Research Report

International Prescription Drug Price Comparisons

Current Empirical Estimates and Comparisons with Previous Studies

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Preface

This report describes how price indices are used to compare prescription drug prices between countries, summarizes findings related to international prescription drug price comparisons presented in prior studies, and presents new price comparisons that are based on 2018 data. The overall result from the new price comparison is then compared with narrower analyses on specific categories of drugs, such as brand-name originator drugs, unbranded generic drugs, biologics, and nonbiologic drugs. The report also presents results from sensitivity analyses using different methodological steps and assumptions, such as prices and volume aggregated at different levels and volume weights calculated in different ways.

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Summary

The United States spends more on prescription drugs on a per capita basis than other countries in the Organisation for Economic Co-operation and Development (OECD).[1] Understanding the extent to which drug prices are higher in the United States than in other countries—after accounting for differences in the volume and mix of drugs—is useful when developing and targeting policies to address both growth in drug spending and the financial impact of prescription drugs on consumers. Although several prior studies systematically compared drug prices in the United States with those in other countries,[2] the most recent of these studies used data that are almost a decade old.

In this report, we (1) describe the use of price indices as a tool to compare drug prices between countries, (2) list the methodological decisions required to calculate price indices, (3) summarize prior studies in terms of their methodologies and results, and (4) present results from a new comparison of 2018 drug prices in the United States with those in 32 OECD countries. We also calculate and compare prices for several subsets of drugs using different methodological steps and assumptions in sensitivity analyses.

Our results are described in detail in the main report. In brief, when analyzing data for all prescription drugs available in the United States and comparison countries, we found that U.S. prices for drugs in 2018 were 256 percent of those in the 32 OECD comparison countries combined. U.S. prices were even higher than those in comparison countries for brand-name originator drugs (with U.S. prices at 344 percent of those in comparison countries) but were lower, on average, than those in comparison countries for unbranded generic drugs (with U.S. prices at 84 percent of those in comparison countries). Unbranded generics represent 84 percent of volume in the United States, compared with 35 percent of volume for the other OECD countries in the study. Although different methodological decisions and assumptions did change the magnitude of results, we found a consistent pattern of considerably higher overall drug prices in the United States than in the comparison OECD countries.

[1] Dana O. Sarnak, David Squires, and Shawn Bishop, "Paying for Prescription Drugs Around the World: Why Is the U.S. an Outlier?" webpage, Commonwealth Fund, October 5, 2017.

[2] U.S. Department of Commerce, International Trade Administration, *Pharmaceutical Price Controls in OECD Countries: Implications for US Consumers, Pricing, Research and Development and Innovation*, Washington, D.C., 2004; Patricia Danzon and Michael F. Furukawa, "International Prices and Availability of Pharmaceuticals in 2005," *Health Affairs*, Vol. 27, No. 1, January/February 2008; Panos Kanavos, Alessandra Ferrario, Sotiris Vandoros, and Gerard F. Anderson, "Higher US Branded Drug Prices and Spending Compared to Other Countries May Stem Partly from Quick Uptake of New Drugs," *Health Affairs*, Vol. 32, No. 4, 2013.

Price Indices as a Tool to Compare Prices

Creating a price index rather than looking at specific prices is an approach used to compare differences in prices for a basket of goods over time or across markets (such as countries). The rationale behind price indices is that a comparison of prices is most meaningful when it avoids the risk of interference stemming from differences in volume and/or mix. Price indices accomplish this by holding the mix and volume constant while allowing prices to vary. Several methodological decisions, such as the following, must be made before calculating prescription drug price indices:

- **Which drugs to include in the analysis.** Prices can be compared for the top drugs by U.S. sales or volume, all drugs sold in the United States and one or more comparison countries,[3] brand-name originator drugs, unbranded generic drugs, or many other subsets of drugs. Certain types of drugs (for example, over-the-counter drugs) can be excluded.
- **Which prices to use.** The price for prescription drugs can be measured at different levels, such as the prices at which drugs are sold to wholesalers ("manufacturer prices") or the prices offered to the public by retail pharmacies, which include both wholesale and retail markups ("retail prices"). Although prices net of rebates and other discounts paid by manufacturers after drugs are dispensed are particularly relevant in the United States, these prices are generally not available to researchers.
- **The granularity of prices and quantities.** For example, prices and quantities can be calculated narrowly for each combination of active ingredient, formulation, and strength (which we define as a *presentation*), or more broadly, at the active ingredient level.
- **The units for measuring sales and volume.** Sales can be measured in local currencies or U.S. dollars converted using exchange rates. Volume is usually measured in terms of standard units—standardized units of volume based on counting pills or 5mL of a drug, depending on formulation—or in terms of kilograms of active ingredient.
- **The basis for calculating volume weights.** Volume weights are used to hold the mix of drugs constant. For comparisons between the United States and other countries, U.S. volume weights, other-country volume weights, or blended shares are used.
- **Whether to exclude outliers.** Quantity and sales data sometimes result in extremely high or low prices in a market that can have significant leverage over the resulting calculated price index. These outlier values can be excluded from the market basket.
- **Whether to present adjusted or unadjusted price indices.** Prior studies adjust price index results to account for differences in per capita gross domestic product (GDP) purchasing power parity (PPP) or for differences in health care system and drug market characteristics.

[3] Because of differences in competitive and regulatory landscapes, there are relatively few drugs sold both in the United States and in each of many comparison countries. As an alternative, analyses can include drugs sold in the United States and individual comparison countries (in "bilateral" comparisons of prices).

Prior Studies Comparing International Drug Prices

Prior studies that we reviewed varied in the periods studied, drugs and countries used in price index calculations, granularity of prices and quantities, choice of volume weights, and use of retail prices versus manufacturer prices. Most notably, two of the most relevant studies focused on brand-name originator drugs and did not include unbranded generic drugs.[4] For these reasons, we focused on comparing broad patterns of results from prior studies rather than comparing price indices for specific countries.

Each of the studies that we reviewed in detail used a price index methodology and IQVIA's MIDAS data.[5] The MIDAS data contain estimates of prescription drug sales and volume that are based on audits of prescription drug transactions in each source country. The audit methodology varies from country to country, but the MIDAS data are generally an estimate of all prescription drug sales regardless of distribution channel. We use the same data for the empirical estimates in this report.

In general, the studies that we reviewed found that U.S. prices are considerably higher than those in comparison countries when analyzing all drugs together, including brand-name originator and unbranded generic drugs. Calculated price indices for individual countries varied across studies, but there was some consistency across studies in the relative ranking of price differences (e.g., prices in Germany were consistently found across studies to be generally closer to prices in the United States than they were to most other comparison countries). With the exception of estimates from one study for Japan and Mexico, all compared countries across all studies had prices that were at least 20 percent lower than those in the United States.

