.03	1.24	1.30	1.31	1.34	1.68	2.37
CANADA	1.18	1.09	1.00	1.82	9.65	7.80	2.57	2.70	2.28	2.19
FINLAND	1.30	1.07	1.00	1.06	1.26	1.34	1.30	1.27	1.61	2.19
FRANCE		1.11	1.00	1.00	1.21	1.32	1.32	1.31	1.42	1.58
GERMANY	1.63	1.17	1.00	1.01	1.09	1.13	1.14	1.08	1.29	2.06
GREECE	1.28	1.01	1.00	1.08	1.32	1.47	1.47	1.53	1.78	1.95
ITALY	1.27	1.08	1.00	0.99	1.12	1.14	1.07	1.14	1.52	2.14
JAPAN	2.35	2.39	1.00	0.93	0.88	0.87	0.88	0.81	0.92	1.26
KOREA	1.38	1.18	1.00	1.01	1.02	1.05	1.18	1.29	1.40	1.32
NETHERLANDS	1.36	1.11	1.00	1.04	1.21	1.27	1.18	1.16	1.31	1.39
PORTUGAL	1.38	1.09	1.00	1.02	1.15	1.24	1.19	1.16	1.24	1.35
SAUDI ARABIA	1.14	1.02	1.00	0.97	0.86	0.78	0.83	0.83	0.85	0.76
SINGAPORE	1.17	1.13	1.00	0.97	0.99	0.92	0.81	0.86	0.92	1.02
SPAIN	1.33	1.09	1.00	1.04	1.20	1.25	1.21	1.22	1.41	1.56
SWEDEN	1.36	1.18	1.00	1.07	1.23	1.30	1.30	1.37	1.79	2.49
SWITZERLAND	1.30	1.02	1.00	1.06	1.19	1.25	1.07	0.99	1.04	1.17
TAIWAN	1.05	1.11	1.00	0.92	0.91	0.95	0.98	0.97	0.98	1.03
UNITED KINGDOM	1.39	1.14	1.00	1.00	1.03	1.13	1.03	1.01	1.13	1.08

10. P_B [2001BASE]: PRICES RELATIVE TO UNITED STATES PRICES BASED ON BILATERALLY-MATCHED SAMPLE, PAASCHE PRICE INDICES (US=1)

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
AUSTRALIA	1.29	1.08	1.00	0.92	1.09	1.26	1.26	1.18	1.23	1.20
AUSTRIA	1.12	0.77	1.00	1.03	1.23	1.32	1.27	1.23	1.15	1.31
BELGIUM	1.08	0.94	1.00	1.03	1.23	1.36	1.31	1.25	0.76	1.41
CANADA	0.85	0.96	1.00	1.29	1.48	1.64	1.72	1.79	1.59	1.62
FINLAND	0.79	0.76	1.00	1.09	1.23	1.41	1.46	1.35	1.48	1.59
FRANCE		0.72	1.00	0.99	1.14	1.33	1.35	1.33	1.38	1.45
GERMANY	0.83	0.67	1.00	0.94	1.20	1.37	1.34	1.35	1.27	1.55
GREECE	0.84	0.76	1.00	1.07	1.30	1.56	1.66	1.72	1.78	2.09
ITALY	1.16	1.03	1.00	1.01	1.14	1.20	1.14	1.11	1.04	1.07
JAPAN	0.97	1.04	1.00	0.94	1.01	1.08	1.05	0.97	0.94	1.02
KOREA	0.95	0.72	1.00	1.21	1.31	1.48	1.78	2.04	2.32	1.74
NETHERLANDS	1.14	0.89	1.00	1.01	1.17	1.22	1.20	1.18	1.32	1.30
PORTUGAL	1.15	1.00	1.00	1.05	1.21	1.37	1.32	1.27	1.29	1.41
SAUDI ARABIA	0.57	0.73	1.00	0.88	0.88	0.80	0.77	0.74	0.56	0.51
SINGAPORE	1.00	0.97	1.00	1.03	1.06	1.01	1.10	1.13	1.23	1.23
SPAIN	1.11	0.96	1.00	1.04	1.25	1.37	1.37	1.36	1.34	1.47
SWEDEN	0.94	0.83	1.00	1.07	1.25	1.37	1.40	1.39	0.91	1.50
SWITZERLAND	1.15	0.99	1.00	1.09	1.26	1.39	1.37	1.23	1.13	1.33
TAIWAN	0.98	1.01	1.00	0.85	0.90	1.09	1.07	1.09	0.93	0.94
UNITED KINGDOM	1.03	0.97	1.00	1.05	1.11	1.22	1.14	1.09	1.19	1.10

11. L_M^{DISC}: PRICES RELATIVE TO DISCOUNTED UNITED STATES PRICES BASED ON MULTILATERALLY-MATCHED SAMPLE, LASPEYRES PRICE INDICES, PRICE PER STANDARD UNIT (US=1)

	2000	2001	2002	2003	2004	2005	2006	2007	2008
AUSTRALIA	0.49	0.42	0.42	0.52	0.57	0.60	0.59	0.72	0.81
AUSTRIA	0.48	0.44	0.45	0.51	0.54	0.53	0.55	0.65	0.76
BELGIUM	0.57	0.50	0.54	0.62	0.66	0.62	0.61	0.71	0.81
CANADA	0.60	0.56	0.54	0.59	0.66	0.70	0.77	0.91	1.00
FINLAND	0.50	0.46	0.48	0.55	0.57	0.54	0.54	0.67	0.77
FRANCE	0.46	0.43	0.42	0.51	0.57	0.55	0.55	0.65	0.73
GERMANY	0.49	0.46	0.47	0.55	0.60	0.59	0.60	0.70	0.79
GREECE	0.38	0.36	0.37	0.46	0.53	0.50	0.55	0.68	0.81
ITALY	0.57	0.54	0.54	0.61	0.64	0.61	0.61	0.71	0.79
JAPAN	3.32	0.65	0.64	0.69	0.73	0.73	0.69	0.81	1.00
KOREA	0.49	0.41	0.41	0.42	0.43	0.48	0.58	0.67	0.67
NETHERLANDS	0.59	0.53	0.53	0.60	0.60	0.56	0.57	0.68	0.73
PORTUGAL	0.54	0.49	0.49	0.55	0.60	0.58	0.59	0.69	0.79
SAUDI ARABIA	0.77	0.75	0.68	0.61	0.57	0.58	0.61	0.62	0.57
SINGAPORE	0.56	0.44	0.43	0.45	0.44	0.43	0.48	0.57	0.65
SPAIN	0.43	0.40	0.41	0.48	0.50	0.49	0.52	0.66	0.75
SWEDEN	0.56	0.48	0.49	0.53	0.55	0.54	0.53	0.66	0.73
SWITZERLAND	0.81	0.77	0.80	0.91	0.97	0.93	0.85	0.91	1.07
TAIWAN	0.53	0.48	0.44	0.43	0.45	0.46	0.50	0.53	0.58
UNITED KINGDOM	0.59	0.53	0.52	0.56	0.60	0.52	0.54	0.62	0.61

12. L_B^{DISC}: PRICES RELATIVE TO DISCOUNTED US BASED ON BILATERALLY-MATCHED SAMPLE, LASPEYRES PRICE INDICES, PRICE PER STANDARD UNIT (US=1)

	1999	**2000**	**2001**	**2002**	**2003**	**2004**	**2005**	**2006**	**2007**	**2008**
AUSTRALIA	0.94	0.77	0.61	0.61	0.71	0.81	1.31	1.14	1.24	1.26
AUSTRIA	1.53	0.97	0.82	0.81	0.66	0.70	0.60	0.63	0.84	1.15
BELGIUM	0.78	0.61	0.56	0.58	0.69	0.73	0.73	0.75	0.94	1.32
CANADA	0.78	0.72	0.66	1.20	6.40	5.18	1.70	1.79	1.51	1.45
FINLAND	0.60	0.50	0.47	0.49	0.59	0.62	0.60	0.59	0.75	1.02
FRANCE		0.49	0.44	0.44	0.54	0.58	0.59	0.58	0.63	0.70
GERMANY	1.29	0.92	0.79	0.80	0.86	0.90	0.90	0.85	1.02	1.63
GREECE	0.50	0.39	0.39	0.42	0.52	0.57	0.57	0.60	0.70	0.76
ITALY	0.69	0.59	0.55	0.54	0.61	0.62	0.59	0.62	0.83	1.17
JAPAN	2.50	2.55	1.07	1.00	0.94	0.93	0.94	0.86	0.99	1.34
KOREA	0.60	0.52	0.44	0.44	0.45	0.46	0.52	0.57	0.61	0.58
NETHERLANDS	0.73	0.60	0.54	0.56	0.65	0.68	0.63	0.62	0.70	0.74
PORTUGAL	0.68	0.54	0.49	0.50	0.57	0.61	0.59	0.57	0.61	0.67
SAUDI ARABIA	0.89	0.80	0.79	0.76	0.68	0.61	0.65	0.65	0.67	0.59
SINGAPORE	0.67	0.65	0.58	0.56	0.57	0.53	0.47	0.49	0.53	0.58
SPAIN	0.56	0.46	0.43	0.44	0.51	0.53	0.52	0.52	0.60	0.66
SWEDEN	0.66	0.57	0.48	0.52	0.59	0.63	0.63	0.66	0.86	1.20
SWITZERLAND	1.10	0.86	0.84	0.90	1.00	1.05	0.90	0.84	0.88	0.99
TAIWAN	0.52	0.55	0.50	0.46	0.45	0.47	0.49	0.48	0.49	0.51
UNITED KINGDOM	0.86	0.71	0.62	0.62	0.64	0.70	0.64	0.63	0.70	0.67

13. P_B^{DISC}: PRICES RELATIVE TO DISCOUNTED US PRICES BASED ON BILATERALLY-MATCHED SAMPLE, PAASCHE PRICE INDICES, PRICE PER STANDARD UNIT (US=1)

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
AUSTRALIA	0.36	0.30	0.28	0.26	0.30	0.35	0.35	0.33	0.34	0.34
AUSTRIA	0.40	0.27	0.36	0.36	0.44	0.47	0.45	0.44	0.41	0.47
BELGIUM	0.41	0.36	0.38	0.39	0.46	0.51	0.50	0.47	0.29	0.53
CANADA	0.26	0.30	0.31	0.40	0.46	0.51	0.53	0.55	0.49	0.50
FINLAND	0.25	0.24	0.31	0.34	0.38	0.44	0.45	0.42	0.46	0.49
FRANCE		0.21	0.29	0.28	0.32	0.38	0.38	0.38	0.39	0.41
GERMANY	0.32	0.26	0.38	0.36	0.46	0.53	0.51	0.52	0.49	0.60
GREECE	0.21	0.19	0.25	0.27	0.33	0.39	0.42	0.43	0.45	0.53
ITALY	0.47	0.42	0.40	0.41	0.46	0.48	0.46	0.45	0.42	0.43
JAPAN	0.35	0.38	0.36	0.34	0.36	0.39	0.38	0.35	0.34	0.37
KOREA	0.18	0.13	0.19	0.22	0.24	0.28	0.33	0.38	0.43	0.32
NETHERLANDS	0.46	0.36	0.40	0.40	0.47	0.49	0.48	0.47	0.53	0.52
PORTUGAL	0.42	0.36	0.36	0.38	0.44	0.49	0.48	0.46	0.47	0.51
SAUDI ARABIA	0.32	0.41	0.56	0.50	0.50	0.45	0.43	0.42	0.31	0.29
SINGAPORE	0.26	0.25	0.26	0.27	0.28	0.26	0.29	0.29	0.32	0.32
SPAIN	0.33	0.29	0.30	0.31	0.38	0.41	0.41	0.41	0.40	0.44
SWEDEN	0.29	0.26	0.31	0.33	0.39	0.43	0.44	0.44	0.29	0.47
SWITZERLAND	0.53	0.46	0.46	0.50	0.58	0.64	0.63	0.57	0.52	0.61
TAIWAN	0.16	0.17	0.16	0.14	0.15	0.18	0.18	0.18	0.15	0.15
UNITED KINGDOM	0.37	0.35	0.36	0.38	0.40	0.44	0.41	0.40	0.43	0.40

14. P_M [DISC]: PRICES RELATIVE TO DISCOUNTED UNITED STATES PRICES BASED ON MULTILATERALLY-MATCHED SAMPLE, PAASCHE PRICE INDICES, PRICE PER STANDARD UNIT (US=1)

	2000	2001	2002	2003	2004	2005	2006	2007	2008
AUSTRALIA	0.36	0.31	0.32	0.40	0.44	0.45	0.43	0.49	0.51
AUSTRIA	0.41	0.37	0.37	0.45	0.46	0.44	0.46	0.40	0.54
BELGIUM	0.49	0.42	0.44	0.51	0.56	0.52	0.51	0.60	0.74
CANADA	0.53	0.26	0.42	0.52	0.57	0.59	0.66	0.72	0.64
FINLAND	0.43	0.40	0.41	0.47	0.49	0.46	0.42	0.50	0.54
FRANCE	0.38	0.36	0.36	0.43	0.48	0.48	0.48	0.49	0.55
GERMANY	0.40	0.39	0.40	0.46	0.50	0.47	0.51	0.40	0.58
GREECE	0.34	0.34	0.35	0.42	0.48	0.50	0.53	0.50	0.70
ITALY	0.49	0.45	0.46	0.51	0.55	0.52	0.53	0.46	0.52
JAPAN	0.47	0.44	0.46	0.49	0.48	0.48	0.47	0.51	0.68
KOREA	0.31	0.30	0.34	0.34	0.35	0.43	0.51	0.61	0.42
NETHERLANDS	0.48	0.44	0.44	0.50	0.49	0.45	0.46	0.57	0.57
PORTUGAL	0.48	0.45	0.43	0.49	0.54	0.53	0.52	0.54	0.68
SAUDI ARABIA	0.74	0.76	0.70	0.63	0.58	0.61	0.68	0.38	0.44
SINGAPORE	0.31	0.31	0.28	0.26	0.21	0.25	0.26	0.37	0.35
SPAIN	0.39	0.35	0.34	0.41	0.45	0.44	0.46	0.44	0.54
SWEDEN	0.44	0.37	0.37	0.40	0.41	0.40	0.41	0.48	0.53
SWITZERLAND	0.59	0.59	0.63	0.72	0.78	0.74	0.66	0.51	0.75
TAIWAN	0.29	0.30	0.31	0.31	0.33	0.39	0.36	0.34	0.38
UNITED KINGDOM	0.48	0.44	0.44	0.48	0.51	0.44	0.42	0.48	0.44

15. L_M^{UK}: PRICES RELATIVE TO UNITED KINGDOM BASED ON MULTILATERALLY-MATCHED SAMPLE, LASPEYRES PRICE INDICES, PRICE PER STANDARD UNIT

	2000	2001	2002	2003	2004	2005	2006	2007	2008
AUSTRALIA	0.84	0.79	0.83	0.93	0.99	1.23	1.21	1.35	1.64
AUSTRIA	0.87	0.88	0.90	0.92	0.90	1.01	1.07	1.21	1.49
BELGIUM	1.11	1.04	1.10	1.15	1.13	1.26	1.23	1.29	1.54
CANADA	1.19	1.26	1.20	1.20	1.26	1.62	1.79	1.99	2.35
FINLAND	0.94	0.95	0.96	0.99	0.97	1.07	1.02	1.12	1.38
FRANCE	0.91	0.93	0.92	1.01	1.05	1.20	1.18	1.28	1.52
GERMANY	0.92	0.93	0.92	0.99	1.01	1.14	1.15	1.21	1.49
GREECE	0.72	0.75	0.77	0.87	0.92	1.12	1.25	1.38	1.79
ITALY	1.12	1.15	1.14	1.16	1.16	1.30	1.35	1.50	1.55
JAPAN	2.70	1.42	1.39	1.38	1.37	1.62	1.52	1.65	2.18
KOREA	0.97	0.90	0.89	0.80	0.78	1.06	1.27	1.33	1.41
NETHERLANDS	1.02	1.02	1.01	1.05	0.95	1.04	1.06	1.19	1.30
PORTUGAL	1.05	1.04	1.01	1.03	1.04	1.24	1.28	1.31	1.64
SAUDI ARABIA	1.60	1.73	1.53	1.23	1.06	1.40	1.43	1.30	1.28
SINGAPORE	0.94	0.83	0.76	0.69	0.59	0.69	0.78	0.83	0.99
SPAIN	0.82	0.82	0.81	0.89	0.84	0.95	1.00	1.07	1.29
SWEDEN	0.98	0.91	0.92	0.89	0.83	0.97	0.97	1.08	1.29
SWITZERLAND	1.32	1.41	1.47	1.53	1.53	1.69	1.58	1.59	2.00
TAIWAN	0.98	0.96	0.88	0.82	0.78	1.04	1.07	1.03	1.17
UNITED STATES	2.25	2.49	2.45	2.25	2.13	2.48	2.57	2.27	2.44

16. P_M^{UK}: PRICES RELATIVE TO UNITED KINGDOM BASED ON MULTILATERALLY-MATCHED SAMPLE, PAASCHE PRICE INDICES, PRICE PER STANDARD UNIT

	2000	2001	2002	2003	2004	2005	2006	2007	2008
AUSTRALIA	0.77	0.73	0.75	0.85	0.91	1.06	0.99	1.01	1.16
AUSTRIA	0.74	0.75	0.75	0.83	0.82	0.95	1.02	1.06	1.27
BELGIUM	0.90	0.89	0.90	0.96	0.94	1.05	1.05	1.12	1.34
CANADA	1.03	1.02	1.01	1.05	1.07	1.28	1.33	1.32	1.45
FINLAND	0.77	0.78	0.79	0.84	0.82	0.91	0.86	0.93	1.13
FRANCE	0.77	0.79	0.78	0.89	0.92	1.05	1.01	1.01	1.16
GERMANY	0.76	0.82	0.80	0.86	0.88	1.05	1.05	1.05	1.25
GREECE	0.50	0.52	0.60	0.70	0.74	0.87	0.94	1.01	1.25
ITALY	0.95	0.97	0.96	0.97	0.95	1.02	1.04	1.05	1.19
JAPAN	0.89	0.89	0.89	0.88	0.80	0.98	1.03	1.07	1.33
KOREA	0.44	0.49	0.59	0.57	0.52	0.70	0.84	0.89	0.91
NETHERLANDS	0.99	0.98	0.96	1.00	0.89	1.00	1.01	1.07	1.15
PORTUGAL	0.84	0.87	0.88	0.94	0.97	1.14	1.17	1.21	1.46
SAUDI ARABIA	1.32	1.49	1.39	1.15	0.96	1.04	0.97	0.84	0.80
SINGAPORE	0.59	0.66	0.58	0.50	0.39	0.51	0.55	0.57	0.69
SPAIN	0.67	0.67	0.69	0.76	0.74	0.83	0.87	0.87	1.08
SWEDEN	0.90	0.81	0.82	0.80	0.75	0.85	0.83	0.87	1.01
SWITZERLAND	1.14	1.20	1.29	1.35	1.34	1.54	1.39	1.33	1.65
TAIWAN	0.42	0.44	0.44	0.43	0.45	0.52	0.54	0.51	0.64
UNITED STATES	1.84	2.04	2.09	1.95	1.82	2.10	2.02	1.74	1.79

17. L_B^{UK}: PRICES RELATIVE TO UNITED KINGDOM BASED ON BILATERALLY-MATCHED SAMPLE, LASPEYRES PRICE INDICES, PRICE PER STANDARD UNIT