Danzon and Furukawa was the only systematic study presenting separate results for unbranded generic drugs.[6] These drugs account for approximately 85 percent of U.S. prescription volume and approximately 15 percent of U.S. prescription spending. This study found that other countries had higher prices for unbranded generic drugs, with prices ranging from 108 percent of U.S. prices in France to 216 percent of U.S. prices in Mexico. All the studies we reviewed found that U.S. brand-name originator prices were higher than those in other countries.

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[4] A *brand-name originator drug* is manufactured by the company that obtained the first regulatory approval for the presentation (or by that company's successor).

[5] IQVIA was IMS Health when these studies were conducted. MIDAS is a data set that allows analysis of sales and volume data for prescription and other drugs from more than 90 countries. (IQVIA, "MIDAS," webpage, undated.)

[6] Danzon and Furukawa, 2008. A 2004 U.S. Department of Health and Human Services report does not present results from a systematic comparison of generic prices but reports comparisons of generic prices for a narrower set of 29 top-selling generics based on 2002 U.S. sales, and it lists findings of generally lower prices in the United States than in other countries. U.S. Department of Health and Human Services Task Force on Drug Importation, *Report on Prescription Drug Importation*, Washington, D.C., December 2004.

Empirical Estimates of Price Differences

Data and Methodology

We used 2018 MIDAS data to calculate price indices comparing prescription drug prices in the United States with those in 32 OECD comparison countries. For our main results, we used presentation-level data from all prescription drugs in the MIDAS data set, excluding presentations in countries with low volume or sales and with extreme ratios of U.S. prices to other-country prices; we excluded these to avoid outlier presentations from exerting undue influence on our overall results. These steps resulted in a different number of presentations being analyzed for each pairwise comparison of the United States with another country.[7] Separately, we compared U.S. prices with those in all other countries in our data aggregated together as a summary measure. We used U.S. volume weights (i.e., the share of total volume accounted for by each presentation) to calculate price indices because of our interest in price differences from a U.S. policy perspective.

We applied the same price index methodology to the following subsets of drugs:

- brand-name originator drugs
- unbranded generic drugs excluding biologics
- unbranded generic and brand-name non-originator ("branded generic") drugs combined
- the top 60 active ingredients by U.S. sales, excluding combination drugs
- biologics
- nonbiologic drugs
- drugs that are typically covered by Medicare Part B, Part D, or both
- drugs that are sorted into groups based on the year in which they were first marketed.

We also conducted sensitivity analyses in which we did the following:

- used other-country and blended volume weights rather than U.S. volume weights
- used active ingredient rather than presentation-level data
- used retail prices rather than manufacturer prices
- applied an adjustment to U.S. manufacturer prices to approximate prices net of rebates and other discounts from manufacturers
- used different approaches to exclude outlier presentations.

This report presents both our main results and other results for seven countries (Mexico and the G7 countries excluding the United States: Canada, France, Germany, Italy, Japan, and the United Kingdom) in bar charts. (Results for other countries are available in Appendix C.) We separately report a comparison of U.S. prices with prices in the 32 comparison countries

[7] The share of volume and sales contributing to each analysis varied widely but was generally considerably less than 100 percent. For example, for the United States–Canada comparison, 72 and 63 percent of Canadian and U.S. volume, respectively, and 84 and 71 percent of Canadian and U.S. sales contributed to our analysis. Among the Group of Seven (G7) countries, Japan had the smallest overlap with the United States, with only 17 and 30 percent of Japanese and U.S. volume and 48 and 46 percent of Japanese and U.S. sales contributing to our analyses.

combined. Price indices greater than 100 indicate that U.S. prices are higher than those in the comparison country; indexes less than 100 indicate that U.S. prices are lower than those in the comparison country. We did not adjust price indices by per capita GDP PPP or for other differences across markets.

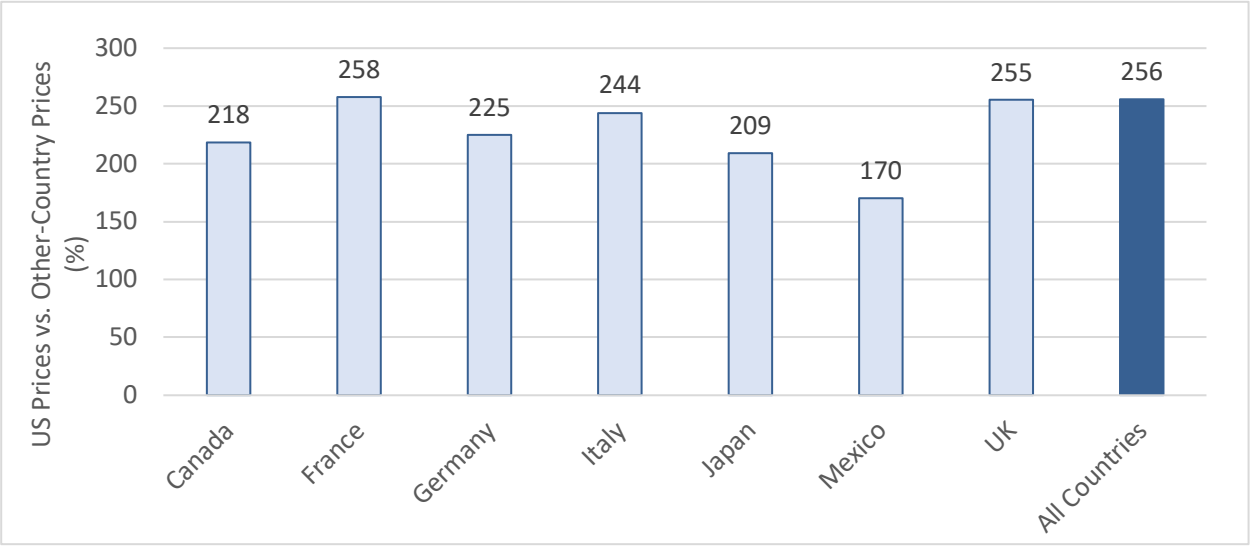
Results

Prices in the United States are higher than those in all comparison countries (see Figure S.1 for comparisons of U.S. prices with those in Mexico and the G7 countries, and see Appendix C for comparisons with other OECD countries). Each result illustrated in Figure S.1 reports U.S. prices relative to a comparison country or, in the right-most column, relative to all 32 OECD comparison countries combined. For example, U.S. prices were 218 percent of prices in Canada (or, alternatively, Canadian prices were 46 percent of U.S. prices). U.S. prices were 256 percent of those in the 32 OECD comparison countries combined. In comparisons with individual countries, U.S. prices ranged from 170 percent of prices in Mexico to 779 percent of prices in Turkey. Among comparisons with individual G7 countries, U.S. prices ranged from 209 percent of prices in Japan to 258 percent of prices in France.