	1999	**2000**	**2001**	**2002**	**2003**	**2004**	**2005**	**2006**	**2007**	**2008**
AUSTRALIA	0.99	0.93	0.87	0.90	1.00	1.06	1.23	1.20	1.26	1.46
AUSTRIA	1.06	0.93	0.96	0.96	1.00	0.97	1.08	1.14	1.19	1.45
BELGIUM	1.15	1.02	1.05	1.05	1.13	1.10	1.20	1.25	1.22	1.48
CANADA	1.39	1.98	1.44	1.33	1.60	2.11	2.37	2.49	1.83	2.08
FINLAND	1.03	0.98	1.03	1.07	1.20	1.17	1.24	1.15	1.18	1.45
FRANCE		0.91	0.95	0.93	1.02	1.03	1.18	1.18	1.20	1.46
GERMANY	1.72	1.12	1.17	1.15	1.24	1.33	1.34	1.30	1.25	1.53
GREECE	0.82	0.76	0.77	0.84	0.97	0.96	1.11	1.21	1.31	1.58
ITALY	1.14	1.07	1.11	1.10	1.15	1.11	1.21	1.25	1.30	1.50
JAPAN	1.96	2.28	1.47	1.38	1.41	1.39	1.62	1.55	1.52	1.90
KOREA	1.00	0.99	0.92	0.90	0.86	0.82	1.08	1.22	1.23	1.25
NETHERLANDS	1.16	1.04	1.05	1.04	1.10	1.02	1.10	1.10	1.17	1.29
PORTUGAL	1.13	1.02	1.04	1.02	1.08	1.07	1.20	1.21	1.21	1.44
SPAIN	0.87	0.78	0.79	0.79	0.89	0.85	0.95	0.98	0.98	1.17
SAUDI ARABIA	1.48	1.45	1.60	1.44	1.15	0.98	1.22	1.26	1.35	1.37
SINGAPORE	0.78	0.84	0.82	0.80	0.74	0.64	0.76	0.83	0.83	1.00
SWEDEN	1.10	1.06	0.99	1.01	1.05	1.01	1.12	1.12	1.15	1.36
SWITZERLAND	1.45	9.41	1.40	1.43	1.50	1.46	1.63	1.57	1.52	1.81
TAIWAN	0.86	1.00	0.99	0.87	0.82	0.79	0.99	1.02	0.95	1.08
UNITED STATES	2.92	3.09	3.00	2.86	2.70	2.46	2.63	2.75	2.51	2.73

18. P_B^{UK}: PRICES RELATIVE TO UNITED KINGDOM BASED ON BILATERALLY-MATCHED SAMPLE, PAASCHE PRICE INDICES, PRICE PER STANDARD UNIT

	1999	**2000**	**2001**	**2002**	**2003**	**2004**	**2005**	**2006**	**2007**	**2008**
AUSTRALIA	0.73	0.71	0.67	0.64	0.68	0.71	0.81	0.72	0.72	0.77
AUSTRIA	0.53	0.51	0.53	0.56	0.62	0.57	0.62	0.63	0.62	0.71
BELGIUM	0.73	0.68	0.71	0.74	0.83	0.83	0.89	0.85	0.85	0.96
CANADA	0.75	0.89	0.90	0.86	0.91	0.92	1.07	1.14	1.06	1.08
FINLAND	0.63	0.59	0.65	0.67	0.77	0.75	0.82	0.78	0.78	0.88
FRANCE		0.53	0.58	0.62	0.71	0.73	0.81	0.80	0.78	0.88
GERMANY	0.53	0.51	0.57	0.58	0.68	0.70	0.81	0.82	0.81	0.94
GREECE	0.44	0.41	0.45	0.49	0.58	0.59	0.67	0.69	0.70	0.83
ITALY	0.69	0.69	0.72	0.74	0.80	0.82	0.87	0.87	0.84	0.91
JAPAN	0.65	0.74	0.74	0.69	0.76	0.73	0.82	0.80	0.76	0.88
KOREA	0.40	0.45	0.46	0.48	0.45	0.46	0.59	0.68	0.68	0.68
NETHERLANDS	0.68	0.60	0.65	0.65	0.83	0.74	0.83	0.85	0.83	0.85
PORTUGAL	0.57	0.55	0.58	0.61	0.67	0.71	0.78	0.76	0.73	0.85
SPAIN	0.59	0.56	0.58	0.60	0.69	0.68	0.74	0.74	0.71	0.81
SAUDI ARABIA	0.84	0.88	1.01	0.98	0.83	0.69	0.73	0.69	0.62	0.56
SINGAPORE	0.51	0.52	0.57	0.55	0.50	0.42	0.48	0.50	0.48	0.55
SWEDEN	0.52	0.51	0.50	0.51	0.58	0.50	0.56	0.56	0.57	0.66
SWITZERLAND	0.53	0.55	0.62	0.69	0.76	0.75	0.84	0.77	0.73	0.82
TAIWAN	0.35	0.43	0.46	0.43	0.39	0.41	0.48	0.48	0.42	0.51
UNITED STATES	1.26	1.53	1.75	1.74	1.70	1.54	1.70	1.73	1.55	1.63

19. L_M^{FR}: PRICES RELATIVE TO FRANCE BASED ON MULTILATERALLY-MATCHED SAMPLE, LASPEYRES PRICE INDICES, PRICE PER STANDARD UNIT

	2000	**2001**	**2002**	**2003**	**2004**	**2005**	**2006**	**2007**	**2008**
AUSTRALIA	1.67	1.49	1.10	1.19	1.03	1.11	1.08	1.13	1.15
AUSTRIA	1.10	1.11	1.16	1.04	0.99	0.97	1.05	1.16	1.20
BELGIUM	1.32	1.24	1.32	1.26	1.22	1.16	1.14	1.17	1.20
CANADA	1.57	1.47	1.40	1.24	1.23	1.37	1.50	1.54	1.46
FINLAND	1.19	1.19	1.23	1.17	1.12	1.08	1.07	1.13	1.17
GERMANY	1.22	1.17	1.17	1.12	1.11	1.09	1.13	1.12	1.15
GREECE	0.88	0.90	0.91	0.92	0.95	1.00	1.08	1.09	1.14
ITALY	1.38	1.38	1.38	1.28	1.22	1.19	1.21	1.28	1.17
JAPAN	3.80	1.78	1.74	1.56	1.46	1.49	1.40	1.37	1.45
KOREA	1.14	0.99	0.96	0.80	0.77	0.90	1.07	1.07	0.93
NETHERLANDS	1.31	1.27	1.25	1.16	1.02	0.98	1.02	1.14	1.09
PORTUGAL	1.23	1.19	1.16	1.08	1.06	1.08	1.09	1.06	1.09
SAUDI ARABIA	1.92	2.00	1.74	1.26	1.05	1.19	1.23	1.04	0.84
SINGAPORE	1.30	1.07	1.04	0.84	0.67	0.70	0.81	0.81	0.83
SPAIN	0.97	0.96	0.96	0.95	0.90	0.90	0.96	1.10	1.11
SWEDEN	1.54	1.39	1.39	1.14	1.03	1.06	1.05	1.13	1.14
SWITZERLAND	1.62	1.68	1.79	1.71	1.63	1.61	1.49	1.43	1.48
TAIWAN	1.14	1.10	1.00	0.82	0.78	0.87	0.92	0.82	0.76
UNITED KINGDOM	1.30	1.27	1.28	1.13	1.09	0.95	0.99	0.99	0.86
UNITED STATES	2.85	3.03	3.05	2.52	2.26	2.27	2.28	2.22	1.96

20. P_M^{FR}: PRICES RELATIVE TO FRANCE BASED ON MULTILATERALLY-MATCHED SAMPLE, PAASCHE PRICE INDICES, PRICE PER STANDARD UNIT

	2000	2001	2002	2003	2004	2005	2006	2007	2008
AUSTRALIA	0.85	0.83	0.86	0.89	0.92	0.97	0.98	1.01	0.99
AUSTRIA	0.95	0.93	0.93	0.90	0.85	0.83	0.89	0.87	0.90
BELGIUM	1.17	1.13	1.14	1.07	1.01	0.96	0.98	1.00	1.00
CANADA	1.20	1.17	1.19	1.09	1.09	1.17	1.30	1.30	1.24
FINLAND	0.89	0.92	0.96	0.91	0.88	0.87	0.85	0.85	0.87
GERMANY	0.89	0.91	0.89	0.88	0.87	0.86	0.92	0.89	0.87
GREECE	0.73	0.74	0.78	0.79	0.82	0.86	0.94	0.97	1.04
ITALY	1.18	1.17	1.18	1.08	1.03	0.99	1.02	0.95	0.94
JAPAN	1.21	1.16	1.15	1.04	0.95	0.99	0.97	0.99	1.11
KOREA	0.50	0.54	0.66	0.61	0.58	0.73	0.89	0.87	0.78
NETHERLANDS	1.17	1.14	1.12	1.03	0.89	0.86	0.91	0.93	0.84
PORTUGAL	1.10	1.09	1.07	1.00	0.97	0.98	1.04	1.01	1.05
SAUDI ARABIA	1.47	1.56	1.44	1.10	0.92	0.92	0.93	0.81	0.67
SINGAPORE	0.68	0.71	0.64	0.50	0.36	0.41	0.47	0.48	0.47
SPAIN	0.84	0.81	0.81	0.79	0.73	0.73	0.80	0.76	0.79
SWEDEN	0.92	0.86	0.90	0.79	0.72	0.74	0.78	0.78	0.76
SWITZERLAND	1.37	1.44	1.55	1.45	1.40	1.37	1.27	1.22	1.31
TAIWAN	0.44	0.43	0.44	0.42	0.43	0.51	0.57	0.51	0.55
UNITED KINGDOM	1.10	1.07	1.09	0.99	0.95	0.83	0.85	0.78	0.66
UNITED STATES	2.36	2.55	2.56	2.12	1.91	1.96	1.98	1.68	1.49

21. L_B^{FR}: PRICES RELATIVE TO FRANCE BASED ON BILATERALLY-MATCHED SAMPLE, LASPEYRES PRICE INDICES, PRICE PER STANDARD UNIT

	2000	2001	2002	2003	2004	2005	2006	2007	2008
AUSTRALIA	1.69	1.57	1.43	1.57	1.48	2.73	2.53	2.49	2.31
AUSTRIA	1.18	1.19	1.21	1.17	1.15	1.13	1.17	1.24	1.26
BELGIUM	2.17	2.04	1.98	1.99	1.80	1.57	1.22	1.20	1.22
CANADA	3.13	2.88	3.06	2.94	7.34	3.71	3.29	4.00	4.25
FINLAND	1.26	1.31	1.38	1.29	1.26	1.25	1.19	1.17	1.22
GERMANY	1.33	1.31	1.30	1.28	1.27	1.25	1.26	1.25	1.28
GREECE	1.01	1.08	1.54	1.34	1.43	1.42	1.39	1.33	1.37
ITALY	1.35	1.36	1.37	1.31	1.26	1.20	1.20	1.22	1.18
JAPAN	2.98	1.86	1.77	1.61	1.52	1.48	1.38	1.26	1.28
KOREA	2.07	1.02	1.17	0.88	0.82	1.17	1.04	1.01	0.87
NETHERLANDS	1.35	1.31	1.31	1.25	1.17	1.12	1.13	1.18	1.14
PORTUGAL	1.24	1.24	1.23	1.18	1.16	1.66	1.12	1.09	1.09
SPAIN	1.47	1.68	1.95	2.00	1.74	1.45	0.95	1.01	1.01
SAUDI ARABIA	1.92	2.02	1.82	1.36	1.12	1.29	1.28	1.09	0.86
SINGAPORE	1.65	1.29	1.26	1.05	0.87	0.92	0.94	0.90	0.91
SWEDEN	2.34	2.05	2.04	1.83	1.70	1.62	1.56	1.39	1.54
SWITZERLAND	2.68	1.81	1.82	1.70	1.64	1.60	1.52	1.46	1.49
TAIWAN	1.28	1.17	1.06	1.02	0.97	0.99	1.00	0.89	0.83
UNITED KINGDOM	1.88	1.73	1.62	1.41	1.37	1.23	1.26	1.28	1.14
UNITED STATES	5.28	3.81	3.84	3.35	2.87	2.83	2.87	2.76	2.63

22. P_B^{FR}: PRICES RELATIVE TO FRANCE BASED ON BILATERALLY-MATCHED SAMPLE, PAASCHE PRICE INDICES, PRICE PER STANDARD UNIT

	2000	2001	2002	2003	2004	2005	2006	2007	2008
AUSTRALIA	0.82	0.78	0.81	0.81	0.84	0.87	0.84	0.86	0.63
AUSTRIA	0.71	0.69	0.71	0.72	0.70	0.70	0.71	0.73	0.75
BELGIUM	0.99	1.00	1.02	0.98	0.96	0.94	0.92	0.95	0.96
CANADA	1.07	1.10	1.09	1.02	1.03	1.10	1.22	1.15	1.05
FINLAND	0.85	0.88	0.93	0.91	0.90	0.90	0.86	0.87	0.88
GERMANY	0.82	0.83	0.84	0.85	0.88	0.87	0.87	0.86	0.87
GREECE	0.63	0.67	0.70	0.71	0.74	0.76	0.81	0.85	0.88
ITALY	1.03	1.04	1.04	0.99	0.95	0.92	0.84	0.81	0.81
JAPAN	1.17	1.16	1.10	1.02	0.93	0.84	0.79	0.78	0.84
KOREA	0.35	0.41	0.47	0.46	0.48	0.59	0.78	0.75	0.64
NETHERLANDS	1.00	1.00	1.01	0.99	0.92	0.90	0.92	0.95	0.88
PORTUGAL	0.92	0.93	0.93	0.90	0.90	0.88	0.91	0.89	0.93
SPAIN	0.81	0.80	0.82	0.81	0.78	0.78	0.81	0.79	0.81
SAUDI ARABIA	1.25	1.37	1.30	0.96	0.81	0.79	0.76	0.70	0.55
SINGAPORE	0.68	0.72	0.69	0.55	0.44	0.44	0.47	0.45	0.44
SWEDEN	0.74	0.69	0.72	0.69	0.67	0.67	0.68	0.70	0.70
SWITZERLAND	1.10	1.19	1.28	1.23	1.23	1.25	1.13	1.10	1.12
TAIWAN	0.50	0.49	0.47	0.38	0.40	0.46	0.50	0.44	0.46
UNITED KINGDOM	1.09	1.06	1.07	0.98	0.97	0.85	0.85	0.83	0.68
UNITED STATES	2.22	2.46	2.46	2.03	1.86	1.86	1.87	1.73	1.55

BRIEF SUMMARY OF FINDINGS

The results of the sensitivity analysis are described in Paper 2. Using the Paasche indices, discounting led to an average increase of 0.03 in index values across all years and all countries. Using Laspeyres indices led to an average increase of 0.063. Whilst these changes are not entirely insignificant, they pale in comparison to range provided by the different types of indices themselves. This is discussed to a greater extent in the text. In general, it highlights that, whilst potentially important to account for the various types of discounts, this may be secondary concern coming after gaining a clearer picture of the indices themselves.

The relative changes in the rebased indices over time provide insight into the underlying evolution of consumption patterns and individual drug prices. It is thus convenient to normalize the indices to their value in a given reference year to study the change of drug prices relative to the US over time. Because 2001 is generally the year in which the indices were lowest, it was chosen as the reference year for our calculations. This choice avoids the complication posed by very large (and

possibly wrong) values of indices for Japan and Canada in 1999 and 2000. The four indices, L_B, L_M, P_M and P_B, normalized to their 2001 values are given in Tables 7-10. For most countries, all four indices increase over time between 2001 and 2008 with a mean increase of about 50% for the Laspeyres indices and of 30% for the Paasche indices. The two exceptions are Saudi Arabia and the United Kingdom. In Saudi Arabia, all four indices decrease systematically over time whilst in the UK, all the indices remain approximately constant. In other words, whilst the drug prices in most high income countries increased compared to the US between 2001 and 2008, they decreased in Saudi Arabia and remained relatively constant in the UK. As mentioned in the text, in the case of the UK this would be suggestive of an overall containment pressure from the combination of policy tools in place at the time, including health technology assessments and the Pharmaceutical Price Regulation Scheme (previous model), as well as policies promoting generic prescription and dispensing.

APPENDIX 3
SUPPORT MATERIAL FOR PAPER 3

CONTENTS

- Summary statistics for samples 1-13

TABLE 1. SUMMARY STATISTICS - SAMPLE 1

**signifies that variable is time-invariant*

	count	mean	p50	sd	variance	min	max
Price wtd(ln)	1756134	-21.23062	-20.95811	2.945369	8.675198	-64.49702	-10.02197
Global penetration (ln)	2782980	3.183688	3.401197	.5190588	.2694221	.6931472	3.465736
Strength (ln)*	1692900	4.008496	4.094345	1.668212	2.782932	.0953102	6.898715
Form count (ln)	2292250	1.501842	1.386294	.6310742	.3982546	.6931472	3.332205
Manufacturer count (ln)	2457700	2.497889	2.484907	1.081841	1.17038	.6931472	5.062595
Therapeutic alternatives (ln)	2741850	2.429366	2.484907	.7219274	.5211792	.6931472	4.934474
Time-since-global-launch (ln)*	2404840	5.910278	5.968708	.6572496	.4319771	1.791759	7.156956
Time-since-incountry-launch (ln)*	2340220	4.814804	4.927254	1.005194	1.010414	.6931472	7.17549
Entry lag (ln)*	2327860	6.49298	6.719013	.6749448	.4555504	.6931472	7.154615
Older population	2512605	11.63002	12.3647	5.515276	30.41827	2.6661	20.7631
GNI per capita (ln)	2512605	9.253956	10.04238	1.46466	2.14523	6.086775	11.0001
population growth	2512605	.8701814	.863316	.606995	.3684429	-.1313045	2.583598
rural population	2512605	33.05606	26.72	17.89445	320.2115	2.66	72.52
Trade	2281425	66.13367	59.55613	39.43946	1555.471	18.96887	228.8752
Death rate	2008145	8.41447	8.5	2.234812	4.994384	3.6896	21.77128
Year	2808680	2003.5	2003.5	2.872282	8.250003	1999	2008
Countrycode	2808680	17.74127	20	11.51821	132.6692	1	37
N	2808680						

TABLE 2. SUMMARY STATISTICS - SAMPLE 2

	count	mean	p50	sd	variance	min	max
Price wtd(ln)	578244	-20.46381	-20.19951	2.808055	7.885173	-30.92904	-11.97883
Global penetration (ln)	969650	2.378876	2.564949	.3531762	.1247335	.6931472	2.564949
Strength (ln)	598240	4.184541	4.60517	1.68388	2.835452	.1823216	6.898715
Form count (ln)	833820	1.573754	1.609438	.6196328	.3839448	.6931472	3.258096
Manufacturer count (ln)	879070	2.81669	2.833213	1.179744	1.391795	.6931472	5.062595
Therapeutic alternatives (ln)	952740	2.29552	2.397895	.6978719	.4870252	.6931472	3.637586
Time-since-global-launch (ln)	864930	5.932373	6.008813	.6359174	.4043909	2.639057	7.156956
Time-since-incountry-launch (ln)	733000	4.577637	4.65396	.913402	.8343033	.6931472	7.166266
Entry lag (ln)	724960	6.462282	6.572282	.621976	.3868541	.6931472	7.154615
Older population	875922	5.150692	4.9766	.9881426	.9764257	3.4482	8.1544
GNI per capita (ln)	875922	7.432131	7.408531	.8774175	.7698615	6.086775	9.028818
population growth	875922	1.427417	1.407728	.3925453	.1540918	.4138161	2.477053
rural population	875922	49.30685	49.66	19.55823	382.5244	14.88	72.52
trade	870652	68.54445	54.69402	48.91105	2392.291	20.22726	228.8752
Death rate	567223	7.571139	7.5	3.322725	11.0405	4.4764	21.77128
Year	982030	2003.5	2003.5	2.872283	8.250008	1999	2008
Countrycode	982030	8.089407	6	4.973471	24.73541	2	25
N	982030						