The gap between U.S. prices and prices in other countries was larger for brand-name originator drugs (Figure S.2). U.S. prices were 344 percent of prices in all non-U.S. countries for these drugs. However, prices for unbranded generic drugs were generally lower in the United States than in other countries (Figure S.3). U.S. prices were 84 percent of prices in all non-U.S. countries for unbranded generics. We found that U.S. prices were higher than most comparison countries when combining data for all non-originator drugs, including unbranded generics and brand-name non-originator drugs.[8]

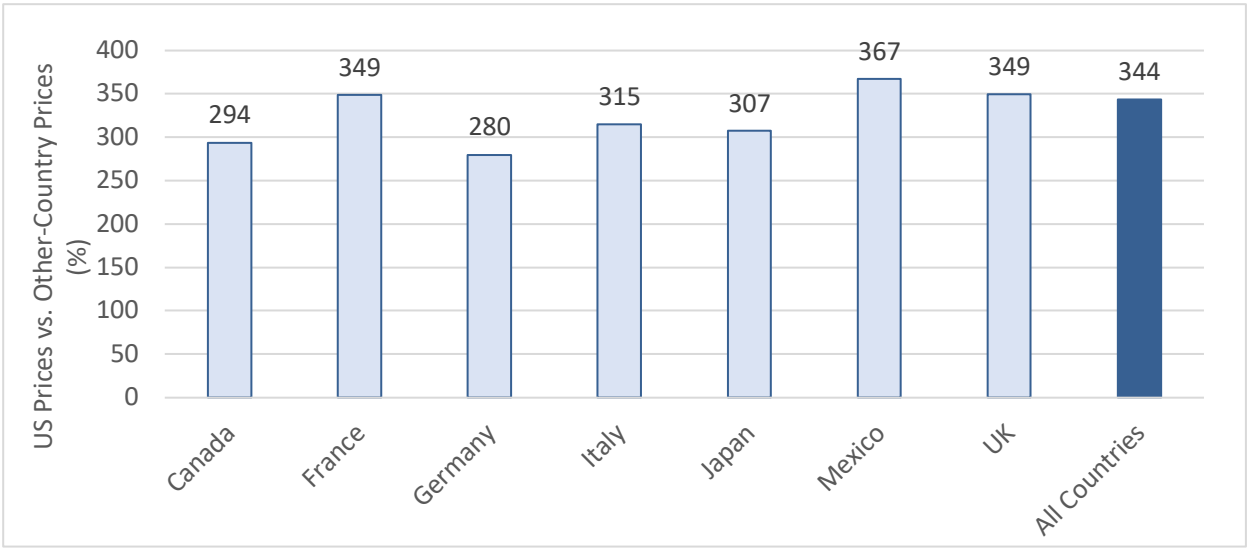
[8] Prices in the United States were 121 percent of those in all other countries combined when unbranded generics and brand-name non-originator drugs were combined. While drugs labeled in MIDAS as "unbranded non-originator" drugs are primarily unbranded generics, drugs designated as brand-name non-originators are more diverse and include (1) multisource branded generics (i.e., generic drugs marketed under a brand name, which is common in some countries outside the United States but very rare in the United States) and (2) brand-name drugs approved in the United States via the 505(b)(2) regulatory approval pathway (such as EpiPen). Drugs in the second category are often non-originator drugs but they may be priced and marketed as brand-name originator drugs.

Figure S.1. U.S. Prescription Drug Prices as a Percentage of Prices in Selected Other Countries, All Drugs, 2018



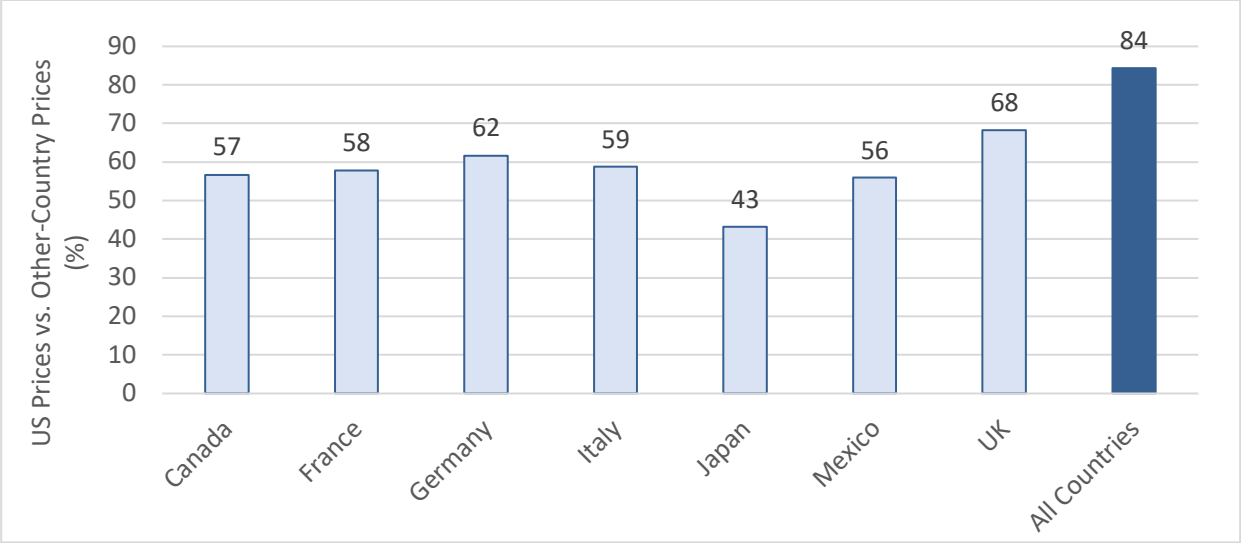
SOURCE: Author analysis of IQVIA MIDAS sales and volume data for calendar year 2018 (run date October 28, 2019).
NOTE: "All Countries" refers to all 32 OECD comparison countries combined. Other-country prices are set to 100. Only some presentations sold in each country contribute to bilateral comparisons.

Figure S.2. U.S. Brand-Name Originator Drug Prices as a Percentage of Other-Country Prices, 2018



SOURCE: Author analysis of IQVIA MIDAS sales and volume data for calendar year 2018 (run date October 28, 2019).
NOTE: "All Countries" refers to all 32 OECD comparison countries combined. Other-country prices are set to 100. Only some presentations sold in each country contribute to bilateral comparisons.