TABLE 3. SUMMARY STATISTICS - SAMPLE 3

	count	mean	p50	sd	variance	min	max
Price wtd(ln)	1177890	-20.6244	-20.36437	2.951387	8.710682	-64.21597	-9.75285
Global penetration (ln)	1798050	2.678114	2.890372	.491886	.2419518	.6931472	2.944439
Strength (ln)	1094660	3.912285	3.912023	1.651678	2.728039	.0953102	6.887553
Form count (ln)	1458430	1.460728	1.386294	.6338684	.4017892	.6931472	3.332205
Manufacturer count (ln)	1578630	2.320362	2.397895	.979272	.9589736	.6931472	4.59512
Therapeutic alternatives (ln)	1789110	2.500642	2.564949	.7243942	.5247469	.6931472	4.934474
Time-since-global-launch (ln)	1539910	5.897867	5.953243	.6686132	.4470436	1.791759	7.156956
Time-since-incountry-launch (ln)	1607220	4.922968	5.068904	1.026343	1.053381	.6931472	7.17549
Entry lag (ln)	1597040	6.450512	6.682108	.7087528	.5023305	.6931472	7.154615
Older population	1636683	15.09763	16.0507	3.418018	11.68285	2.6661	20.7631
GNI per capita (ln)	1636683	10.22896	10.31923	.3929025	.1543724	8.961879	11.0001
population growth	1636683	.5719593	.5028359	.4775386	.2280431	-.1313045	2.583598
rural population	1636683	24.35894	23.3	8.359893	69.88781	2.66	46.26
trade	1410773	64.64587	66.40145	32.14394	1033.233	18.96887	172.7742
Death rate	1440922	8.74645	8.8	1.491355	2.22414	3.6896	11.1
Year	1826650	2003.5	2003.5	2.872282	8.250005	1999	2008
Countrycode	1826650	22.93024	26	10.66242	113.6872	1	37
N	1826650						

TABLE 4. SUMMARY STATISTICS - SAMPLE 4

	count	mean	p50	sd	variance	min	max
lnpricesuregrD	1761832	-5.805162	-6.114752	2.120089	4.494775	-41.05474	32.58273
Global penetration (ln)	2782980	3.183688	3.401197	.5190588	.2694221	.6931472	3.465736
Strength (ln)	1692900	4.008496	4.094345	1.668212	2.782932	.0953102	6.898715
Form count (ln)	2292250	1.501842	1.386294	.6310742	.3982546	.6931472	3.332205
Manufacturer count (ln)	2457700	2.497889	2.484907	1.081841	1.17038	.6931472	5.062595
Therapeutic alternatives (ln)	2741850	2.429366	2.484907	.7219274	.5211792	.6931472	4.934474
Time-since-global-launch (ln)	2404840	5.910278	5.968708	.6572496	.4319771	1.791759	7.156956
Time-since-incountry-launch (ln)	2340220	4.814804	4.927254	1.005194	1.010414	.6931472	7.17549
Entry lag (ln)	2327860	6.49298	6.719013	.6749448	.4555504	.6931472	7.154615
Older population	2512605	11.63002	12.3647	5.515276	30.41827	2.6661	20.7631
GNI per capita (ln)	2512605	9.253956	10.04238	1.46466	2.14523	6.086775	11.0001
population growth	2512605	.8701814	.863316	.606995	.3684429	-.1313045	2.583598
rural population	2512605	33.05606	26.72	17.89445	320.2115	2.66	72.52
trade	2281425	66.13367	59.55613	39.43946	1555.471	18.96887	228.8752
Death rate	2008145	8.41447	8.5	2.234812	4.994384	3.6896	21.77128
Year	2808680	2003.5	2003.5	2.872282	8.250003	1999	2008
Countrycode	2808680	17.74127	20	11.51821	132.6692	1	37
N	2808680						

TABLE 5. SUMMARY STATISTICS - SAMPLE 5

	count	mean	p50	sd	variance	min	max
lnpricesuregrD	568430	-6.193923	-6.331256	1.704947	2.906845	-41.05474	28.16475
Strength (ln)	646920	4.121017	4.382027	1.660847	2.758413	.1823216	6.882438
Form count (ln)	821750	1.651143	1.609438	.5853108	.3425888	.6931472	3.091043
Manufacturer count (ln)	895440	2.821801	2.833213	1.0117	1.023537	.6931472	5.056246
Therapeutic alternatives (ln)	731120	1.190945	1.386294	.4121921	.1699023	.6931472	1.94591
Time-since-global-launch (ln)	876600	5.983136	6.025866	.5917638	.3501844	4.343805	7.118826
Time-since-incountry-launch (ln)	744990	4.761928	4.890349	1.003971	1.007959	.6931472	7.17549
Entry lag (ln)	717440	5.710104	5.888878	.909806	.8277469	.6931472	7.116394
Older population	815756	11.1592	12.3077	5.550833	30.81174	2.6661	20.7631
GNI per capita (ln)	815756	9.122021	9.891415	1.48294	2.199111	6.086775	11.0001
population growth	815756	.9157726	.9290047	.61089	.3731866	-.1313045	2.583598
rural population	815756	33.82889	26.72	18.35819	337.0232	2.66	72.52
trade	747701	68.83116	61.5735	40.24016	1619.271	18.96887	228.8752
Death rate	638456	8.39149	8.5	2.342234	5.486059	3.6896	21.77128
Year	913680	2003.5	2003.5	2.872283	8.250009	1999	2008
Countrycode	913680	17.58133	18	11.37751	129.4476	1	37
N	913680						

TABLE 6. SUMMARY STATISTICS - SAMPLE 6

	count	mean	p50	sd	variance	min	max
Price wtd(ln)	566737	-20.20571	-19.94178	2.954671	8.730079	-46.98684	-9.003541
Strength (ln)	646920	4.121017	4.382027	1.660847	2.758413	.1823216	6.882438
Form count (ln)	821750	1.651143	1.609438	.5853108	.3425888	.6931472	3.091043
Manufacturer count (ln)	895440	2.821801	2.833213	1.0117	1.023537	.6931472	5.056246
Therapeutic alternatives (ln)	731120	1.190945	1.386294	.4121921	.1699023	.6931472	1.94591
Time-since-global-launch (ln)	876600	5.983136	6.025866	.5917638	.3501844	4.343805	7.118826
Time-since-incountry-launch (ln)	744990	4.761928	4.890349	1.003971	1.007959	.6931472	7.17549
Entry lag (ln)	717440	5.710104	5.888878	.909806	.8277469	.6931472	7.116394
Older population	815756	11.1592	12.3077	5.550833	30.81174	2.6661	20.7631
GNI per capita (ln)	815756	9.122021	9.891415	1.48294	2.199111	6.086775	11.0001
population growth	815756	.9157726	.9290047	.61089	.3731866	-.1313045	2.583598
rural population	815756	33.82889	26.72	18.35819	337.0232	2.66	72.52
trade	747701	68.83116	61.5735	40.24016	1619.271	18.96887	228.8752
Death rate	638456	8.39149	8.5	2.342234	5.486059	3.6896	21.77128
Year	913680	2003.5	2003.5	2.872283	8.250009	1999	2008
Countrycode	913680	17.58133	18	11.37751	129.4476	1	37
N	913680						

TABLE 7. SUMMARY STATISTICS - SAMPLE 7

	count	mean	p50	sd	variance	min	max
Price wtd(ln)	292372	-19.78657	-19.57155	2.818619	7.944611	-30.2012	-11.2258
Strength (ln)	322930	4.256916	4.60517	1.677497	2.813997	.4054651	6.856462
Form count (ln)	452050	1.691861	1.609438	.6080064	.3696718	.6931472	3.258096
Manufacturer count (ln)	481670	3.1239	3.218876	1.101687	1.213714	.6931472	5.056246
Therapeutic alternatives (ln)	428010	1.332855	1.386294	.4620242	.2134664	.6931472	1.94591
Time-since-global-launch (ln)	476960	5.99459	6.086775	.5648756	.3190845	4.343805	7.118826
Time-since-incountry-launch (ln)	362350	4.629425	4.718499	.8823354	.7785158	.6931472	7.166266
Entry lag (ln)	353120	5.898615	6.011267	.6985856	.4880219	1.386294	7.116394
Older population	438060	5.159214	4.9766	1.026081	1.052843	3.4482	8.1544
GNI per capita (ln)	438060	7.43365	7.408531	.8644594	.74729	6.086775	9.028818
population growth	438060	1.425945	1.407728	.399913	.1599304	.4138161	2.477053
rural population	438060	49.18096	49.66	19.50809	380.5657	14.88	72.52
trade	434486	70.19077	56.20589	49.16403	2417.102	20.22726	228.8752
Death rate	279205	7.518441	7.5	3.285774	10.79631	4.4764	21.77128
Year	492690	2003.5	2003.5	2.872284	8.250017	1999	2008
Countrycode	492690	8.29682	7	5.177163	26.80302	2	25
N	492690						

TABLE 8. SUMMARY STATISTICS - SAMPLE 8

	count	mean	p50	sd	variance	min	max
Price wtd(ln)	463928	-19.60297	-19.37584	2.927789	8.571946	-46.91167	-8.89033
Strength (ln)	509680	3.958703	3.912023	1.632863	2.666241	.1823216	6.882438
Form count (ln)	623660	1.534378	1.386294	.5819112	.3386206	.6931472	3.091043
Manufacturer count (ln)	690710	2.522176	2.564949	.9267525	.8588701	.6931472	4.59512
Therapeutic alternatives (ln)	599560	1.438214	1.386294	.4674106	.2184726	.6931472	2.197225
Time-since-global-launch (ln)	692860	5.938188	5.968708	.6091416	.3710535	3.367296	7.118826
Time-since-incountry-launch (ln)	632370	4.823988	4.983607	1.040103	1.081815	.6931472	7.17549
Entry lag (ln)	612890	5.761689	5.958425	.95204	.9063801	.6931472	7.113956
Older population	646939	15.09681	16.0507	3.364927	11.32274	2.6661	20.7631
GNI per capita (ln)	646939	10.20944	10.26011	.3966066	.1572968	8.961879	11.0001
population growth	646939	.5809915	.5038087	.483348	.2336253	-.1313045	2.583598
rural population	646939	24.24119	23.3	8.633626	74.5395	2.66	46.26
trade	561273	68.1322	66.89499	32.1571	1034.079	18.96887	172.7742
Death rate	568818	8.806273	8.917869	1.496649	2.239957	3.6896	11.1
Year	722130	2003.5	2003.5	2.872283	8.250011	1999	2008
Countrycode	722130	23.73161	26	10.08705	101.7486	1	37
N	722130						

TABLE 9. SUMMARY STATISTICS – SAMPLE 9

	count	mean	p50	sd	variance	min	max
olderpop	2512605	11.63002	12.3647	5.515276	30.41827	2.6661	20.7631
lngnicap	2512605	9.253956	10.04238	1.46466	2.14523	6.086775	11.0001
popgrowth	2512605	.8701814	.863316	.606995	.3684429	-.1313045	2.583598
ruralpop	2512605	33.05606	26.72	17.89445	320.2115	2.66	72.52
tradepgdp	2281425	66.13367	59.55613	39.43946	1555.471	18.96887	228.8752
deathrate	2008145	8.41447	8.5	2.234812	4.994384	3.6896	21.77128
year	2808680	2003.5	2003.5	2.872282	8.250003	1999	2008
N	2808680						

TABLE 10. SUMMARY STATISTICS – SAMPLE 10

	count	mean	p50	sd	variance	min	max
olderpop	875922	5.150692	4.9766	.9881426	.9764257	3.4482	8.1544
lngnicap	875922	7.432131	7.408531	.8774175	.7698615	6.086775	9.028818
popgrowth	875922	1.427417	1.407728	.3925453	.1540918	.4138161	2.477053
ruralpop	875922	49.30685	49.66	19.55823	382.5244	14.88	72.52
tradepgdp	870652	68.54445	54.69402	48.91105	2392.291	20.22726	228.8752
deathrate	567223	7.571139	7.5	3.322725	11.0405	4.4764	21.77128
year	982030	2003.5	2003.5	2.872283	8.250008	1999	2008
N	982030						

TABLE 11. SUMMARY STATISTICS – SAMPLE 11

	count	mean	p50	sd	variance	min	max
olderpop	1636683	15.09763	16.0507	3.418018	11.68285	2.6661	20.7631
lngnicap	1636683	10.22896	10.31923	.3929025	.1543724	8.961879	11.0001
popgrowth	1636683	.5719593	.5028359	.4775386	.2280431	-.1313045	2.583598
ruralpop	1636683	24.35894	23.3	8.359893	69.88781	2.66	46.26
tradepgdp	1410773	64.64587	66.40145	32.14394	1033.233	18.96887	172.7742
deathrate	1440922	8.74645	8.8	1.491355	2.22414	3.6896	11.1
year	1826650	2003.5	2003.5	2.872282	8.250005	1999	2008
N	1826650						

TABLE 12. SUMMARY STATISTICS – SAMPLE 12

	count	mean	p50	sd	variance	min	max
lnwtpricesuregrD	1756134	-21.23062	-20.95811	2.945369	8.675198	-64.49702	-10.02197
lnpenetration	2782980	3.183688	3.401197	.5190588	.2694221	.6931472	3.465736
lnstrength1	1692900	4.008496	4.094345	1.668212	2.782932	.0953102	6.898715
lnformcount	2292250	1.501842	1.386294	.6310742	.3982546	.6931472	3.332205
lnmnfcount	2457700	2.497889	2.484907	1.081841	1.17038	.6931472	5.062595
lnthalternatives	2741850	2.429366	2.484907	.7219274	.5211792	.6931472	4.934474
lnageG	2404840	5.910278	5.968708	.6572496	.4319771	1.791759	7.156956
lnageL	2340220	4.814804	4.927254	1.005194	1.010414	.6931472	7.17549
lnentrylag	2327860	6.49298	6.719013	.6749448	.4555504	.6931472	7.154615
lngnicap	2512605	9.253956	10.04238	1.46466	2.14523	6.086775	11.0001
tradepgdp	2281425	66.13367	59.55613	39.43946	1555.471	18.96887	228.8752
deathrate	2008145	8.41447	8.5	2.234812	4.994384	3.6896	21.77128
year	2808680	2003.5	2003.5	2.872282	8.250003	1999	2008
Countrycode	2808680	17.74127	20	11.51821	132.6692	1	37
N	2808680						

TABLE 13. SUMMARY STATISTICS – SAMPLE 13

	count	mean	p50	sd	variance	min	max
lnwtpricesuregrD	578244	-20.46381	-20.19951	2.808055	7.885173	-30.92904	-11.97883
lnpenetration	969650	2.378876	2.564949	.3531762	.1247335	.6931472	2.564949
lnstrength1	598240	4.184541	4.60517	1.68388	2.835452	.1823216	6.898715
lnformcount	833820	1.573754	1.609438	.6196328	.3839448	.6931472	3.258096
lnmnfcount	879070	2.81669	2.833213	1.179744	1.391795	.6931472	5.062595
lnthalternatives	952740	2.29552	2.397895	.6978719	.4870252	.6931472	3.637586
lnageG	864930	5.932373	6.008813	.6359174	.4043909	2.639057	7.156956
lnageL	733000	4.577637	4.65396	.913402	.8343033	.6931472	7.166266
lnentrylag	724960	6.462282	6.572282	.621976	.3868541	.6931472	7.154615
olderpop	875922	5.150692	4.9766	.9881426	.9764257	3.4482	8.1544
lngnicap	875922	7.432131	7.408531	.8774175	.7698615	6.086775	9.028818
popgrowth	875922	1.427417	1.407728	.3925453	.1540918	.4138161	2.477053
tradepgdp	870652	68.54445	54.69402	48.91105	2392.291	20.22726	228.8752
deathrate	567223	7.571139	7.5	3.322725	11.0405	4.4764	21.77128
year	982030	2003.5	2003.5	2.872283	8.250008	1999	2008
Countrycode	982030	8.089407	6	4.973471	24.73541	2	25
N	982030						

APPENDIX 4
SUPPORT MATERIAL FOR PAPER 4

CONTENTS

The material presented here describe the data used in the price index calculations of Paper 4. It provides a picture of the relative size of the individual country markets by molecule presentation (also a decent proxy for variability) and the degree to which the samples used in calculating the indices were representative of the individual country markets.

1. Number of molecule presentations per OECD country market
2. Number of unique ATCMOLs on market by country by year
3. OECD sample representativeness: Proportion of total country market (by SU volume) captured in samples bilaterally-matched with United States

1. NUMBER OF MOLECULE PRESENTATIONS PER OECD COUNTRY MARKET (THOSE INCLUDED IN THE DATABASE)

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
AUSTRALIA	7911	8046	8138	8251	8289	8315	8268	8293	8328	8288
AUSTRIA	5726	5798	5815	5852	5870	5902	5898	5913	5904	5850
BELGIUM	4685	4716	4787	4844	4845	4845	4782	4794	4761	4677
CANADA	10370	10438	10622	10596	10589	10616	10746	10926	11010	10937
FINLAND	4185	4222	4245	4258	4292	4319	4340	4330	4330	4310
GERMANY	33291	33634	33970	34105	34196	34146	34139	34128	34027	33936
GREECE	5585	5611	5715	5816	5818	5829	5864	5897	5876	5892
ITALY	9061	9165	9203	9396	9379	9358	9322	9272	9254	9231
JAPAN	17371	17390	17478	17490	17504	17503	17482	17510	17510	17483
KOREA	11168	12506	12647	12882	12914	12994	12931	12996	13022	12929
NETHERLANDS	11772	11973	12168	12202	12278	12350	12388	12373	12394	12377
PORTUGAL	5287	5359	5404	5450	5498	5533	5454	5455	5455	5412
SPAIN	7773	7849	7885	7912	7916	7926	7950	7879	7874	7840
SWEDEN	5553	5702	5791	5940	5971	6020	6029	6067	6084	6078
SWITZERLAND	8320	8342	8356	8367	8311	8236	8202	8139	8106	8021
UNITED KINGDOM	7504	7573	7627	7643	7666	7677	7655	7660	7655	7592
UNITED STATES	37904	38057	38260	38602	38669	38764	38751	38220	38230	38195

2. NUMBER OF UNIQUE ATCMOLS ON MARKET BY COUNTRY BY YEAR

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
AUSTRALIA	1430	1465	1494	1547	1569	1575	1536	1544	1564	1558
AUSTRIA	1205	1225	1216	1231	1244	1248	1242	1252	1252	1224
BELGIUM	1147	1156	1172	1182	1176	1173	1120	1129	1109	1067
CANADA	1447	1436	1495	1458	1461	1457	1509	1608	1640	1618
FINLAND	784	784	784	790	795	795	800	803	799	792
GERMANY	2471	2516	2629	2630	2616	2509	2497	2481	2493	2486
GREECE	996	1002	1035	1088	1080	1087	1103	1120	1111	1118
ITALY	1348	1375	1367	1392	1369	1345	1330	1312	1304	1305
JAPAN	1735	1733	1742	1749	1738	1732	1720	1737	1735	1731
KOREA	1016	1333	1334	1492	1462	1501	1479	1496	1514	1482
NETHERLANDS	994	1006	1013	996	974	978	990	982	982	974
PORTUGAL	924	943	953	960	973	990	937	935	929	918
SPAIN	1193	1219	1221	1220	1215	1208	1211	1181	1174	1171
SWEDEN	799	824	856	897	892	900	906	919	931	934
SWITZERLAND	1994	1990	1976	1966	1926	1858	1834	1794	1780	1739
UNITED KINGDOM	1354	1369	1388	1381	1391	1390	1387	1389	1382	1348
UNITED STATES	2172	2152	2150	2203	2200	2214	2196	2127	2160	2192

3. OECD SAMPLE REPRESENTATIVENESS: PROPORTION OF TOTAL COUNTRY MARKET (BY SU VOLUME) CAPTURED IN SAMPLES BILATERALLY-MATCHED WITH UNITED STATES

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
AUSTRALIA	99	99	99	99	99	99	99	99	99	99
AUSTRIA	71	72	72	72	72	72	72	72	74	74
BELGIUM	80	80	80	80	81	81	81	80	82	82
FINLAND	85	85	85	85	84	85	85	86	86	87
FRANCE		62	63	63	62	63	65	68	70	71
GERMANY	79	80	80	79	79	80	80	76	79	80
ITALY	67	68	69	70	70	72	72	73	75	77
JAPAN	72	72	72	72	71	70	69	67	66	65
KOREA	99	99	98	98	98	97	97	97	97	97
NETHERLANDS	92	93	93	93	93	93	93	92	92	92
POLAND	67	68	68	69	68	70	70	65	66	67
PORTUGAL	88	88	89	90	90	91	92	92	93	94
SPAIN	75	76	75	75	75	77	77	76	78	78
SWEDEN	94	94	94	93	93	93	93	92	92	92
SWITZERLAND	79	79	79	78	78	78	78	75	78	78
UNITED KINGDOM	86	86	86	87	87	87	87	86	85	85

APPENDIX 5
SUPPORT MATERIAL TO OVERALL DISSERTATION AND ADDITIONAL GLOBAL INDICES

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IMPACT OF POLITICAL MOTIVATIONS ON THE TECHNICAL PREFERENCES FOR CALCULATING PRICE INDICES

The Introduction lists the various agents who may be interested in understanding price differentials for different reasons. Depending on their interest they may prefer to use indices calculated in a different manner. Some examples of the potential technical preferences of various agents are included here-below.

Health authorities wanting to predict and manage out-going patient migration (or medical tourism) may want price indices based on bilateral matches with the physically-accessible neighbouring country using its own country for weighting given that patients would value drugs according to local, in-country, patterns (which is determined by exposure to marketing activities such as advertisements, habits of local prescribers, general attitudes towards drug consumption, etc.). With such indices and an understanding of transport considerations the agency could arguably be in a position to devise reasonable policy responses.

National authorities concerned by the potential for parallel importing to "distort" the in-country market may prefer Laspeyres indices based on product-specific (e.g. brand, strength, and formulation) multilaterally-matched samples given that an importer may be more likely to look

across several neighbouring markets for clear signs of large price differentials to exploit. Such price comparisons would likely focus on drugs sold in-country at clearly high prices and in high volumes.

National-level payors wanting greater leverage in price negotiations with manufacturers may use either manufacturer-specific indices across all products sold into the national market (Laspeyres indices, possibly unweighted) but matched bilaterally with other countries each in order to maximize the representativeness of the products with respect to wider market. However, if manufacturer-specific arguments to lower prices are based on the notion of "fairness", then the national-level payor may prefer product-by-product price multilateral comparisons to be able to demand, for example, the lowest or the median price offered within the list of comparison countries. (Indeed this type of external price referencing can be a powerful tool for national payors to use their buying power to drive down prices, arguably down lower than their position of relative national wealth would accord in a "fairer" system.)

Patients seeking a bargain are likely to look at relative prices of specific drugs in close neighbouring markets if they can access those places cheaply. As only their own consumption needs are of relevance (assuming only legal purchase of a single drug and no re-selling), there is no need for weighting, or the use of an index. If however they are interested in purchasing numerous drugs for own-use, the savvy patient may indeed construct an index to compile all the drugs of interest to see if there is an appreciable difference in prices across the national borders in order to see if the trip is worthwhile.

The public and civil society organizations fighting for better and fairer access to pharmaceuticals globally may prefer price comparisons for "essential" drugs (those needed for basic survival such as antibiotics, antimalarials, ARVs, etc.). Such comparisons may not be consumption-weighted and may include generics and brands as needed to make a political message of unfairness regarding price or access. With regards to the latter, indices based on availability in high-income markets (e.g. the latest treatments) may be chosen to highlight extreme differentials in access.

ADDITIONAL INDICES AGGREGATING GLOBAL DATA

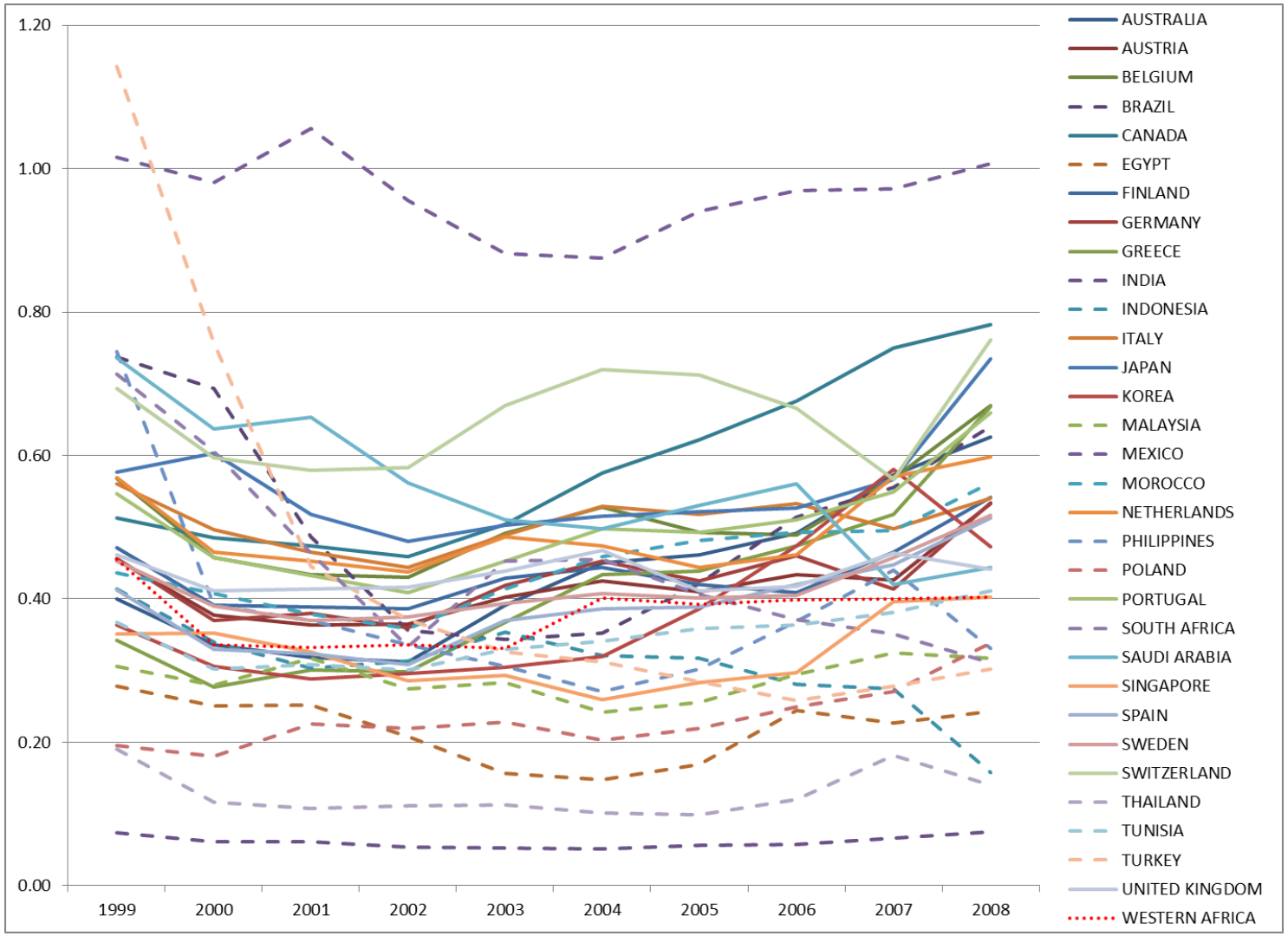
The additional indices presented below present different variations of indices constructed for the papers in the dissertation itself. They are intended to explore how overall price relatives change when a key parameter, for example, the base country or sampling method, changes. In this sense they act much like a sensitivity analysis of the overall work.

The indices here utilize Fisher calculations, thereby intended to present findings in a manner as country independent as possible. It should be noted that some of the indices originally included in this appendix have been transformed into an additional paper (Paper 4). The rest have been included in this Appendix (5). These results could themselves be used as part of an additional paper. Indeed the results presented here offer the widest possible comparison using the available dataset, spanning low-, middle-, and high-income countries. However, most of the interesting points deriving from an additional analysis of this data (for example, with respect to differential pricing by income category, similarities/differences across markets, etc.) may not have a tremendous amount of added value given the findings already presented in the papers themselves. Indeed each of the countries here have already been included in the analysis of at least one chapter of this dissertation. Also, as mentioned in the limitations of this doctoral work, by expanding the price comparison out to so many countries, the number of pharmaceuticals (the number going down to about 100 in the 33-country multilaterally-matched sample, representing between only 20-30% of the market by volume) and indeed the like-for-like nature of the comparison is diminished. In sum, whilst the findings of these more global comparisons presented in this appendix are interesting, it should be cautioned that they derive from a sample that is less robust than those analysed in the main chapters.

1. F_M: Prices relative to United States prices based on multilaterally-matched sample, Fisher price indices, price per standard unit

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
AUSTRALIA	0.40	0.34	0.32	0.31	0.39	0.45	0.46	0.49	0.57	0.63
AUSTRIA	0.45	0.38	0.36	0.37	0.40	0.42	0.41	0.43	0.43	0.53
BELGIUM	0.57	0.46	0.43	0.43	0.49	0.53	0.49	0.49	0.57	0.67
BRAZIL	0.74	0.69	0.49	0.36	0.34	0.35	0.42	0.51	0.56	0.64
CANADA	0.51	0.49	0.47	0.46	0.50	0.58	0.62	0.68	0.75	0.78
EGYPT	0.28	0.25	0.25	0.21	0.16	0.15	0.17	0.24	0.23	0.24
FINLAND	0.47	0.39	0.39	0.39	0.43	0.44	0.42	0.41	0.47	0.54
GERMANY	0.46	0.37	0.38	0.36	0.42	0.45	0.42	0.46	0.41	0.53
GREECE	0.34	0.28	0.30	0.30	0.37	0.43	0.44	0.47	0.52	0.67
INDIA	0.07	0.06	0.06	0.05	0.05	0.05	0.06	0.06	0.07	0.07
INDONESIA	0.41	0.34	0.30	0.31	0.35	0.32	0.32	0.28	0.27	0.16
ITALY	0.56	0.50	0.47	0.44	0.49	0.53	0.52	0.53	0.50	0.54
JAPAN	0.58	0.60	0.52	0.48	0.50	0.52	0.52	0.53	0.57	0.74
KOREA	0.36	0.31	0.29	0.30	0.30	0.32	0.39	0.47	0.58	0.47
MALAYSIA	0.31	0.28	0.32	0.27	0.28	0.24	0.26	0.30	0.32	0.32
MEXICO	1.02	0.98	1.06	0.95	0.88	0.87	0.94	0.97	0.97	1.01
MOROCCO	0.44	0.41	0.38	0.36	0.41	0.46	0.48	0.49	0.50	0.56
NETHERLANDS	0.57	0.47	0.45	0.44	0.49	0.47	0.44	0.46	0.57	0.60
PHILIPPINES	0.74	0.39	0.37	0.34	0.31	0.27	0.30	0.37	0.44	0.33
POLAND	0.20	0.18	0.23	0.22	0.23	0.20	0.22	0.25	0.27	0.34
PORTUGAL	0.55	0.46	0.43	0.41	0.45	0.50	0.49	0.51	0.55	0.66
SOUTH AFRICA	0.71	0.61	0.46	0.33	0.45	0.46	0.41	0.37	0.35	0.31
SAUDI ARABIA	0.74	0.64	0.65	0.56	0.51	0.50	0.53	0.56	0.42	0.44
SINGAPORE	0.35	0.35	0.33	0.29	0.29	0.26	0.28	0.30	0.40	0.40
SPAIN	0.41	0.33	0.32	0.31	0.37	0.39	0.39	0.42	0.45	0.51
SWEDEN	0.45	0.39	0.37	0.37	0.39	0.41	0.40	0.41	0.46	0.52
SWITZERLAND	0.69	0.60	0.58	0.58	0.67	0.72	0.71	0.67	0.57	0.76
THAILAND	0.19	0.12	0.11	0.11	0.11	0.10	0.10	0.12	0.18	0.14
TUNISIA	0.37	0.30	0.31	0.30	0.33	0.34	0.36	0.36	0.38	0.41
TURKEY	1.14	0.76	0.44	0.37	0.33	0.31	0.29	0.26	0.28	0.30
UNITED KINGDOM	0.46	0.41	0.41	0.42	0.44	0.47	0.41	0.42	0.46	0.44
WESTERN AFRICA	0.46	0.34	0.33	0.34	0.33	0.40	0.39	0.40	0.40	0.40

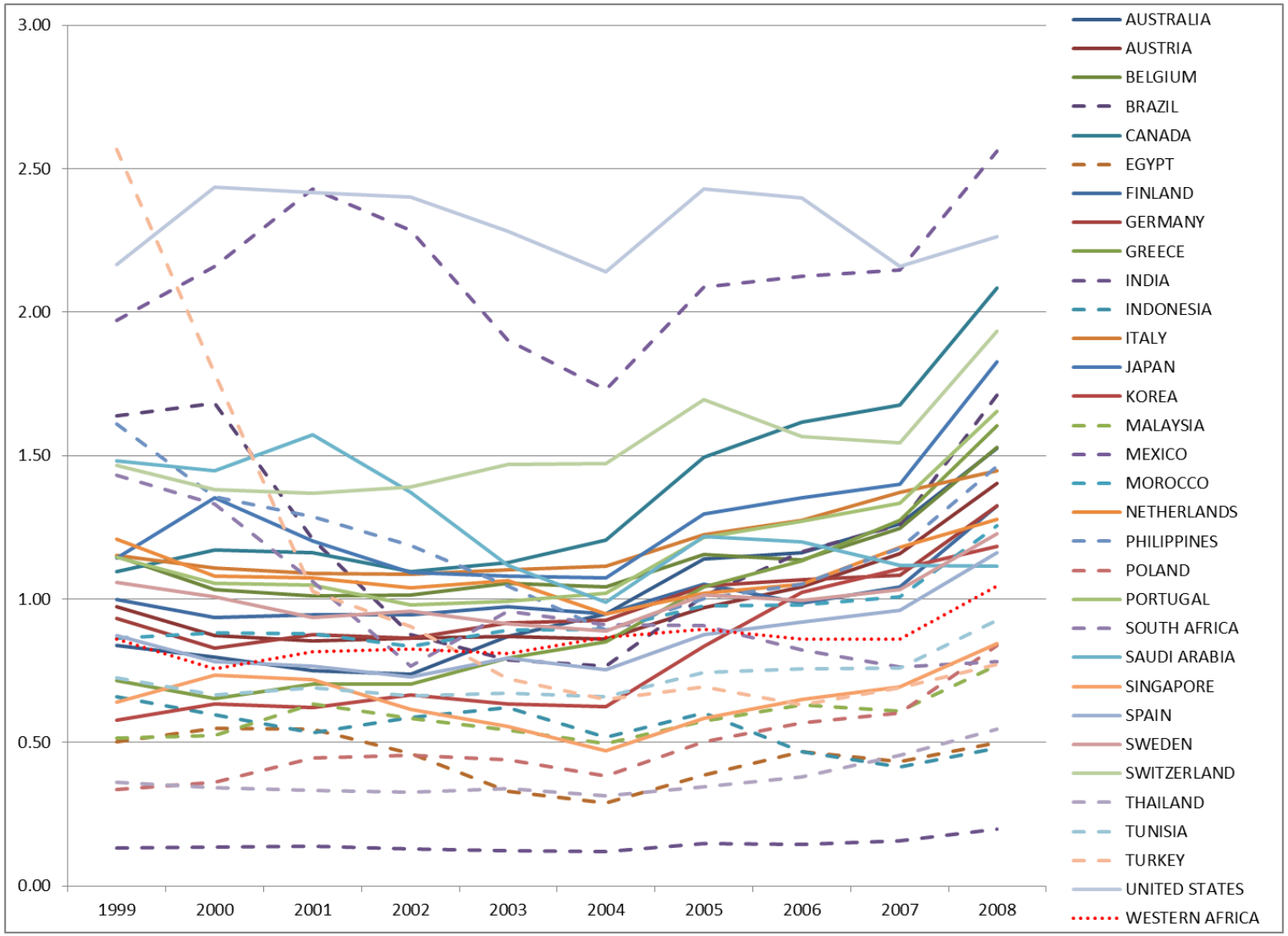
2. FM PRICES RELATIVE TO UNITED STATES PRICES BASED ON MULTILATERALLY-MATCHED SAMPLE, FISHER PRICE INDICES, PRICE PER STANDARD UNIT (US=1)



3. F_M^{UK}: Prices relative to United Kingdom prices based on multilaterally-matched sample, Fisher price indices, price per standard unit

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
AUSTRALIA	0.84	0.80	0.75	0.74	0.87	0.95	1.14	1.16	1.26	1.53
AUSTRIA	0.97	0.87	0.85	0.86	0.87	0.86	0.97	1.04	1.16	1.40
BELGIUM	1.15	1.03	1.01	1.01	1.06	1.04	1.16	1.14	1.25	1.53
BRAZIL	1.64	1.68	1.21	0.88	0.79	0.76	1.01	1.16	1.26	1.71
CANADA	1.10	1.17	1.16	1.10	1.13	1.20	1.49	1.62	1.68	2.08
EGYPT	0.50	0.55	0.55	0.46	0.33	0.29	0.39	0.47	0.43	0.50
FINLAND	1.00	0.94	0.95	0.94	0.97	0.95	1.05	0.99	1.04	1.32
GERMANY	0.93	0.83	0.87	0.86	0.92	0.93	1.05	1.07	1.08	1.32
GREECE	0.72	0.65	0.70	0.70	0.79	0.85	1.04	1.13	1.28	1.60
INDIA	0.13	0.13	0.14	0.13	0.12	0.12	0.15	0.14	0.16	0.20
INDONESIA	0.66	0.60	0.54	0.59	0.62	0.52	0.60	0.47	0.41	0.48
ITALY	1.15	1.11	1.09	1.08	1.10	1.11	1.22	1.27	1.37	1.45
JAPAN	1.14	1.35	1.20	1.09	1.08	1.07	1.30	1.35	1.40	1.83
KOREA	0.58	0.63	0.62	0.67	0.63	0.62	0.83	1.02	1.10	1.18
MALAYSIA	0.51	0.53	0.63	0.58	0.54	0.50	0.57	0.63	0.61	0.77
MEXICO	1.97	2.16	2.43	2.29	1.90	1.73	2.09	2.13	2.15	2.56
MOROCCO	0.86	0.88	0.88	0.84	0.89	0.89	0.98	0.98	1.01	1.26
NETHERLANDS	1.21	1.08	1.07	1.04	1.07	0.95	1.02	1.05	1.18	1.28
PHILIPPINES	1.61	1.35	1.29	1.19	1.05	0.89	1.00	1.05	1.18	1.46
POLAND	0.34	0.36	0.45	0.46	0.44	0.38	0.50	0.57	0.60	0.84
PORTUGAL	1.15	1.05	1.05	0.98	0.99	1.02	1.21	1.27	1.34	1.66
SOUTH AFRICA	1.43	1.33	1.06	0.77	0.96	0.91	0.91	0.82	0.76	0.78
SAUDI ARABIA	1.48	1.45	1.57	1.37	1.12	0.99	1.22	1.20	1.12	1.12
SINGAPORE	0.64	0.73	0.72	0.61	0.56	0.47	0.58	0.65	0.69	0.84
SPAIN	0.87	0.78	0.76	0.73	0.79	0.75	0.88	0.92	0.96	1.16
SWEDEN	1.06	1.01	0.93	0.96	0.91	0.89	1.01	0.99	1.03	1.23
SWITZERLAND	1.47	1.38	1.37	1.39	1.47	1.47	1.70	1.57	1.54	1.93
THAILAND	0.36	0.34	0.33	0.33	0.34	0.31	0.34	0.38	0.45	0.55
TUNISIA	0.73	0.66	0.69	0.66	0.67	0.66	0.74	0.76	0.76	0.93
TURKEY	2.57	1.79	1.03	0.90	0.72	0.65	0.69	0.63	0.69	0.77
UNITED STATES	2.17	2.43	2.42	2.40	2.28	2.14	2.43	2.40	2.16	2.26
WESTERN AFRICA	0.86	0.76	0.81	0.82	0.81	0.87	0.90	0.86	0.86	1.04