Figure S.3. U.S. Unbranded Generic Drug Prices as a Percentage of Other-Country Prices, 2018



SOURCE: Author analysis of IQVIA MIDAS sales and volume data for calendar year 2018 (run date October 28, 2019).
NOTE: Biologics are excluded. "All Countries" refers to all 32 OECD comparison countries combined. Other-country prices are set to 100. Only some presentations sold in each country contribute to bilateral comparisons.

The United Kingdom, France, and Italy generally have the lowest prices among the comparison countries for all drugs and for brand-name originator, biologic, and nonbiologic drugs separately. Canada, Germany, and Japan tend to have higher prices across each subset of drugs.

Our main findings—that U.S. prices are higher than those in comparison countries for all drugs and for brand-name originator drugs but lower for unbranded generic drugs—held through several additional sensitivity analyses related to how price indices were calculated. These tests, described in detail in Chapter 3, included using different prices, calculating results with and without outlier presentations in terms of price, and calculating results using different volume weights.

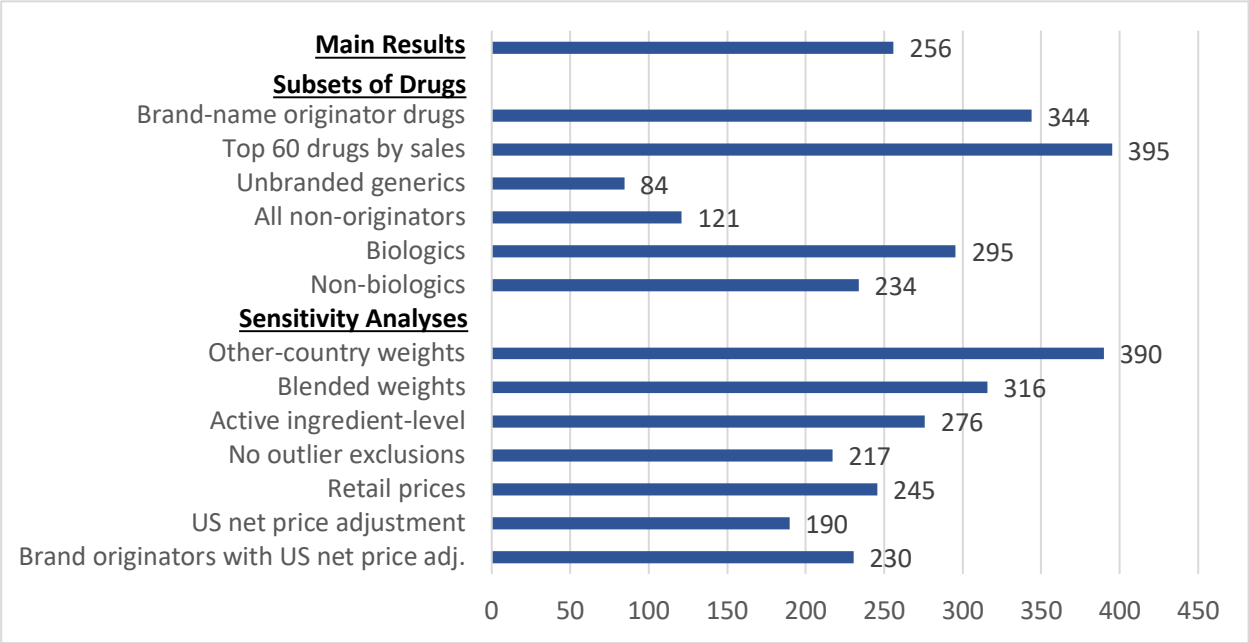
U.S. prices remained substantially higher than prices in other countries when we calculated price indices using retail prices rather than manufacturer prices, but the gap between U.S. and other-country prices shrank in some bilateral comparisons, suggesting higher wholesale and retail markups in these countries than in the United States.

One important limitation of our analysis is that we use manufacturer prices for the purposes of comparison because net prices—that is, the prices ultimately paid for drugs after negotiated rebates and other discounts are applied—are not systematically available. The magnitude of the difference between manufacturer and net prices is difficult to quantify. Net prices reflect confidential rebates negotiated between manufacturers and buyers that vary depending on market conditions and negotiating leverage. Net prices also reflect Medicaid best price and rebate program provisions, discounts from the 340B prescription drug discount program that may or may not be applied as drugs are sold by manufacturers, and discounts from other sources. To

assess how our results might change if net price information were available, we conducted a final set of sensitivity analyses in which we adjusted U.S. prices downward based on published estimates of the relative differences between manufacturer and net prices.[9] The resulting U.S. prices remained substantially higher than prices in other countries—but with a smaller difference than in our main results. Because of a lack of available estimates, we did not adjust prices in other countries downward to reflect increasingly common discounts on manufacturer prices. U.S. prices would appear relatively higher—i.e., more in line with our main results—if we were able to also adjust for rebates and other discounts applied to manufacturer prices in other countries.

Figure S.4 compares our main result with selected results from subsets of drugs and with results from these sensitivity analyses.

Figure S.4. Summary of Selected Results: U.S. Prices as a Percentage of Other-Country Prices, 2018



SOURCE: Author analysis of IQVIA MIDAS sales and volume data for calendar year 2018 (run date October 28, 2019).
NOTE: "Other-Country Prices" refers to all 32 OECD comparison countries combined. For "Top 60," we compared prices for the top 60 drugs by U.S. sales at the active ingredient level, excluding combination products. "Adj." is adjustment. Only some presentations sold in each country contribute to bilateral comparisons.

Conclusion

Although several prior studies compare drug prices in the United States with those in other countries, the most recent of these studies used data that are nearly a decade old. In our analysis

[9] IQVIA Institute for Human Data Science, *Medicine Use and Spending in the U.S.: A Review of 2018 and Outlook to 2023*, Durham, N.C., May 9, 2019b.

using 2018 data, we found that, with the exception of unbranded generics, 2018 drug prices in the United States were substantially higher than those in other countries. The United States had lower prices for unbranded generics than most comparator countries. Unbranded generics account for 84 percent of U.S. prescription drug volume—a much larger share than the 35 percent for the OECD comparison countries—but only 12 percent of prescription drug spending at manufacturer prices. In contrast, brand-name originator drugs accounted for only 11 percent of U.S. prescription drug volume and 82 percent of U.S. prescription drug spending. Overall, the United States' considerable unbranded generic market share and low average unbranded generic prices did not fully offset higher brand-name originator prices.