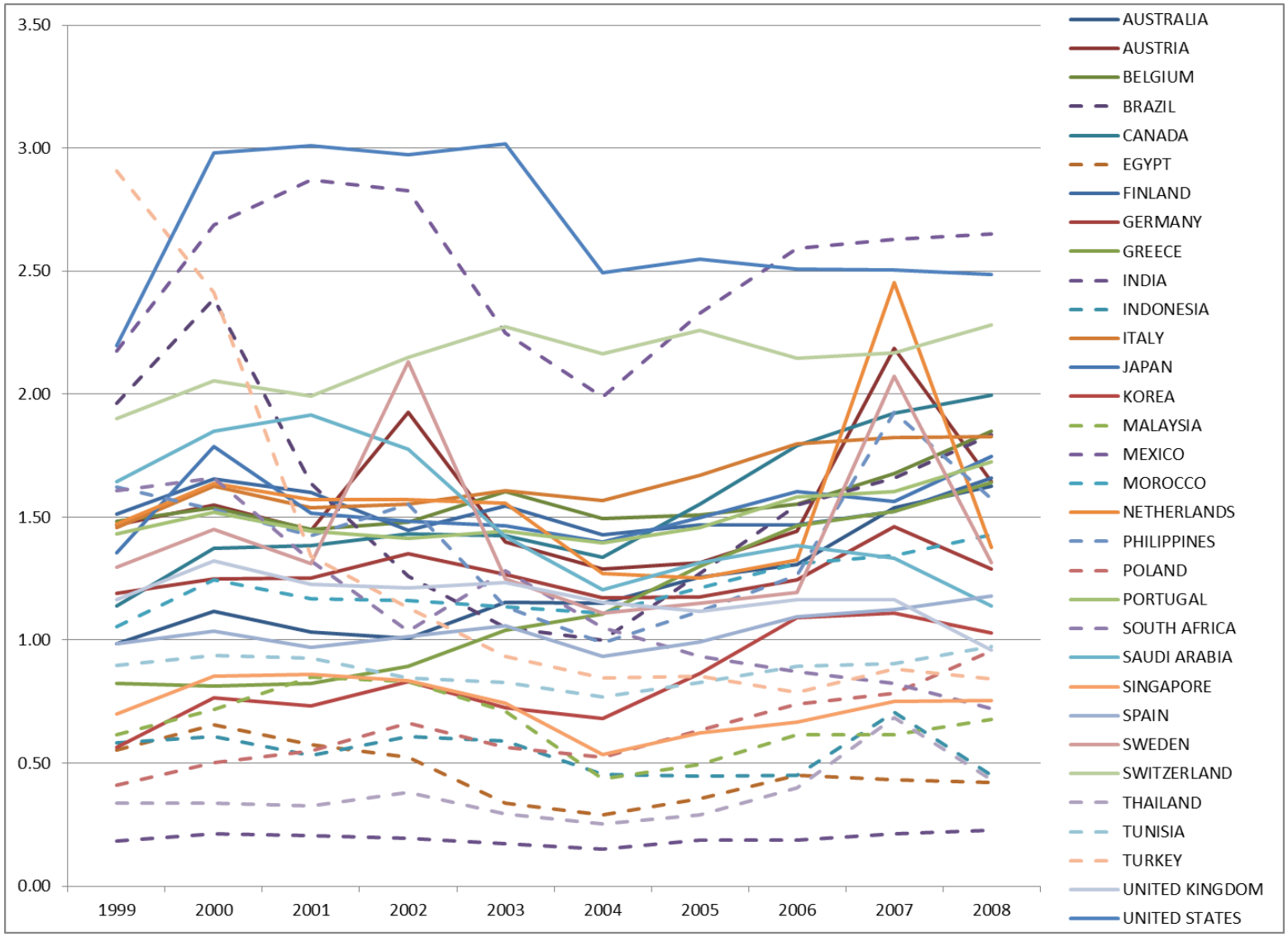
4. F_M^{UK}: PRICES RELATIVE TO UNITED KINGDOM PRICES BASED ON MULTILATERALLY-MATCHED SAMPLE, FISHER PRICE INDICES, PRICE PER STANDARD UNIT (UK=1)



5. F_M^{WA}: Prices relative to western Africa prices based on multilaterally-matched sample, Fisher price indices, price per standard unit

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
AUSTRALIA	0.98	1.12	1.03	1.01	1.15	1.15	1.26	1.31	1.54	1.62
AUSTRIA	1.47	1.55	1.45	1.93	1.40	1.29	1.31	1.44	2.19	1.64
BELGIUM	1.48	1.54	1.45	1.48	1.60	1.49	1.51	1.55	1.68	1.85
BRAZIL	1.96	2.39	1.64	1.26	1.05	1.00	1.27	1.55	1.66	1.83
CANADA	1.14	1.37	1.38	1.43	1.42	1.34	1.55	1.79	1.92	2.00
EGYPT	0.55	0.65	0.57	0.53	0.34	0.29	0.36	0.45	0.43	0.42
FINLAND	1.51	1.65	1.60	1.45	1.54	1.43	1.47	1.47	1.52	1.66
GERMANY	1.19	1.25	1.25	1.35	1.27	1.17	1.18	1.25	1.46	1.29
GREECE	0.82	0.81	0.82	0.89	1.04	1.11	1.30	1.46	1.52	1.64
INDIA	0.18	0.21	0.21	0.20	0.17	0.15	0.19	0.19	0.21	0.23
INDONESIA	0.58	0.61	0.53	0.61	0.59	0.45	0.45	0.45	0.71	0.45
ITALY	1.46	1.63	1.54	1.55	1.61	1.57	1.67	1.80	1.82	1.83
JAPAN	1.36	1.79	1.52	1.48	1.46	1.40	1.50	1.60	1.56	1.75
KOREA	0.56	0.77	0.73	0.83	0.72	0.68	0.87	1.09	1.11	1.03
MALAYSIA	0.62	0.72	0.85	0.83	0.71	0.44	0.50	0.61	0.61	0.68
MEXICO	2.18	2.69	2.87	2.83	2.25	1.99	2.33	2.59	2.63	2.65
MOROCCO	1.05	1.25	1.17	1.16	1.14	1.11	1.21	1.31	1.35	1.43
NETHERLANDS	1.47	1.64	1.57	1.57	1.56	1.27	1.25	1.33	2.45	1.38
PHILIPPINES	1.62	1.53	1.43	1.55	1.14	0.99	1.12	1.27	1.93	1.57
POLAND	0.41	0.50	0.55	0.66	0.56	0.52	0.63	0.74	0.79	0.96
PORTUGAL	1.43	1.52	1.44	1.41	1.44	1.40	1.46	1.58	1.60	1.73
SOUTH AFRICA	1.61	1.66	1.32	1.04	1.28	1.05	0.93	0.87	0.82	0.72
SAUDI ARABIA	1.64	1.85	1.92	1.78	1.42	1.21	1.32	1.38	1.33	1.14
SINGAPORE	0.70	0.85	0.86	0.83	0.74	0.54	0.62	0.67	0.75	0.75
SPAIN	0.99	1.03	0.97	1.02	1.06	0.93	0.99	1.10	1.12	1.18
SWEDEN	1.30	1.45	1.31	2.13	1.25	1.11	1.15	1.19	2.07	1.32
SWITZERLAND	1.90	2.05	1.99	2.15	2.27	2.16	2.26	2.15	2.17	2.28
THAILAND	0.34	0.34	0.33	0.38	0.29	0.25	0.29	0.40	0.69	0.43
TUNISIA	0.90	0.94	0.93	0.85	0.83	0.77	0.83	0.89	0.91	0.97
TURKEY	2.91	2.41	1.34	1.13	0.93	0.85	0.85	0.79	0.88	0.84
UNITED KINGDOM	1.16	1.32	1.23	1.21	1.23	1.15	1.12	1.16	1.16	0.96
UNITED STATES	2.20	2.98	3.01	2.97	3.02	2.49	2.55	2.51	2.50	2.49

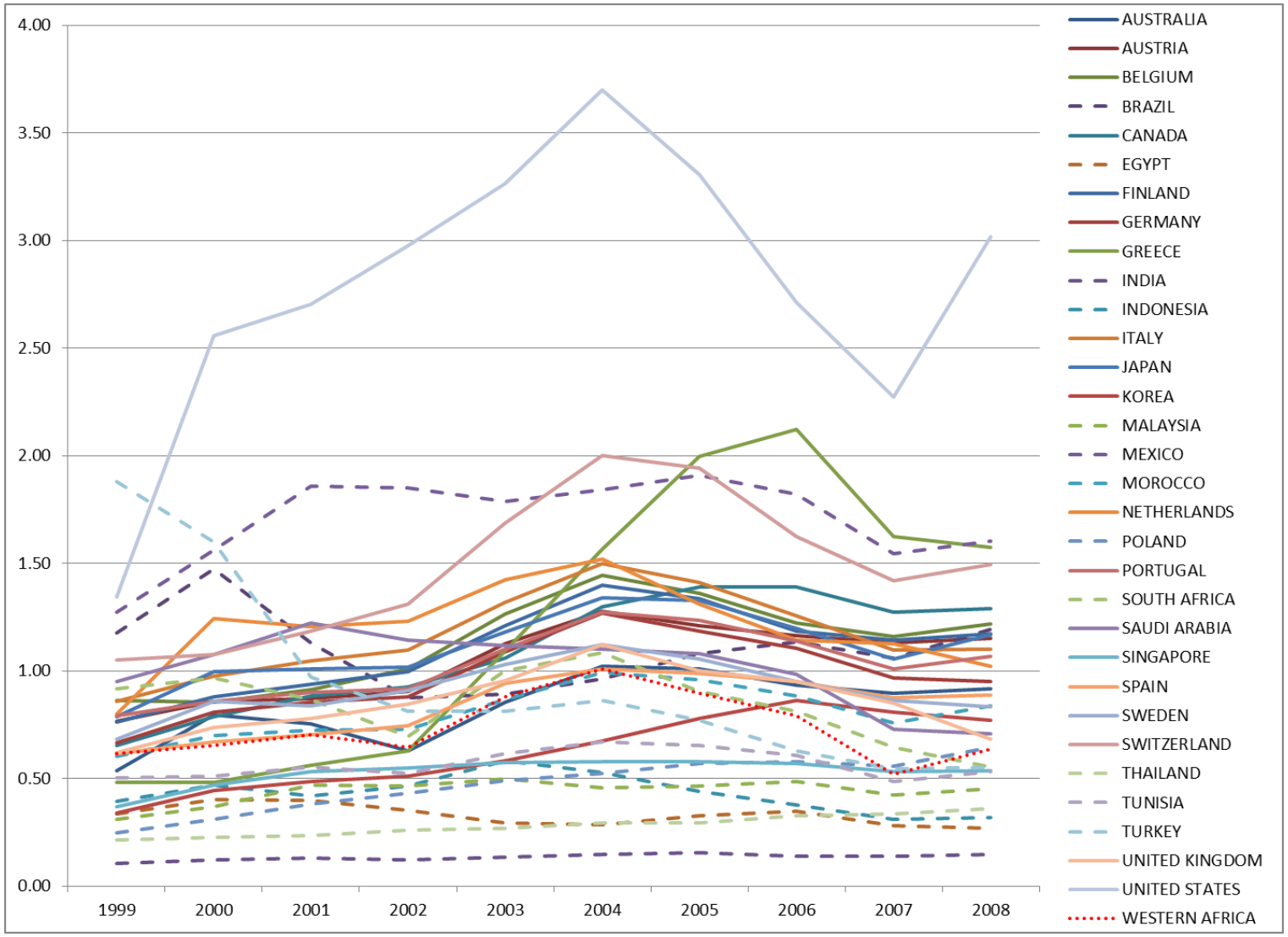
6. F_M^{WA}: Prices relative to western Africa prices based on multilaterally-matched sample, Fisher price indices, price per standard unit (western Africa =1)



7. F_M^{PH}: Prices relative to the Philippines prices based on multilaterally-matched sample, Fisher price indices, price per standard unit

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
AUSTRALIA	0.53	0.79	0.75	0.63	0.85	1.02	1.01	0.94	0.89	0.92
AUSTRIA	0.77	0.86	0.87	0.90	1.13	1.28	1.21	1.16	1.13	1.15
BELGIUM	0.86	0.85	0.91	1.01	1.26	1.44	1.36	1.22	1.16	1.22
BRAZIL	1.18	1.47	1.13	0.87	0.89	0.96	1.08	1.13	1.06	1.19
CANADA	0.65	0.79	0.88	0.93	1.06	1.30	1.39	1.39	1.27	1.29
EGYPT	0.34	0.40	0.40	0.35	0.29	0.29	0.33	0.35	0.28	0.27
FINLAND	0.76	0.88	0.94	0.99	1.21	1.40	1.33	1.18	1.14	1.17
GERMANY	0.67	0.81	0.85	0.88	1.09	1.27	1.19	1.10	0.97	0.95
GREECE	0.48	0.48	0.56	0.63	1.09	1.57	2.00	2.12	1.62	1.57
INDIA	0.11	0.12	0.13	0.12	0.13	0.14	0.16	0.14	0.14	0.15
INDONESIA	0.39	0.47	0.42	0.47	0.58	0.53	0.44	0.38	0.31	0.32
ITALY	0.86	0.98	1.05	1.10	1.32	1.50	1.41	1.26	1.09	1.10
JAPAN	0.79	1.00	1.01	1.02	1.18	1.34	1.33	1.20	1.06	1.17
KOREA	0.34	0.44	0.48	0.51	0.58	0.68	0.78	0.86	0.81	0.77
MALAYSIA	0.31	0.37	0.47	0.47	0.50	0.46	0.46	0.48	0.42	0.45
MEXICO	1.27	1.56	1.86	1.85	1.79	1.84	1.91	1.82	1.54	1.60
MOROCCO	0.60	0.70	0.72	0.73	0.87	0.99	0.96	0.88	0.76	0.84
NETHERLANDS	0.80	1.24	1.21	1.23	1.42	1.52	1.31	1.14	1.13	1.02
POLAND	0.25	0.31	0.38	0.43	0.49	0.52	0.57	0.58	0.56	0.65
PORTUGAL	0.79	0.86	0.90	0.92	1.10	1.27	1.24	1.14	1.01	1.07
SOUTH AFRICA	0.92	0.97	0.86	0.70	1.00	1.08	0.91	0.81	0.64	0.55
SAUDI ARABIA	0.95	1.07	1.22	1.14	1.12	1.10	1.08	0.98	0.73	0.71
SINGAPORE	0.37	0.47	0.53	0.55	0.57	0.58	0.58	0.57	0.53	0.54
SPAIN	0.61	0.67	0.70	0.75	0.94	1.01	0.99	0.95	0.87	0.89
SWEDEN	0.68	0.86	0.84	0.91	1.03	1.12	1.05	0.95	0.86	0.83
SWITZERLAND	1.05	1.08	1.18	1.31	1.68	2.00	1.94	1.62	1.42	1.49
THAILAND	0.21	0.23	0.24	0.26	0.27	0.29	0.29	0.33	0.34	0.36
TUNISIA	0.50	0.51	0.55	0.52	0.61	0.67	0.65	0.61	0.49	0.53
TURKEY	1.88	1.60	0.97	0.81	0.81	0.86	0.77	0.63	0.54	0.55
UNITED KINGDOM	0.62	0.74	0.78	0.84	0.96	1.12	1.00	0.95	0.85	0.68
UNITED STATES	1.34	2.56	2.71	2.97	3.26	3.70	3.31	2.71	2.27	3.02
WESTERN AFRICA	0.62	0.65	0.70	0.64	0.88	1.01	0.89	0.79	0.52	0.64

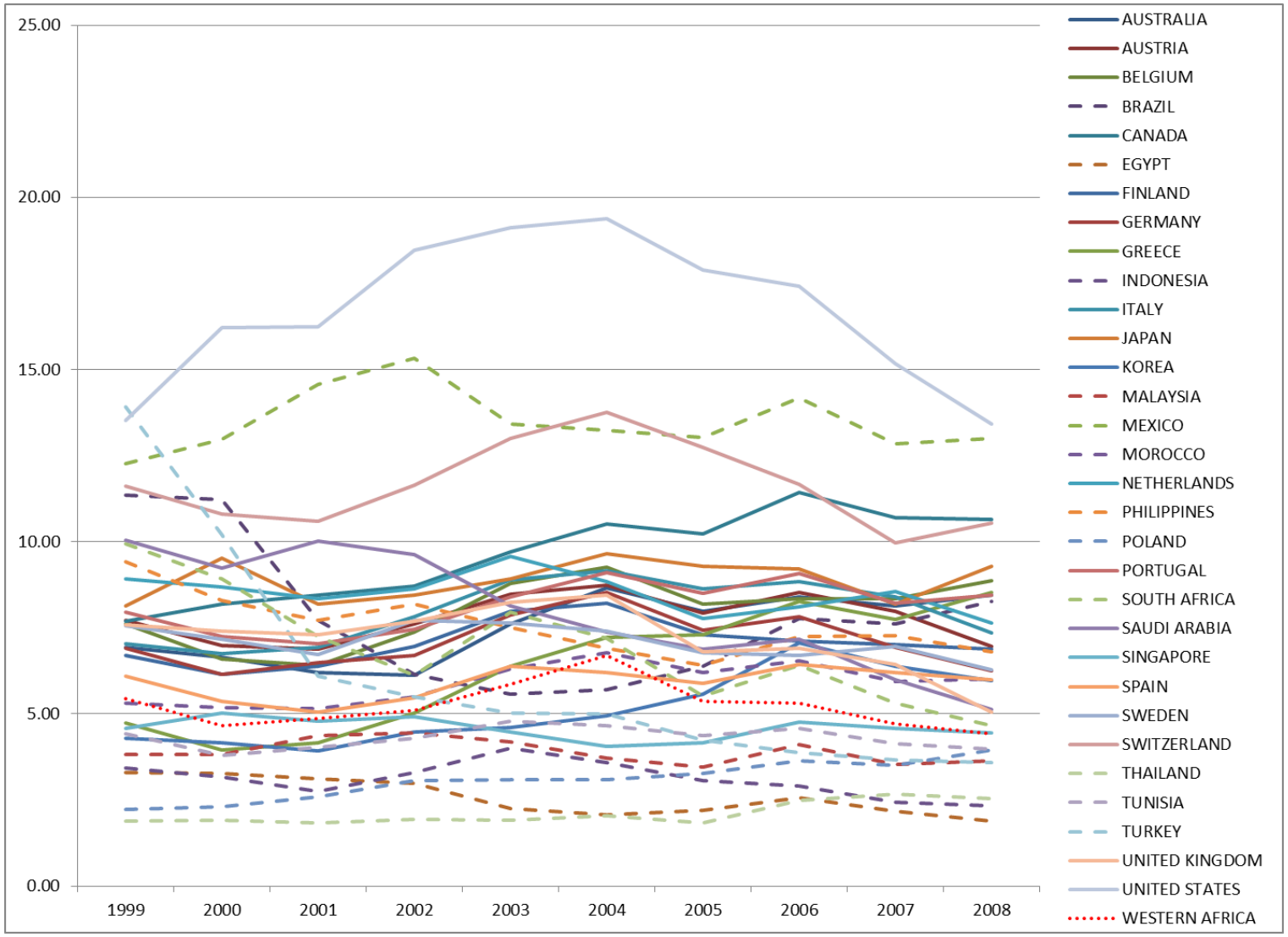
8. F_M^{PH}: Prices relative to the Philippines prices based on multilaterally-matched sample, Fisher price indices, price per standard unit (Philippines = 1)