The magnitude of the difference between prices in the United States and those in other countries was substantial. For all drugs, U.S. prices were 256 percent of prices in other countries. U.S. prices for brand-name originator drugs were 344 percent of prices in other countries. U.S. prices for unbranded generics were 84 percent of prices in other countries. Although different methodological decisions did change the magnitude of results, the overall pattern of higher drug prices in the United States was generally consistent—again, with the exception of unbranded generics. All G7 comparator countries had lower prices than the United States; France, Italy, and the United Kingdom had particularly low prices across drug categories regardless of methodological decisions.

The results of our study provide evidence that prescription drug prices are higher in the United States than in comparison countries. These results are consistent with the existing literature. Although we apply an estimated adjustment to U.S. prices to approximate rebates and other discounts applied to manufacturer prices as one of our sensitivity analyses, we recognize that the resulting prices will almost certainly differ from the actual net price to payers for individual presentations. We also recognize that resulting price indices will understate differences between prices in the United States and other countries because they adjust only U.S. prices downward even though rebates and similar discounts are increasingly common in other countries.

Future analyses should examine the association between purchasing power and drug prices across countries. We also recommend studying specific active ingredients and presentations that contribute most to the differences in aggregate prices between the United States and other countries, and we recommend long-term tracking of price indices that are relevant to the nascent U.S. biosimilars market.

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We thank Amber Jessup, Kenneth Finegold, Zeid El-Kilani, and Nancy De Lew at the U.S. Department of Health and Human Services, Office of the Assistant Secretary for Planning and Evaluation, for their contributions throughout our project and the development of this report. We also thank Christine Eibner and Erin Taylor of RAND and Patricia Danzon of the University of Pennsylvania for their suggestions and comments as peer reviewers of this report. We are indebted to Arwen Bicknell for her careful editing of the report.

Abbreviations

ASPE	Office of the Assistant Secretary for Planning and Evaluation
CPI	Consumer Price Index
G7 countries	Canada, France, Germany, Italy, Japan, the United Kingdom, and the United States
GDP	gross domestic product
N/A	not applicable
OECD	Organisation for Economic Co-operation and Development
PBM	pharmacy benefit manager
PPP	purchasing power parity
SU	standard unit
UK	United Kingdom

1. Introduction and Background

Annual U.S. spending on prescription drugs was recently estimated at $457 billion.[10] Even after adjusting for general inflation, U.S. prescription drug spending increased by 76 percent from 2000 to 2017,[11] and spending is expected to increase at a higher rate than other areas of health care over the next decade.[12] Much of the increase in drug spending is expected to come from new advances in medicine, such as expensive specialty drugs.[13] At the same time, the list prices for existing drugs are increasing.[14]

Previous research demonstrates that spending on prescription drugs is higher in the United States than in other countries on a per capita basis but is relatively similar as a share of total health care spending.[15] The volume of dispensed drugs, the mix of dispensed drugs, and prices per drug all contribute to higher U.S. spending on drugs—which, in turn, contributes to higher health insurance premiums and higher out-of-pocket spending by patients on health care more broadly.

The relationships among volume, mix, and price are complex. But if the volume and mix of drugs are the same and prices are higher, this will translate directly to higher spending on drugs. The robust policy discussion surrounding U.S. prescription drug prices focuses on whether prices in the United States are too high or appropriate relative to the benefits that they offer to patients. Although comparisons of U.S. drug prices with those in other countries are useful for informing this discussion, the most recent systematic comparison of international drug prices used data that are almost a decade old.

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[10] Office of the Assistant Secretary for Planning and Evaluation (ASPE), "Observations on Trends in Prescription Drug Spending," Washington, D.C.: U.S. Department of Health and Human Services, ASPE Issue Brief, March 8, 2016.

[11] Rabah Kamal, Cynthia Cox, and Daniel McDermott, "What Are the Recent and Forecasted Trends in Prescription Drug Spending?" Kaiser Family Foundation, February 20, 2019. (Calculations based on the chart titled "Nominal and Inflation-Adjusted Per Capita Spending on Retail Prescription Drugs, 1960–2017.")

[12] Andrea M. Sisko, Sean P. Keehan, John A. Poisal, Gigi A. Cuckler, Sheila D. Smith, Andrew J. Madison, Kathryn E. Rennie, and James C. Hardesty, "National Health Expenditure Projections, 2018–27: Economic and Demographic Trends Drive Spending and Enrollment Growth," *Health Affairs*, Vol. 38, No. 3, February 20, 2019.

[13] IQVIA Institute for Human Data Science, *Medicine Use and Spending in the U.S.: A Review of 2017 and Outlook to 2022*, Durham, N.C., April 19, 2018. This report notes that specialty drugs, many of which are new drugs, accounted for a large share of U.S. spending growth in recent years.

[14] Inmaculada Hernandez, Chester B. Good, David M. Cutler, Walid F. Gellad, Natasha Parekh, and William H. Shrank, "The Contribution of New Product Entry Versus Existing Product Inflation in the Rising Costs of Drugs," *Health Affairs*, Vol. 38, No. 1, 2019.

[15] Dana O. Sarnak, David Squires, and Shawn Bishop, "Paying for Prescription Drugs Around the World: Why Is the U.S. an Outlier?" webpage, Commonwealth Fund, October 5, 2017.

The Importance of Systematic International Drug Price Comparisons

Systematic comparisons of drug *prices* among countries are based on data from a broad set of drugs, and, unlike comparisons of drug *spending* among countries, they focus narrowly on differences in prices absent the influences of different volumes and mixes of drugs.[16] Results from systematic comparisons of drug prices are more generalizable than comparisons of prices for individual or small samples of drugs. As a result, these systematic comparisons are more helpful as an input in the development of policies that are designed to address high prices overall or for certain categories of prescription drugs.

In this report, we describe the methods and challenges involved in systematically comparing drug prices among countries, summarize prior studies presenting results of systematic comparisons of drug prices among countries, and present updated descriptive comparisons of prices between the United States and Organisation for Economic Co-operation and Development (OECD) countries using 2018 data. The prior studies that we describe in our literature review were published between 2004 and 2013 and used even older data, which highlights the importance of our updated empirical analysis.

The Motivation for Price Indices

Calculating the average price for drugs in one country by dividing total drug sales and volume yields a result that reflects both prices and the volumes and mixes of drugs used. Volumes and mixes of drugs can vary from country to country on many dimensions, such as the following:

- volume per capita
- mix of *active ingredients* (i.e., specific molecules or combinations of molecules)
- mix of *presentations* (i.e., prices and quantities can be calculated narrowly for each combination of an active ingredient, formulation, and strength)
- mix of manufacturers for each active ingredient and presentation
- mix of brand-name originator, brand-name non-originator, and unbranded generic drugs
- mix of drugs that reach patients through retail outlets, health care facilities, and other channels.

Without addressing differences in volume and mix, a comparison of average prices in two countries says as much about differences in the "market baskets" of drugs in those countries as it does about prices directly.

Differences between countries in terms of prescription drug volume can be addressed by scaling the volume in other countries to match the volume in a target country (e.g., the United States) on a per capita basis. Addressing differences in the mix of drugs is more challenging.

[16] Comparisons of prescription drug spending involve volume and mix in addition to price. Some studies attempt to decompose differences in spending along these dimensions. See, for example, Sarnak, Squires, and Bishop, 2017.

Without some adjustment, differences in the average prices of drugs could just as easily be the result of a difference in the mix of drugs as it could the result of an actual difference in prices. For example, if the mix of drugs in the United States contains a greater number of expensive brand-name originator drugs than the mix in a comparator country, then the resulting difference in average price could be the result of a difference in mix, a difference in price, or both.

Price Indices as a Tool to Compare Prices Across Markets

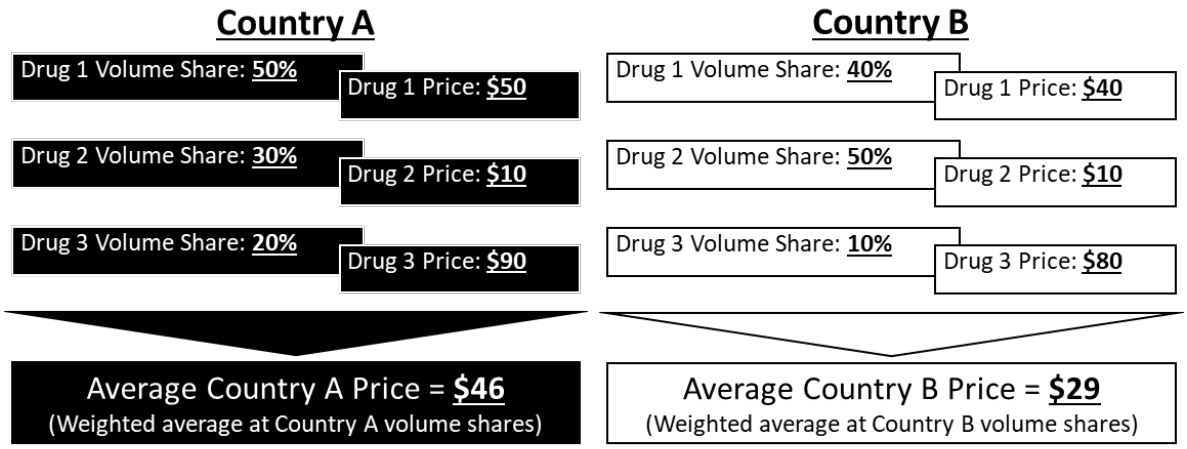
Creating a price index rather than looking at specific prices is an approach used to compare differences in prices for a basket of goods over time or across markets (such as countries). The best-known price index—the Consumer Price Index (CPI)—is calculated by the U.S. Department of Labor's Bureau of Labor Statistics and compares prices for a broad market basket of consumer goods over time. The approach that serves as the foundation for the CPI can be used to compare prices for market baskets of prescription drugs between countries.

The rationale behind price indices is that a comparison of prices is most meaningful when it focuses on prices alone without the risk of interference from differences in volume and/or mix. Price indices accomplish this by holding market baskets constant while allowing prices to vary.

Figures 1.1 and 1.2 illustrate the differences in these approaches and the results from calculating an average drug price difference between "Country A" and "Country B" across a hypothetical set of three drugs. Figure 1.1 reports average volume-weighted prices in Country A and Country B without the price index approach ($46 in Country A and $29 in Country B). The result—that Country A's prices are 159 percent of those in Country B on average—is driven by differences in prices and by each drug's volume weight in each country. Figure 1.2 illustrates a price index approach, in which the Country A volume weights are held constant.[17] The result—that Country A prices are 118 percent of those in Country B on average at Country A volume weights—is driven by price alone.

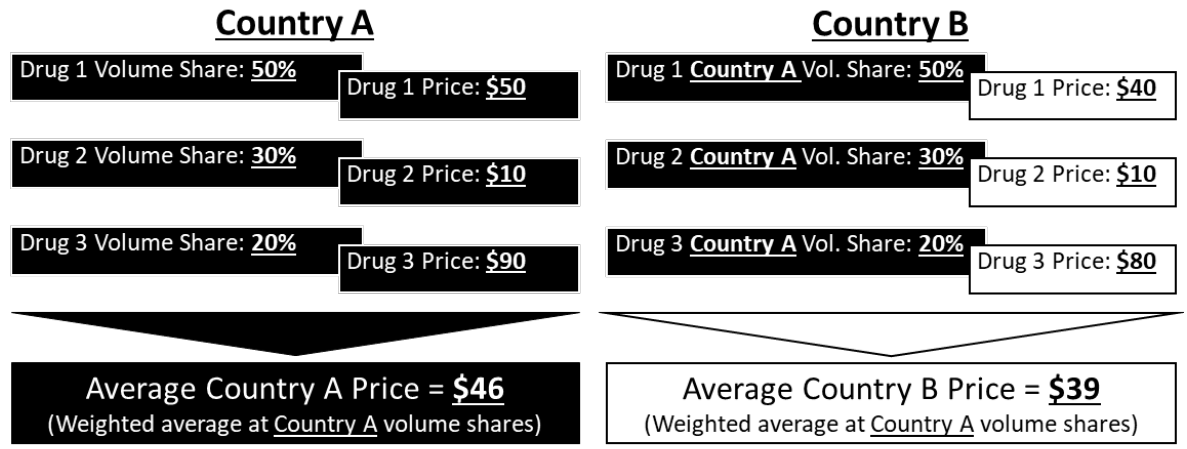
[17] The decision of whether to use U.S. volume weights, another country's volume weights, or some blend of the two is an important one that must be made when implementing the price index approach. The key point is that whichever specific volume weight is chosen, it should be held constant when calculating prices in both countries.

Figure 1.1. Illustrative Average Price Comparison, Without the Price Index Approach



Result of Comparison: Country A prices are 59% higher than Country B prices on average. This result is driven by differences in both price and mix.

Figure 1.2. Illustrative Average Price Comparison, with the Price Index Approach



Result of Comparison: Country A prices are 18% higher than Country B prices holding US volume shares constant.