9. F_M^{IND}: Prices relative to the India prices based on multilaterally-matched sample, Fisher price indices, price per standard unit

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
AUSTRALIA	6.94	6.65	6.20	6.11	7.61	8.67	7.98	8.39	8.14	8.46
AUSTRIA	7.71	6.98	6.89	7.62	8.48	8.73	7.92	8.52	7.98	6.96
BELGIUM	7.61	6.59	6.40	7.37	8.80	9.25	8.19	8.34	8.34	8.86
BRAZIL	11.36	11.22	7.72	6.15	5.56	5.71	6.39	7.76	7.60	8.26
CANADA	7.70	8.18	8.45	8.71	9.69	10.52	10.23	11.43	10.69	10.65
EGYPT	3.29	3.28	3.10	2.98	2.24	2.06	2.20	2.58	2.17	1.89
FINLAND	6.68	6.16	6.37	6.95	7.98	8.20	7.31	7.11	7.02	6.88
GERMANY	6.90	6.16	6.49	6.70	7.88	8.53	7.43	7.81	6.92	6.25
GREECE	4.72	3.96	4.16	5.03	6.39	7.21	7.31	8.27	7.73	8.53
INDONESIA	3.42	3.17	2.74	3.30	4.01	3.58	3.07	2.91	2.43	2.33
ITALY	7.05	6.74	6.93	7.83	8.88	9.15	8.62	8.85	8.40	7.34
JAPAN	8.14	9.51	8.20	8.45	8.91	9.65	9.29	9.22	8.19	9.28
KOREA	4.30	4.16	3.92	4.47	4.59	4.94	5.56	7.05	6.38	5.96
MALAYSIA	3.82	3.81	4.36	4.46	4.19	3.71	3.47	4.12	3.52	3.63
MEXICO	12.26	12.96	14.57	15.33	13.42	13.24	13.03	14.18	12.84	13.01
MOROCCO	5.31	5.18	5.14	5.50	6.32	6.79	6.19	6.55	5.93	6.01
NETHERLANDS	8.93	8.68	8.35	8.62	9.57	8.84	7.77	8.12	8.56	7.64
PHILIPPINES	9.42	8.29	7.72	8.20	7.50	6.90	6.42	7.25	7.26	6.80
POLAND	2.23	2.30	2.60	3.06	3.10	3.09	3.26	3.64	3.50	3.95
PORTUGAL	7.96	7.25	7.04	7.45	8.39	9.11	8.49	9.07	8.20	8.45
SOUTH AFRICA	9.93	8.92	7.24	6.13	7.96	7.20	5.52	6.40	5.32	4.66
SAUDI ARABIA	10.05	9.24	10.02	9.64	8.15	7.37	6.89	7.16	6.00	5.13
SINGAPORE	4.58	5.02	4.79	4.92	4.48	4.07	4.16	4.76	4.59	4.44
SPAIN	6.09	5.35	5.04	5.47	6.39	6.19	5.88	6.43	6.19	5.98
SWEDEN	7.57	7.18	6.72	7.72	7.64	7.39	6.76	6.69	6.95	6.28
SWITZERLAND	11.60	10.81	10.58	11.63	13.01	13.75	12.75	11.66	9.95	10.55
THAILAND	1.89	1.91	1.84	1.95	1.92	2.03	1.83	2.48	2.67	2.54
TUNISIA	4.41	3.79	4.02	4.29	4.79	4.65	4.38	4.59	4.14	3.99
TURKEY	13.93	10.20	6.08	5.48	5.03	4.99	4.23	3.88	3.67	3.58
UNITED KINGDOM	7.57	7.41	7.30	7.68	8.24	8.46	6.81	6.91	6.43	5.04
UNITED STATES	13.53	16.22	16.25	18.47	19.11	19.38	17.89	17.41	15.16	13.41
WESTERN AFRICA	5.45	4.67	4.87	5.11	5.86	6.69	5.36	5.30	4.71	4.41

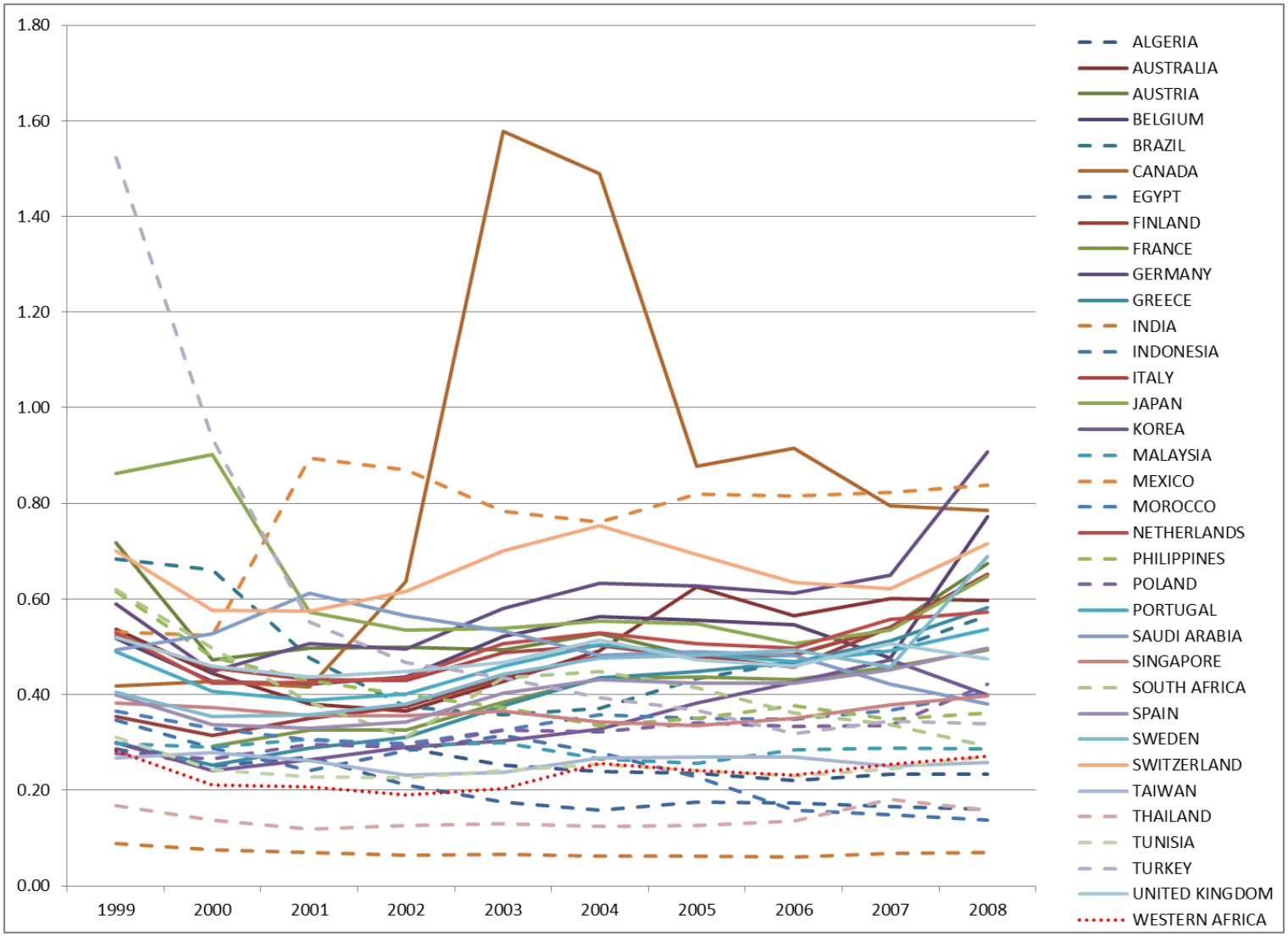
10. F_M^{IND}: Prices relative to the India prices based on multilaterally-matched sample, Fisher price indices, price per standard unit (India=1)



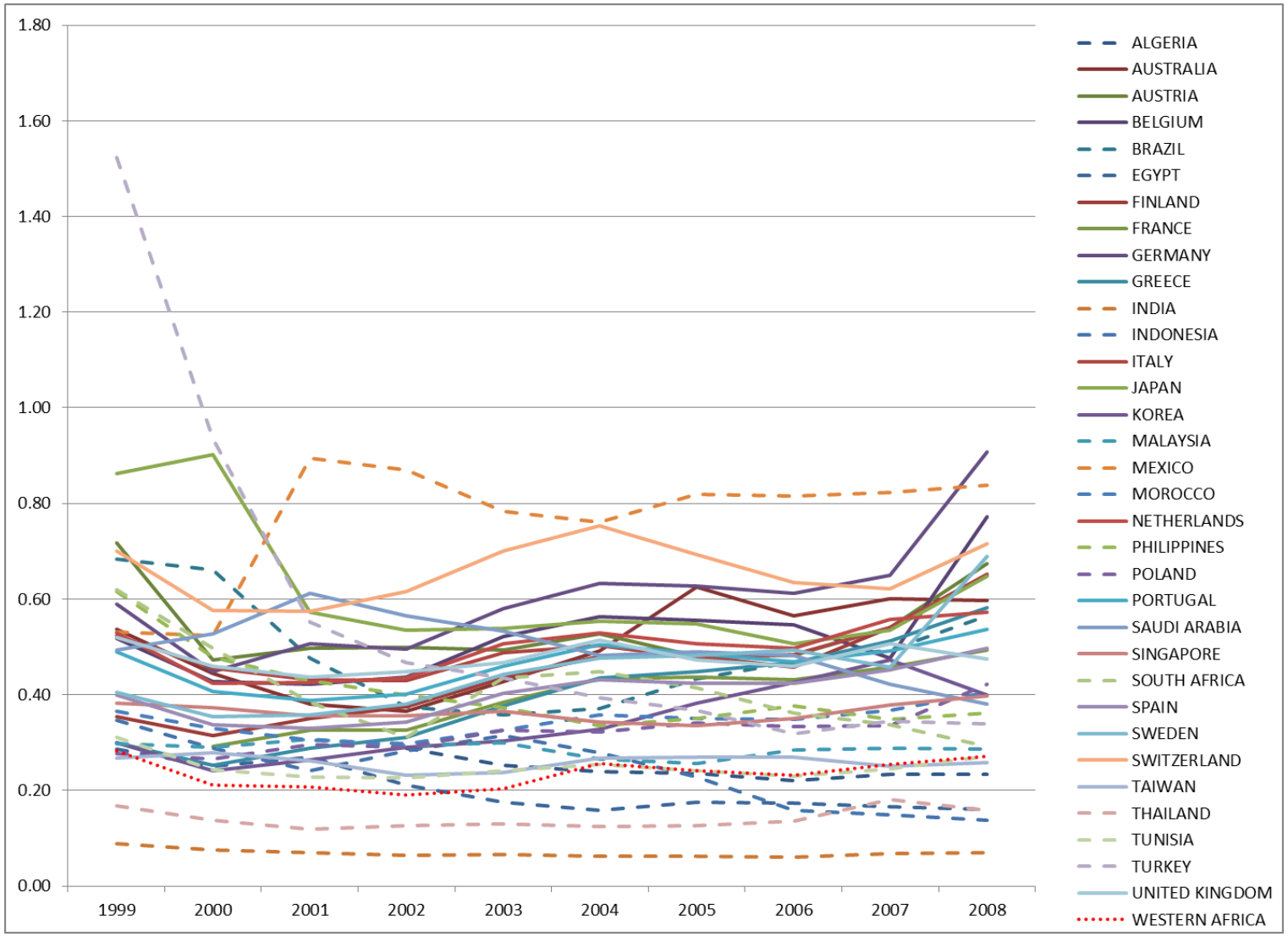
11. F_B Prices relative to United States prices based on bilaterally-matched sample, Fisher price indices, price per standard unit

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
ALGERIA				0.29	0.25	0.24	0.24	0.22	0.23	0.23
AUSTRALIA	0.54	0.44	0.38	0.36	0.43	0.49	0.63	0.56	0.60	0.60
AUSTRIA	0.72	0.47	0.50	0.50	0.49	0.53	0.48	0.48	0.54	0.67
BELGIUM	0.52	0.43	0.42	0.44	0.52	0.56	0.55	0.55	0.48	0.77
BRAZIL	0.68	0.66	0.48	0.37	0.36	0.37	0.43	0.47	0.49	0.57
CANADA	0.42	0.43	0.42	0.64	1.58	1.49	0.88	0.92	0.79	0.79
EGYPT	0.29	0.25	0.27	0.21	0.18	0.16	0.18	0.17	0.17	0.16
FINLAND	0.35	0.32	0.35	0.37	0.44	0.48	0.48	0.46	0.54	0.65
FRANCE		0.29	0.33	0.33	0.38	0.43	0.44	0.43	0.46	0.49
GERMANY	0.59	0.45	0.51	0.49	0.58	0.63	0.63	0.61	0.65	0.91
GREECE	0.30	0.25	0.29	0.31	0.38	0.44	0.45	0.47	0.51	0.58
INDIA	0.09	0.08	0.07	0.06	0.07	0.06	0.06	0.06	0.07	0.07
INDONESIA	0.35	0.29	0.24	0.28	0.31	0.28	0.23	0.16	0.15	0.14
ITALY	0.52	0.46	0.43	0.43	0.49	0.50	0.48	0.48	0.54	0.65
JAPAN	0.86	0.90	0.57	0.54	0.54	0.55	0.55	0.51	0.53	0.65
KOREA	0.30	0.24	0.26	0.29	0.30	0.33	0.38	0.43	0.47	0.40
MALAYSIA	0.30	0.29	0.31	0.29	0.30	0.26	0.26	0.28	0.29	0.29
MEXICO	0.53	0.52	0.89	0.87	0.78	0.76	0.82	0.82	0.82	0.84
MOROCCO	0.37	0.33	0.30	0.30	0.33	0.36	0.35	0.35	0.37	0.40
NETHERLANDS	0.53	0.42	0.43	0.44	0.51	0.53	0.51	0.50	0.56	0.57
PHILIPPINES	0.61	0.48	0.43	0.40	0.37	0.34	0.35	0.38	0.35	0.36
POLAND	0.28	0.27	0.30	0.29	0.33	0.32	0.34	0.33	0.33	0.42
PORTUGAL	0.49	0.41	0.39	0.40	0.46	0.50	0.49	0.47	0.49	0.54
SAUDI ARABIA	0.49	0.53	0.61	0.56	0.53	0.48	0.49	0.48	0.42	0.38
SINGAPORE	0.38	0.37	0.36	0.36	0.36	0.34	0.34	0.35	0.38	0.40
SOUTH AFRICA	0.62	0.50	0.38	0.31	0.43	0.45	0.41	0.36	0.34	0.29
SPAIN	0.40	0.34	0.33	0.34	0.40	0.43	0.42	0.42	0.45	0.50
SWEDEN	0.40	0.35	0.36	0.38	0.44	0.48	0.48	0.49	0.46	0.69
SWITZERLAND	0.70	0.58	0.57	0.62	0.70	0.75	0.69	0.63	0.62	0.71
TAIWAN	0.27	0.28	0.26	0.23	0.24	0.27	0.27	0.27	0.25	0.26
THAILAND	0.17	0.14	0.12	0.13	0.13	0.12	0.13	0.14	0.18	0.16
TUNISIA	0.31	0.24	0.23	0.23	0.24	0.25	0.24	0.23	0.24	0.27
TURKEY	1.52	0.94	0.55	0.47	0.43	0.39	0.37	0.32	0.34	0.34
UNITED KINGDOM	0.52	0.46	0.44	0.45	0.47	0.51	0.47	0.46	0.51	0.47
WESTERN AFRICA	0.28	0.21	0.21	0.19	0.20	0.26	0.24	0.23	0.25	0.27

12. F_B Prices relative to United States prices based on bilaterally-matched sample, Fisher price indices, price per standard unit (US=1)



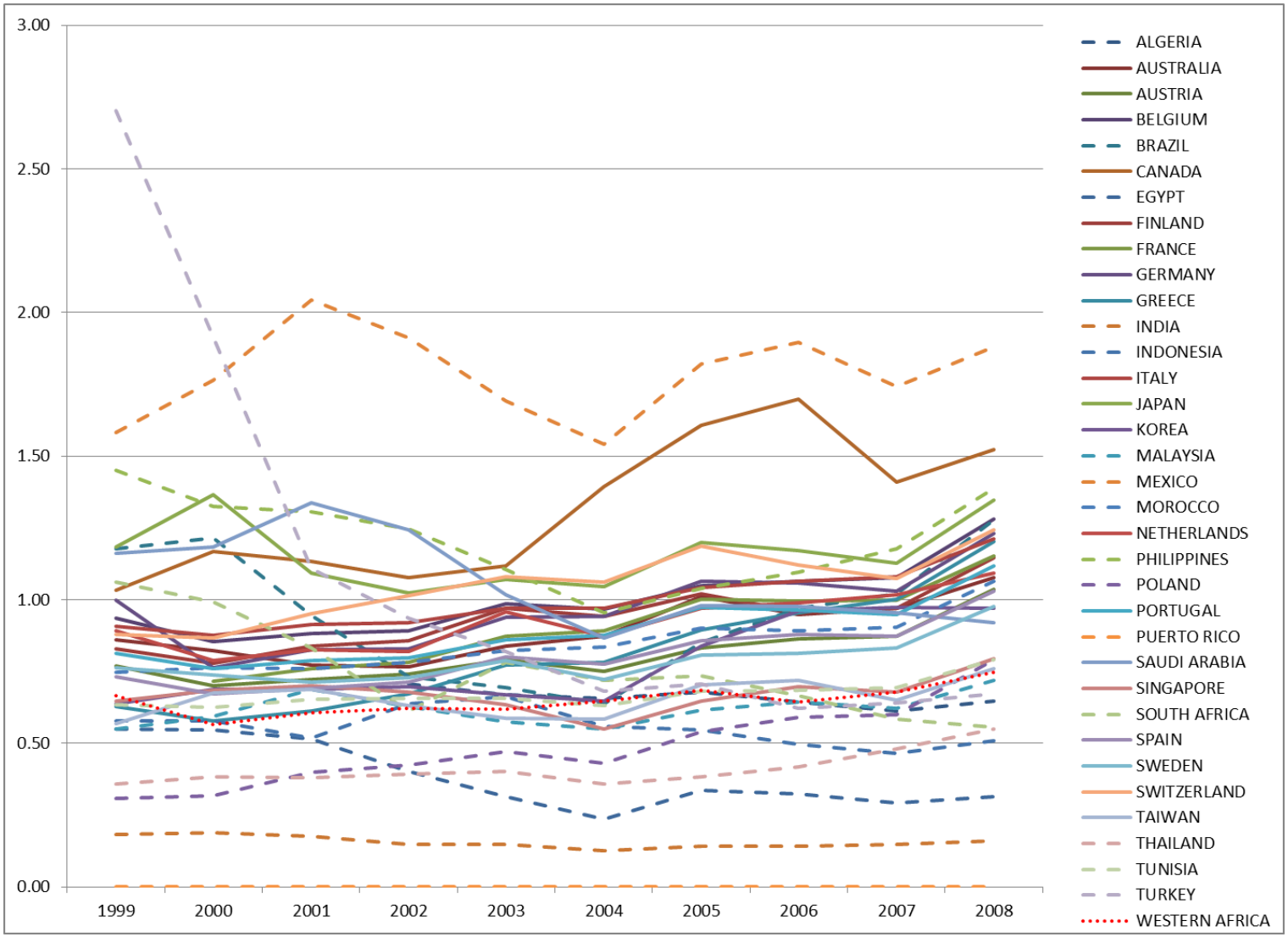
13. F_B Prices relative to United States prices based on bilaterally-matched sample, Fisher price indices, price per standard unit (US=1, excludes Canada)



14. F_B^{UK}: Prices relative to United Kingdom prices based on bilaterally-matched sample, Fisher price indices, price per standard unit

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
ALGERIA				0.71	0.67	0.66	0.68	0.64	0.61	0.65
AUSTRALIA	0.86	0.82	0.77	0.77	0.84	0.87	1.01	0.95	0.97	1.08
AUSTRIA	0.77	0.70	0.72	0.74	0.79	0.75	0.83	0.86	0.87	1.03
BELGIUM	0.94	0.85	0.88	0.89	0.98	0.97	1.05	1.06	1.08	1.28
BRAZIL	1.18	1.22	0.94	0.73	0.69	0.64	0.85	0.97	1.02	1.28
CANADA	1.03	1.17	1.13	1.08	1.12	1.40	1.61	1.70	1.41	1.52
EGYPT	0.55	0.55	0.51	0.40	0.32	0.24	0.33	0.32	0.29	0.31
FINLAND	0.83	0.78	0.84	0.86	0.97	0.94	1.02	0.96	0.97	1.15
FRANCE		0.72	0.76	0.78	0.87	0.89	1.00	0.99	1.00	1.15
GERMANY	1.00	0.76	0.83	0.83	0.94	0.94	1.06	1.06	1.03	1.23
GREECE	0.63	0.58	0.61	0.67	0.77	0.78	0.89	0.95	1.00	1.20
INDIA	0.18	0.19	0.18	0.15	0.15	0.12	0.14	0.14	0.15	0.16
INDONESIA	0.58	0.58	0.52	0.64	0.66	0.56	0.55	0.50	0.46	0.51
ITALY	0.91	0.87	0.91	0.92	0.97	0.97	1.04	1.07	1.08	1.21
JAPAN	1.18	1.36	1.09	1.02	1.07	1.05	1.20	1.17	1.13	1.35
KOREA	0.64	0.69	0.69	0.70	0.67	0.65	0.84	0.96	0.97	0.97
MALAYSIA	0.55	0.59	0.69	0.63	0.57	0.55	0.61	0.64	0.62	0.72
MEXICO	1.58	1.76	2.04	1.91	1.69	1.54	1.82	1.89	1.74	1.88
MOROCCO	0.75	0.76	0.76	0.78	0.82	0.83	0.90	0.89	0.90	1.06
NETHERLANDS	0.89	0.79	0.82	0.82	0.96	0.87	0.97	0.99	1.02	1.09
PHILIPPINES	1.45	1.32	1.30	1.24	1.10	0.95	1.04	1.10	1.18	1.39
POLAND	0.31	0.32	0.40	0.42	0.47	0.43	0.54	0.59	0.60	0.79
PORTUGAL	0.81	0.76	0.79	0.80	0.86	0.88	0.97	0.96	0.95	1.12
PUERTO RICO	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
SAUDI ARABIA	1.16	1.18	1.34	1.24	1.02	0.87	0.98	0.97	0.96	0.92
SINGAPORE	0.65	0.68	0.70	0.68	0.64	0.55	0.65	0.70	0.68	0.79
SOUTH AFRICA	1.06	0.99	0.83	0.61	0.78	0.72	0.74	0.67	0.58	0.55
SPAIN	0.73	0.67	0.69	0.71	0.80	0.77	0.86	0.88	0.87	1.03
SWEDEN	0.76	0.74	0.71	0.73	0.79	0.72	0.81	0.81	0.83	0.97
SWITZERLAND	0.88	0.87	0.95	1.01	1.08	1.06	1.19	1.12	1.07	1.24
TAIWAN	0.57	0.67	0.69	0.63	0.59	0.58	0.70	0.72	0.65	0.76
THAILAND	0.36	0.38	0.38	0.39	0.40	0.36	0.38	0.42	0.48	0.55
TUNISIA	0.63	0.62	0.65	0.66	0.66	0.63	0.68	0.68	0.69	0.79
TURKEY	2.70	1.92	1.11	0.93	0.82	0.68	0.71	0.62	0.64	0.67
WESTERN AFRICA	0.66	0.57	0.61	0.62	0.62	0.65	0.69	0.64	0.68	0.75

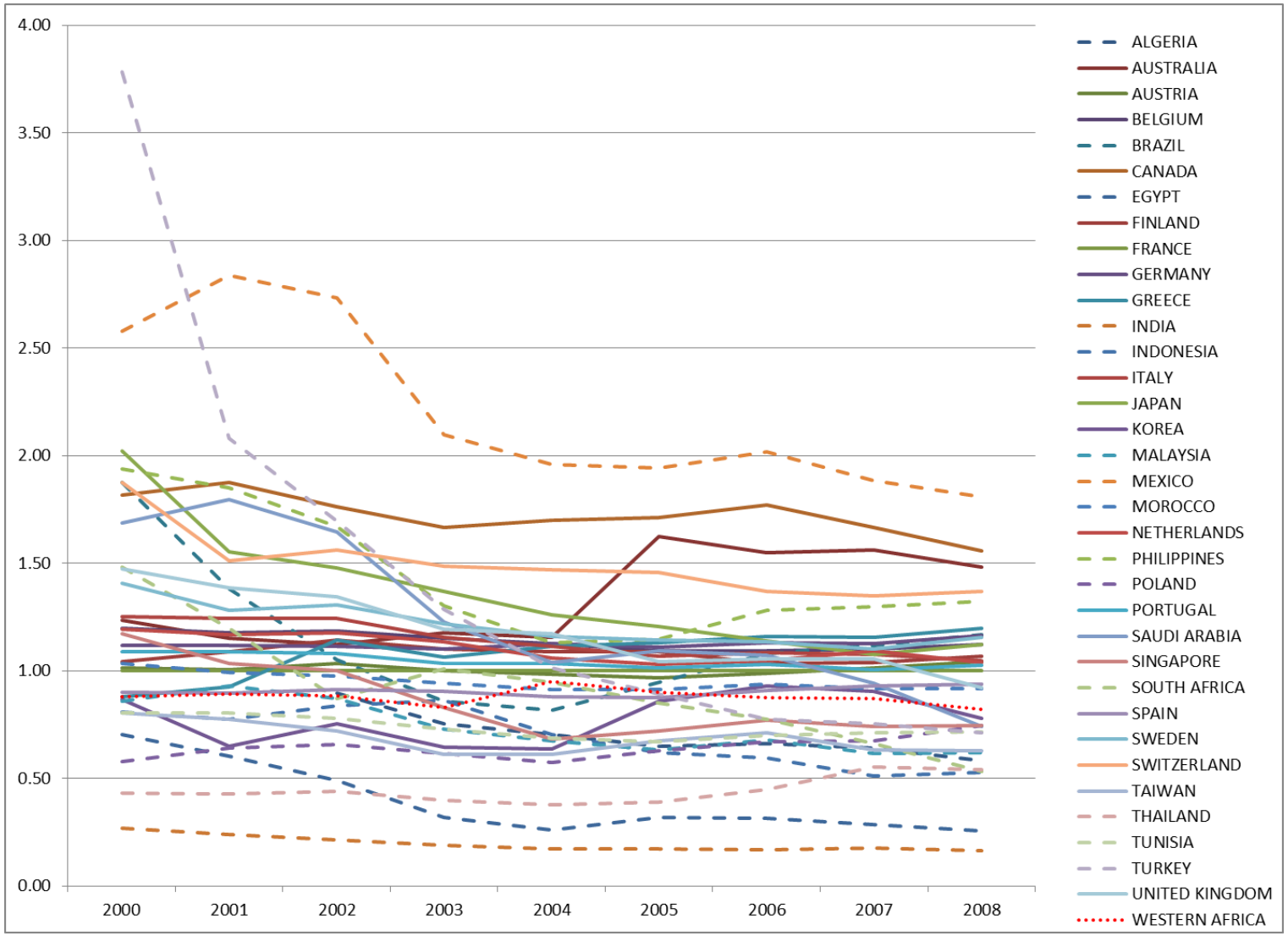
15. F_B^{UK}: Prices relative to United Kingdom prices based on bilaterally-matched sample, Fisher price indices, price per standard unit (UK=1)



16. F_B^{FR}: Prices relative to France prices based on bilaterally-matched sample, Fisher price indices, price per standard unit

	2000	2001	2002	2003	2004	2005	2006	2007	2008
ALGERIA			0.90	0.75	0.70	0.65	0.66	0.64	0.58
AUSTRALIA	1.24	1.15	1.12	1.18	1.16	1.62	1.55	1.56	1.48
AUSTRIA	1.01	1.01	1.03	1.00	0.99	0.96	0.99	1.01	1.04
BELGIUM	1.20	1.18	1.19	1.15	1.13	1.09	1.09	1.10	1.12
BRAZIL	1.87	1.38	1.05	0.86	0.82	0.95	1.08	1.12	1.17
CANADA	1.82	1.88	1.76	1.67	1.70	1.71	1.77	1.67	1.56
EGYPT	0.70	0.60	0.49	0.32	0.26	0.32	0.32	0.28	0.26
FINLAND	1.04	1.09	1.14	1.10	1.09	1.09	1.04	1.04	1.07
FRANCE	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
GERMANY	1.12	1.12	1.11	1.10	1.12	1.11	1.13	1.13	1.16
GREECE	0.88	0.93	1.14	1.06	1.11	1.13	1.16	1.16	1.20
INDIA	0.27	0.24	0.21	0.19	0.17	0.17	0.17	0.17	0.16
INDONESIA	0.81	0.77	0.84	0.86	0.70	0.62	0.60	0.51	0.53
ITALY	1.25	1.24	1.24	1.16	1.11	1.07	1.08	1.07	1.04
JAPAN	2.02	1.55	1.48	1.37	1.26	1.20	1.14	1.07	1.12
KOREA	0.87	0.65	0.75	0.64	0.63	0.86	0.93	0.91	0.78
MALAYSIA	0.86	0.93	0.87	0.73	0.67	0.63	0.68	0.62	0.62
MEXICO	2.58	2.84	2.73	2.10	1.96	1.94	2.02	1.88	1.81
MOROCCO	1.03	0.99	0.98	0.94	0.91	0.91	0.94	0.92	0.92
NETHERLANDS	1.19	1.17	1.18	1.14	1.06	1.03	1.05	1.09	1.04
PHILIPPINES	1.94	1.85	1.67	1.30	1.13	1.15	1.28	1.30	1.32
POLAND	0.58	0.64	0.66	0.61	0.58	0.63	0.67	0.68	0.74
PORTUGAL	1.09	1.09	1.08	1.03	1.03	1.01	1.03	1.01	1.03
PUERTO RICO	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
SAUDI ARABIA	1.68	1.80	1.64	1.23	1.04	1.09	1.07	0.94	0.74
SINGAPORE	1.17	1.03	1.00	0.83	0.68	0.72	0.77	0.74	0.74
SOUTH AFRICA	1.48	1.20	0.87	1.01	0.94	0.85	0.77	0.66	0.53
SPAIN	0.90	0.90	0.91	0.90	0.88	0.87	0.91	0.93	0.94
SWEDEN	1.41	1.28	1.31	1.22	1.16	1.14	1.14	1.10	1.15
SWITZERLAND	1.87	1.51	1.56	1.48	1.47	1.46	1.37	1.35	1.37
TAIWAN	0.81	0.78	0.72	0.61	0.61	0.67	0.71	0.63	0.63
THAILAND	0.43	0.43	0.44	0.40	0.38	0.39	0.45	0.55	0.54
TUNISIA	0.80	0.80	0.78	0.73	0.69	0.67	0.70	0.71	0.72
TURKEY	3.78	2.08	1.69	1.29	1.01	0.89	0.78	0.76	0.71
UNITED KINGDOM	1.47	1.38	1.34	1.19	1.17	1.04	1.05	1.05	0.92
WESTERN AFRICA	0.88	0.89	0.88	0.83	0.95	0.90	0.87	0.87	0.82

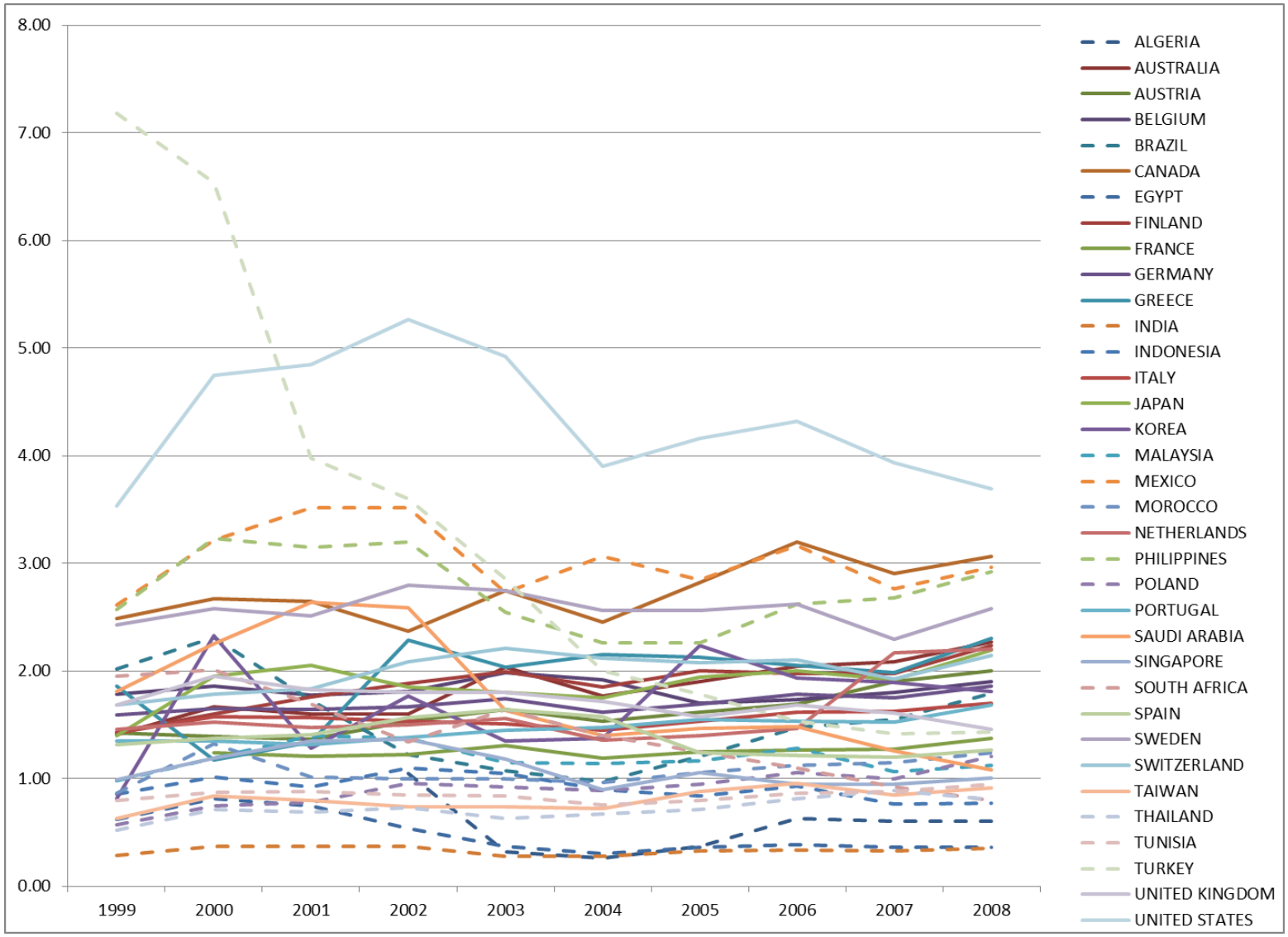
17. F_B^{FR}: Prices relative to France prices based on bilaterally-matched sample, Fisher price indices, price per standard unit (France=1)



18. F_B^{WA}: Prices relative to western Africa based on bilaterally-matched sample, Fisher price indices, price per standard unit

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
ALGERIA				1.04	0.32	0.26	0.37	0.63	0.60	0.60
AUSTRALIA	1.41	1.67	1.60	1.60	2.03	1.77	1.90	2.04	2.08	2.27
AUSTRIA	1.42	1.39	1.36	1.53	1.64	1.53	1.62	1.69	1.90	2.00
BELGIUM	1.78	1.86	1.78	1.81	1.98	1.91	1.70	1.74	1.80	1.90
BRAZIL	2.02	2.31	1.73	1.22	1.07	0.97	1.21	1.47	1.55	1.79
CANADA	2.49	2.67	2.64	2.37	2.75	2.45	2.82	3.19	2.90	3.07
EGYPT	0.62	0.81	0.74	0.53	0.37	0.30	0.36	0.38	0.36	0.36
FINLAND	1.43	1.60	1.76	1.88	1.99	1.85	2.00	1.97	1.97	2.24
FRANCE		1.24	1.21	1.22	1.31	1.19	1.25	1.27	1.27	1.37
GERMANY	1.59	1.65	1.64	1.67	1.74	1.62	1.69	1.78	1.75	1.85
GREECE	1.86	1.17	1.34	2.29	2.03	2.15	2.13	2.05	1.98	2.31
INDIA	0.28	0.37	0.37	0.37	0.28	0.27	0.33	0.33	0.33	0.35
INDONESIA	0.86	1.01	0.92	1.09	1.04	0.89	0.84	0.93	0.76	0.77
ITALY	1.42	1.57	1.57	1.53	1.50	1.45	1.53	1.61	1.62	1.70
JAPAN	1.40	1.95	2.05	1.85	1.80	1.75	1.95	2.00	1.92	2.19
KOREA	0.81	2.33	1.28	1.77	1.35	1.37	2.24	1.93	1.89	1.81
MALAYSIA	0.98	1.19	1.40	1.37	1.15	1.14	1.17	1.28	1.06	1.12
MEXICO	2.61	3.22	3.52	3.52	2.73	3.06	2.84	3.17	2.76	2.97
MOROCCO	0.86	1.32	1.02	1.00	1.00	0.97	1.05	1.12	1.15	1.24
NETHERLANDS	1.46	1.52	1.47	1.50	1.56	1.36	1.40	1.47	2.17	2.20
PHILIPPINES	2.57	3.23	3.15	3.20	2.55	2.26	2.26	2.62	2.68	2.92
POLAND	0.57	0.75	0.78	0.95	0.92	0.89	0.95	1.05	1.00	1.20
PORTUGAL	1.34	1.35	1.32	1.38	1.45	1.48	1.55	1.53	1.53	1.68
SAUDI ARABIA	1.81	2.25	2.64	2.59	1.63	1.40	1.47	1.48	1.25	1.08
SINGAPORE	0.99	1.19	1.35	1.36	1.18	0.90	1.06	0.94	0.94	1.01
SOUTH AFRICA	1.95	2.01	1.69	1.34	1.64	1.40	1.25	1.10	0.92	0.80
SPAIN	1.32	1.37	1.40	1.56	1.64	1.57	1.24	1.22	1.20	1.27
SWEDEN	2.42	2.58	2.51	2.79	2.74	2.56	2.57	2.62	2.29	2.58
SWITZERLAND	1.69	1.78	1.83	2.09	2.21	2.12	2.08	2.10	1.93	2.14
TAIWAN	0.62	0.84	0.80	0.74	0.73	0.72	0.88	0.95	0.85	0.91
THAILAND	0.52	0.72	0.69	0.72	0.63	0.67	0.71	0.81	0.89	0.81
TUNISIA	0.80	0.87	0.88	0.85	0.84	0.75	0.80	0.86	0.88	0.94
TURKEY	7.18	6.53	3.98	3.60	2.86	2.00	1.78	1.53	1.41	1.43
UNITED KINGDOM	1.68	1.95	1.83	1.80	1.80	1.71	1.57	1.68	1.61	1.46
UNITED STATES	3.53	4.75	4.85	5.26	4.92	3.90	4.16	4.32	3.93	3.69