Methodological Decisions Related to Calculating Price Indices

Although price indices facilitate comparison of prices, their implementation requires several methodological decisions, many of which have the potential to substantively affect the magnitude and generalizability of calculated prices. The following are the key decisions that must be made:

- **Which drugs to include in the analysis.** Price can be compared for the top drugs by U.S. sales or volume, all drugs sold in the United States and one or more comparison countries, brand-name originator drugs, unbranded generic drugs, or many other subsets of drugs. Another option is to compare prices for a set of drugs sold in many countries or every country. Because of differences in competitive and regulatory landscapes, there are relatively few drugs sold both in the United States and in each of many comparison countries. As an alternative, analyses can include drugs sold in the United States and individual comparison countries (in "bilateral" comparisons of prices). Certain sets of drugs—for example, vaccines or drugs sold over the counter—can be excluded from the basket because they have very different patterns of prices compared with other drugs.
- **Which prices to use.** The price for prescription drugs can be measured at different levels, such as the prices at which drugs are sold to wholesalers ("manufacturer prices") or the prices offered to the public by retail pharmacies, which include both wholesale and retail markups ("retail prices"). Although prices net of rebates and other discounts paid by manufacturers after drugs are dispensed are particularly relevant in the United States, these prices are generally not available to researchers.
- **The granularity of prices and quantities.** For example, prices and quantities can be calculated narrowly for each combination of an active ingredient, formulation, and strength or more broadly at the active ingredient level or the therapeutic class level.
- **The units for measuring sales and volume.** Sales can be measured in local currencies or U.S. dollars converted using exchange rates. Volume is usually measured in terms of standard units—standardized units of volume based on counting pills or 5mL of a drug, depending on formulation—or in terms of kilograms of active ingredient.
- **The basis for calculating volume weights**. Volume weights are used to hold the mix of drugs constant. For comparisons between the United States and other countries, U.S. volume weights, other-country volume weights, or blended shares are used.
- **Whether to exclude outliers**. Quantity and sales data sometimes result in extremely high or low prices in a market that can have significant leverage over the resulting calculated price index. These outlier values can be excluded from the market basket.
- **The presentation of adjusted or unadjusted price indices.** Prior studies adjusted price index results to account for differences in per capita gross domestic product (GDP) purchasing power parity (PPP) or for differences in health care system and drug market characteristics.

The Choice of Price to Use in Comparisons

The choice of which price to use warrants additional discussion. Prices to payers that are net of rebates from manufacturers and other discounts are likely the prices that are most relevant to ongoing policy discussions in the United States.[18] These prices reflect the set of complex business arrangements that have evolved over time among payers, pharmacy benefit managers (PBMs), and drug manufacturers. U.S. health insurers often work with a PBM to develop

[18] The net price to payers is importantly different than the net price received by drug companies. The difference between these two prices reflects margins retained by distributors, pharmacies, and other organizations along prescription drug supply chains.

prescription drug formularies and benefit designs and to negotiate rebates with drug manufacturers. PBMs use formularies to negotiate lower prices from manufacturers by offering larger shares of volume—driven by such tools as tiered formularies, with preferred drugs tied to lower cost-sharing for patients and fewer authorization steps for prescribing. PBMs realize these lower negotiated prices by collecting rebates from drug manufacturers. The net prices to individual payers are unknown because rebates from manufacturers are considered trade secrets.

Although PBMs are able to negotiate lower prices, the extent to which they pass the lower prices on to health plans (which can then pass savings on to consumers through lower premiums) is not well understood. If a large portion of the rebates and other discounts is passed on to payers, then PBMs could offer value by reducing prescription drug spending even if they retain a share of the discounts. One 2017 study suggests that PBMs retain 7 percent of U.S. spending on prescription drugs.[19] Estimates of the magnitude of rebates tend to be higher, with one 2018 study estimating rebates of 23 percent.[20] Another recent study suggests that U.S. net prices—including rebates and other discounts—are 28 percent lower than wholesale prices.[21]

In other countries, the functions performed by PBMs in the United States are typically performed by government or quasi-governmental entities, often in conjunction with direct and indirect price controls on drugs. Discounts that would not be reflected in manufacturer sales and prices are increasingly important in other countries.[22] For example, German sickness funds (similar to U.S. insurers) receive statutory rebates that are not reflected in manufacturer sales. In the United Kingdom, patient access scheme discounts and formulary-based rebates are not reflected in manufacturer sales.

Although prices to payers net of rebates and all discounts are particularly relevant to U.S. policymakers and payers, data on prices measured in this way are generally not available to researchers. As a result, manufacturer and retail prices have been used for prior price comparisons. The resulting price indices are calculated using manufacturer or retail prices that are likely often substantially higher than prices to payers net of rebates and other discounts. We return to this issue as a limitation of our price index approach in Chapter 4.

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[19] Neeraj Sood, Tiffany Shih, Karen Van Nuys, and Dana Goldman, "Flow of Money Through the Pharmaceutical Distribution System," Los Angeles, Calif.: Leonard D. Schaeffer Center for Health Policy & Economics, June 6, 2017.

[20] Charles Roehrig, *The Impact of Prescription Drug Rebates on Health Plans and Consumers*, Ann Arbor, Mich.: Altarum Institute, April 2018.

[21] IQVIA Institute for Human Data Science, *Medicine Use and Spending in the U.S.: A Review of 2018 and Outlook to 2023*, Durham, N.C., May 9, 2019b.

[22] Ulf Persson and Bengt Jonsson, "The End of the International Reference Pricing System?" *Applied Health Economics and Health Policy*, Vol. 14, No. 1, February 2016.

Report Overview

Each of the methodological decisions we have described can affect the results of systematic price comparisons. In Chapter 2, we compare several studies identified through our literature review, highlighting their methodological decisions and main results. In Chapter 3, we describe the methodological decisions that we made in our new analyses using 2018 data; we also present our main results, our results for several subsets of drugs, and our results from sensitivity analyses in which we varied methodological decisions. Chapter 4 contains a discussion on the usefulness, limitations, and future directions for price index–based systematic international comparisons of drug prices.

2. Prior Studies Presenting Results from Systematic Comparisons of Drug Prices Between Countries

We identified peer-reviewed articles, reports, and other sources that reported comparisons of drug prices between countries by searching such databases as PubMed and Google Scholar.[23] Additional sources were suggested by reviewers. We selected relevant documents for full review based on their title and, when available, abstracts. Of the 16 studies initially selected for review,[24] five reported results from systematic comparisons of U.S. drug prices with those in other countries using a price index approach (see Table 2.1). We abstracted the following information from these five studies:

1. methods for price comparisons
2. prices for baskets of drugs, by country and by drug category
3. prices for individual drugs, by country
4. reasons cited or hypothesized by the authors to drive the price differences.