19. F_B^{WA}: Prices relative to western Africa based on bilaterally-matched sample, Fisher price indices, price per standard unit (western Africa=1)



20. Proportion of total country market (by SU volume) captured in samples bilaterally-matched with United States

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
ALGERIA				80	80	76	85	87	87	86
AUSTRALIA	99	99	99	99	99	99	99	99	99	99
AUSTRIA	71	72	72	72	72	72	72	72	74	74
BELGIUM	80	80	80	80	81	81	81	80	82	82
BRAZIL	71	68	71	69	68	69	69	68	70	71
CANADA	97	97	97	97	97	98	98	95	95	95
EGYPT	83	81	82	81	75	74	76	72	73	73
FINLAND	85	85	85	85	84	85	85	86	86	87
FRANCE		62	63	63	62	63	65	68	70	71
GERMANY	79	80	80	79	79	80	80	76	79	80
GREECE	98	98	98	98	98	98	97	97	98	98
INDIA	97	97	97	97	97	97	97	97	97	97
INDONESIA	94	94	92	93	93	93	93	92	92	93
ITALY	67	68	69	70	70	72	72	73	75	77
JAPAN	72	72	72	72	71	70	69	67	66	65
KOREA	99	99	98	98	98	97	97	97	97	97
MALAYSIA	89	88	88	89	87	86	87	87	89	89
MEXICO	88	87	85	84	80	81	81	80	82	83
MOROCCO	61	63	65	66	66	66	67	68	69	69
NETHERLANDS	92	93	93	93	93	93	93	92	92	92
PHILIPPINES	93	96	96	95	96	96	96	95	96	95
POLAND	67	68	68	69	68	70	70	65	66	67
PORTUGAL	88	88	89	90	90	91	92	92	93	94
PUERTO RICO		100	100	100	100	100	100	100	100	100
SOUTH AFRICA	86	86	86	87	87	88	89	88	89	88
SAUDI ARABIA	92	92	91	90	87	86	86	80	82	81
SINGAPORE	81	81	85	85	82	82	81	83	83	84
SPAIN	75	76	75	75	75	77	77	76	78	78
SWEDEN	94	94	94	93	93	93	93	92	92	92
SWITZERLAND	79	79	79	78	78	78	78	75	78	78
TAIWAN	80	81	83	82	82	81	82	81	82	82
THAILAND	67	62	65	64	58	59	62	67	64	62
TUNISIA	68	69	70	71	70	71	72	71	71	71
TURKEY	76	76	76	77	72	72	73	73	73	73
UNITED KINGDOM	86	86	86	87	87	87	87	86	85	85
WESTERN AFRICA	60	60	61	59	57	55	63	62	63	64

21. Number of molecule presentations per country market in the multilaterally-matched sample

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
AUSTRALIA	1858	1774	1853	1932	2012	1966	1896	2012	2019	1962
AUSTRIA	1384	1340	1392	1547	1625	1594	1481	1545	1648	1672
BELGIUM	1342	1338	1311	1429	1468	1437	1368	1446	1455	1469
BRAZIL	3812	3873	3876	3927	4040	3953	3771	3880	3936	3852
CANADA	2470	2406	2474	2510	2614	2529	2445	2534	2623	2568
EGYPT	1343	1325	1386	1437	1470	1409	1354	1390	1419	1377
FINLAND	1380	1345	1393	1629	1655	1602	1525	1604	1659	1673
GERMANY	7439	7190	7667	8333	8618	8662	8065	8560	8970	8999
GREECE	1477	1467	1481	1654	1693	1624	1525	1613	1652	1606
INDIA	8505	8689	9460	8783	9431	9061	8394	8544	9138	8876
INDONESIA	3179	3069	3140	3067	3152	3007	2907	2996	2980	2916
ITALY	2308	2186	2256	2494	2606	2486	2310	2506	2502	2494
JAPAN	3055	2982	2955	3013	3097	2896	2761	2793	2860	2720
KOREA	2927	2849	3096	3359	3458	3186	3072	3297	3315	3229
MALAYSIA	2196	2111	2178	2167	2220	2104	2018	2043	2060	2017
MEXICO	2890	2892	3045	2962	3096	2872	2704	2800	2839	2715
MOROCCO	1041	1034	1048	1063	1084	1042	976	987	1018	986
NETHERLANDS	3594	3483	3578	4170	4242	4111	3830	4053	4185	4167
PHILIPPINES	2989	2934	3007	2913	2983	2873	2802	2848	2870	2870
POLAND	1622	1605	1671	1857	1942	1898	1815	1903	1977	2023
PORTUGAL	1723	1739	1816	2010	2059	1952	1926	2082	2194	2163
SOUTH AFRICA	1761	1712	1761	1837	1890	1830	1737	1784	1812	1766
SAUDI ARABIA	1132	1119	1185	1217	1235	1184	1141	1167	1187	1165
SINGAPORE	1606	1564	1577	1610	1633	1553	1488	1502	1536	1508
SPAIN	2411	2497	2597	2818	2888	2744	2671	2832	2950	2888
SWEDEN	1525	1501	1588	1818	1856	1805	1696	1825	1921	1950
SWITZERLAND	1681	1675	1725	1845	1867	1863	1769	1833	1883	1882
THAILAND	3491	3446	3629	3595	3616	3457	3362	3375	3431	3277
TUNISIA	701	706	698	762	770	746	701	712	721	716
TURKEY	1221	1192	1313	1374	1432	1301	1228	1286	1348	1302
UK	2128	2034	2046	2230	2274	2255	2082	2186	2187	2218
UNITED STATES	7032	6992	7088	7165	7287	7184	7080	7326	7358	7216
WESTERN AFRICA	1858	1811	1904	1828	1888	1794	1750	1785	1794	1745

22. Number of molecule presentations per country market (included in database)

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
AUSTRALIA	7911	8046	8138	8251	8289	8315	8268	8293	8328	8288
AUSTRIA	5726	5798	5815	5852	5870	5902	5898	5913	5904	5850
BELGIUM	4685	4716	4787	4844	4845	4845	4782	4794	4761	4677
BRAZIL	11262	11417	11493	11539	11544	11529	11630	11562	11544	11561
CANADA	10370	10438	10622	10596	10589	10616	10746	10926	11010	10937
EGYPT	4523	4601	4704	4812	4852	4918	4978	5002	5041	5056
FINLAND	4185	4222	4245	4258	4292	4319	4340	4330	4330	4310
GERMANY	33291	33634	33970	34105	34196	34146	34139	34128	34027	33936
GREECE	5585	5611	5715	5816	5818	5829	5864	5897	5876	5892
INDIA	24120	25136	26192	27394	27935	29117	29494	29850	29971	29836
INDONESIA	8912	8987	9012	9017	9078	9063	9062	9158	9130	9146
ITALY	9061	9165	9203	9396	9379	9358	9322	9272	9254	9231
JAPAN	17371	17390	17478	17490	17504	17503	17482	17510	17510	17483
KOREA	11168	12506	12647	12882	12914	12994	12931	12996	13022	12929
MALAYSIA	6241	6280	6278	6273	6325	6401	6421	6426	6418	6383
MEXICO	8199	8264	8401	8543	8587	8624	8709	8875	8833	8829
MOROCCO	2858	2862	2905	2928	2943	2949	2950	2950	2942	2842
NETHERLANDS	11772	11973	12168	12202	12278	12350	12388	12373	12394	12377
PHILIPPINES	7889	7907	7916	7909	7913	7925	7914	7902	7928	7919
POLAND	6798	6915	6928	6988	6996	6961	6945	6922	6949	6881
PORTUGAL	5287	5359	5404	5450	5498	5533	5454	5455	5455	5412
SOUTH AFRICA	6026	6187	6234	6225	6255	6259	6255	6258	6292	6261
SAUDI ARABIA	3387	3420	3464	3483	3492	3466	3407	3404	3411	3403
SINGAPORE	4944	4963	4941	4917	4912	5016	5055	5070	5002	4947
SPAIN	7773	7849	7885	7912	7916	7926	7950	7879	7874	7840
SWEDEN	5553	5702	5791	5940	5971	6020	6029	6067	6084	6078
SWITZERLAND	8320	8342	8356	8367	8311	8236	8202	8139	8106	8021
THAILAND	10740	10901	10772	10861	10978	11122	11169	11197	11201	11126
TUNISIA	2145	2144	2180	2196	2173	2186	2169	2150	2161	2152
TURKEY	4781	4860	4901	4931	4993	5015	5354	5470	5551	5563
UNITED KINGDOM	7504	7573	7627	7643	7666	7677	7655	7660	7655	7592
UNITED STATES	37904	38057	38260	38602	38669	38764	38751	38220	38230	38195
WESTERN AFRICA	4976	5046	5089	5127	5153	5118	5100	5140	5151	5127

23. Attributes of molecule presentations underpinning multilaterally-matched sample (average across years) MK = Full market, MS = Multilateral sample

	% any brand MK	% any brands MS	% original brands MK	% original brands MS	% OTC MK	% OTC MS
AUSTRALIA	53	13	15	61	28	48
AUSTRIA	71	25	19	69	7	15
BELGIUM	72	27	23	74	14	22
BRAZIL	73	9	6	83	14	26
CANADA	53	11	11	54	5	12
EGYPT	76	10	10	85		
FINLAND	73	29	21	71	12	11
GERMANY	59	19	15	64	12	29
GREECE	87	20	15	92		
INDIA						
INDONESIA	79	10	8	89	10	13
ITALY	66	14	11	63	8	15
JAPAN	66	8	8	77	3	7
KOREA	68	5	4	73	22	29
MALAYSIA	71	14	11	79	19	25
MEXICO	76	13	9	80	7	14
MOROCCO	82	17	16	94		
NETHERLANDS	55	33	26	46	10	9
PHILIPPINES	69	11	8	73	8	12
POLAND	68	15	11	76	15	24
PORTUGAL	58	18	12	51	3	6
SOUTH AFRICA	68	17	14	76	22	38
SAUDI ARABIA	86	23	19	94		
SINGAPORE	71	19	15	78	18	24
SPAIN	57	15	9	50	6	12
SWEDEN	72	37	31	67	10	9
SWITZERLAND	61	18	19	73	13	40
THAILAND	75	6	6	88		
TUNISIA	77	22	20	89		
TURKEY	82	14	11	92		
UNITED KINGDOM	57	19	17	57	19	25
UNITED STATES	47	10	12	54	24	34
WESTERN AFRICA	63	14	13	75		

24. Number of unique ATCMOLs in multilaterally-matched (33-country) sample

1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
101	100	101	111	114	110	100	106	112	108

25. Proportion of total country market (by SU volume) captured in multilaterally-matched samples

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
AUSTRALIA	46	42	43	45	43	41	41	40	38	38
AUSTRIA	25	24	25	27	28	27	27	29	32	32
BELGIUM	30	29	28	31	31	31	32	35	35	36
BRAZIL	33	32	31	32	33	32	31	31	31	31
CANADA	33	35	34	35	35	34	36	39	36	34
EGYPT	34	30	32	32	31	31	30	29	30	30
FINLAND	39	37	38	42	41	39	39	43	42	43
GERMANY	27	26	27	30	31	31	31	32	35	36
GREECE	34	30	29	32	30	29	28	29	31	33
INDIA	40	41	40	41	40	38	36	36	37	35
INDONESIA	34	34	35	34	37	36	36	40	40	39
ITALY	32	30	28	31	30	30	30	32	34	35
JAPAN	17	16	15	16	16	16	15	16	17	16
KOREA	15	17	20	20	20	19	18	19	19	19
MALAYSIA	45	43	42	43	43	41	40	42	43	39
MEXICO	29	27	29	27	27	26	26	27	26	25
MOROCCO	31	31	32	34	33	32	32	34	35	35
NETHERLANDS	38	35	37	44	43	42	41	44	44	43
PHILIPPINES	34	39	42	42	47	47	49	46	48	48
POLAND	32	29	29	30	30	29	30	32	30	31
PORTUGAL	32	31	30	33	34	33	33	35	37	37
SOUTH AFRICA	30	28	29	33	34	35	36	37	38	37
SAUDI ARABIA	37	36	38	43	42	38	39	42	45	43
SINGAPORE	41	37	36	38	39	38	36	39	38	39
SPAIN	34	33	32	36	35	34	34	38	39	39
SWEDEN	41	39	36	37	37	34	34	37	36	37
SWITZERLAND	22	22	23	25	25	24	25	27	30	30
THAILAND	30	27	30	29	26	24	26	27	26	23
TUNISIA	33	33	33	34	34	35	34	35	34	32
TURKEY	30	28	29	31	29	27	27	30	29	29
UNITED KINGDOM	47	41	42	50	48	47	43	45	45	46
UNITED STATES	29	28	30	31	31	30	34	39	36	36

WESTERN AFRICA	26	27	27	26	26	26	30	32	33	33

26. NUMBER OF UNIQUE ATCMOLS ON MARKET BY COUNTRY BY YEAR

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
AUSTRALIA	1430	1465	1494	1547	1569	1575	1536	1544	1564	1558
AUSTRIA	1205	1225	1216	1231	1244	1248	1242	1252	1252	1224
BELGIUM	1147	1156	1172	1182	1176	1173	1120	1129	1109	1067
BRAZIL	1306	1370	1388	1410	1402	1386	1430	1399	1408	1417
CANADA	1447	1436	1495	1458	1461	1457	1509	1608	1640	1618
EGYPT	894	909	925	950	970	1006	1038	1049	1082	1097
FINLAND	784	784	784	790	795	795	800	803	799	792
GERMANY	2471	2516	2629	2630	2616	2509	2497	2481	2493	2486
GREECE	996	1002	1035	1088	1080	1087	1103	1120	1111	1118
INDIA	1136	1205	1291	1390	1265	1547	1622	1686	1728	1751
INDONESIA	1042	1069	1083	1075	1099	1098	1110	1175	1165	1178
ITALY	1348	1375	1367	1392	1369	1345	1330	1312	1304	1305
JAPAN	1735	1733	1742	1749	1738	1732	1720	1737	1735	1731
KOREA	1016	1333	1334	1492	1462	1501	1479	1496	1514	1482
MALAYSIA	1022	1025	1017	1014	1022	1067	1084	1099	1110	1096
MEXICO	1154	1193	1238	1286	1315	1331	1369	1479	1457	1461
MOROCCO	813	808	835	834	842	845	844	840	835	771
NETHERLANDS	994	1006	1013	996	974	978	990	982	982	974
PHILIPPINES	949	943	941	931	925	914	918	916	943	941
POLAND	1387	1411	1393	1416	1409	1371	1360	1350	1368	1342
PORTUGAL	924	943	953	960	973	990	937	935	929	918
SOUTH AFRICA	1234	1320	1355	1330	1335	1326	1329	1324	1357	1338
SAUDI ARABIA	813	814	839	835	826	810	768	771	776	774
SINGAPORE	1132	1135	1106	1091	1075	1123	1138	1158	1115	1083
SPAIN	1193	1219	1221	1220	1215	1208	1211	1181	1174	1171
SWEDEN	799	824	856	897	892	900	906	919	931	934
SWITZERLAND	1994	1990	1976	1966	1926	1858	1834	1794	1780	1739
THAILAND	1033	1041	1030	1052	1062	1063	1093	1105	1114	1094
TUNISIA	691	685	698	696	681	686	675	665	678	667
TURKEY	898	914	923	936	952	974	1092	1172	1228	1249
UNITED KINGDOM	1354	1369	1388	1381	1391	1390	1387	1389	1382	1348
UNITED STATES	2172	2152	2150	2203	2200	2214	2196	2127	2160	2192
WESTERN AFRICA	1082	1109	1128	1146	1161	1124	1107	1140	1145	1136

BRIEF SUMMARY OF ADDITIONAL RESULTS

Findings of the US-based comparison largely echo the main findings of all papers: Most high-income countries had prices higher than most middle- and low-income countries, with the important exception of Mexico (a country categorized as middle-income countries) which had prices higher than all high-income countries, including the US in some years. A few other middle-income countries —such as Philippines and Brazil--had prices close to the average high-income country level. Prices in low-income countries were below high-income countries (except Singapore) and above many middle-income countries. Expanding the sample (through bilaterally-matching with the US) increased the representation of the sample to 65-99% (averaging over 10-year period) of the market by volume. Results altered the magnitude of the price relatives, namely estimating that low-income countries prices were closer to 20% of US prices rather than 40% estimated in the smaller, multilaterally-match sample. Sample size also affected UK prices relative to western Africa. When compared to this low-income aggregate using the smaller, multilaterally-match sample UK prices were actually found to be relatively smaller (a rather startling finding) but were found to be relatively larger when compared bilaterally. Using the UK as a base country further suggests that UK prices fell somewhere between the cheaper of the high-income countries and the more expensive of the middle-income countries. Of perhaps most interest, however, is the echoing of the trend for other countries to experience an increase in prices relative to the UK from approximately 2004 to the end of the study period, especially amongst high-income countries. Using a larger sample size bilaterally-match sampling gives a slightly different picture. Here prices in other high-income countries relative to the UK start mainly below the UK in 1999 but surpass it by 2008. So whilst the overall price trend is similar, the shape of the curve differs depending on the sample. The picture of middle-income country price relatives is largely consistent across the two samples.

This Appendix also includes additional calculations were also made using alternative base countries (Philippines and India) in order examine more directly price differentials to these countries. Results suggest that prices in the Philippines were in general on the higher end of those found across all middle-income countries (Mexico having consistently the highest prices amongst the group) and prices in India were consistently the lowest. This variation in prices across middle-income countries should be taken into account in formulating fairer pricing policies. Indeed the fact that per capita

GDP in 2012 was twice as much in India as in the Philippines should put some stress on the unfairness of relative drug pricing.

Technical notes: Countries are excluded from the indices based on multilaterally-matched samples if they lacked data in at least one year (e.g. France, Algeria) in order to capture price relatives across the full decade.