[23] We used the search terms "drug" AND ("price" OR "payment") AND ("comparison" OR "index") AND "international."

[24] Patricia Danzon and Michael F. Furukawa, "Prices and Availability of Pharmaceuticals: Evidence from Nine Countries," *Health Affairs*, supplemental web exclusives, 2003; U.S. Department of Commerce, International Trade Administration, *Pharmaceutical Price Controls in OECD Countries: Implications for US Consumers, Pricing, Research and Development and Innovation*, Washington, D.C., 2004; U.S. Department of Health and Human Services Task Force on Drug Importation, *Report on Prescription Drug Importation*, Washington, D.C., December 2004; Patricia Danzon and Michael F. Furukawa, "Prices and Availability of Biopharmaceuticals: An International Comparison," *Health Affairs,* Vol. 25, No. 5, 2006; Patricia Danzon and Michael F. Furukawa, "International Prices and Availability of Pharmaceuticals in 2005," *Health Affairs*, Vol. 27**,** No. 1, January/February 2008; Guk-Hee Suh, Anders Wimo, Serge Gauthier, Daniel O'Connor, Manabu Ikeda, Akira Homma, Jacqueline Dominguez, and Bong-Min Yang, "International Price Comparisons of Alzheimer's Drugs: A Way to Close the Affordability Gap," *International Psychogeriatrics*, Vol. 21, No. 6, December 2009; Panos Kanavos and Sotiris Vandoros, "Determinants of Branded Prescription Medicine Prices in OECD Countries," *Health Economics, Policy and Law*, Vol. 6, No. 3, 2011; Panos Kanavos, Alessandra Ferrario, Sotiris Vandoros, and Gerard F. Anderson, "Higher US Branded Drug Prices and Spending Compared to Other Countries May Stem Partly from Quick Uptake of New Drugs," *Health Affairs*, Vol. 32, No. 4, 2013; Robert Langreth, Blacki Migliozz, and Ketaki Gokhale, "The U.S. Pays a Lot More for Top Drugs Than Other Countries," Bloomberg, December 18, 2015; Aaron S. Kesselheim, Jerry Avorn, and Ameet Sarpatwari, "The High Cost of Prescription Drugs in the United States: Origins and Prospects for Reform," *JAMA*, Vol. 316, No. 8, 2016; Sarnak, Squires, and Bishop, 2017. As of September 26, 2018; Philip Savage, Sarah Mahmoud, Yogin Patel, and Hagop M. Kantarjian, "Cancer Drugs: An International Comparison of Postlicensing Price Inflation," *Journal of Oncology Practice*, Vol. 13, No. 6, 2017; Lito E. Papanicolas, David L. Gordon, Steve L. Wesselingh, and Geraint B. Rogers, "Not Just Antibiotics: Is Cancer Chemotherapy Driving Antimicrobial Resistance?" *Trends in Microbiology*, Vol. 26, No. 5, 2018; Patented Medicine Prices Review Board, *Meds Entry Watch, 2016*, Ottawa: Government of Canada, June 2018; Emily Miller, "U.S. Drug Prices vs. the World," Drug Watch, January 25, 2018; ASPE, "Comparison of US and International Prices for Top Spending Medicare Part B Drugs," Washington, D.C.: U.S. Department of Health and Human Services, October 25, 2018.

We standardized the price indices reported in the five source studies so that the comparison country price was set to 100 and U.S. prices were expressed relative to other-country prices in order to facilitate comparisons.[25] After standardization, a price index of 50 indicates that U.S. prices were 50 percent of those in the comparison country; a price index of 150 indicates that U.S. prices were 150 percent of those in the comparison country.[26]

Summary of Reviewed Studies

The five studies that we reviewed used IQVIA's MIDAS prescription drug sales and volume data.[27] They also all used price indices to compare prices between countries, similar to the approach that we used for our own analysis.

IQVIA's MIDAS Data

The MIDAS data contain estimates of prescription drug sales and volume that are based on audits of prescription drug transactions in each source country. The audit methodology varies from country to country, but the MIDAS data generally are an estimate of all prescription drug sales regardless of distribution channel.[28] Both manufacturer and retail sales are available in MIDAS data.[29]

Price Index Methodological Decisions

The studies varied in the key decisions necessary to calculate price indices as summarized in Table 2.1 and as we will describe further in this section. In particular, Danzon and Furukawa, along with Kanavos and Vandoros, presented results from different approaches to comparing prices, such as comparing active ingredient-level with presentation-level prices, using different

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[25] For example, if comparison Country A has a reported price index value of 20 and the United States has a reported value of 50, we set Country A's value to 100 and standardized the U.S. value by the calculation *(50/20) * 100* to get a standardized value of 250.

[26] As a further example, if the market basket of drugs cost $150 in the United States and $100 in a comparison country, the reported price index would be 150.

[27] IQVIA was IMS Health when these studies were conducted. MIDAS is a data set that allows analysis of sales and volume data for prescription and other drugs from more than 90 countries. (IQVIA, "MIDAS," webpage, undated.)

[28] Author analysis of IQVIA MIDAS sales and volume data for calendar year 2018 (run date October 28, 2019). There are some exceptions. For example, data for Chile, Greece, Mexico, and the Netherlands do not capture drugs dispensed via hospitals, and data for the United States exclude Puerto Rico.

[29] The audits underlying the MIDAS data can express price and sales values at either the ex-manufacturer, ex-wholesaler, or retail levels. MIDAS then applies a set of country- and channel-specific markups to calculate the default ex-manufacturer sales level. IQVIA's manufacturer sales values might include any discounts that are reflected in the invoices paid at the point in the distribution chain at which IQVIA audits, in cases where average pack price is determined from sales invoices. For example, volume discounts are typically reflected in the IQVIA manufacturer sales; rebates paid by manufacturers to PBMs or insurers are not. In countries where the pack price is determined from a set list price, discounts are not included at all. IQVIA retail sales include pharmacy markups and dispensing fees.

volume weights, and comparing over different periods.[30] In general, these decisions had important implications for the magnitude of the price differentials.

The **U.S. Department of Commerce** report calculated active ingredient-level price indices to compare U.S. prices with prices in nine other OECD countries (Australia, Canada, France, Germany, Greece, Japan, Poland, Switzerland, and the United Kingdom). The Commerce report used 2004 MIDAS data on the top 60 active ingredients as determined by 2002 U.S. sales, excluding nine active ingredients that were combination products (i.e., drugs with multiple constituent active ingredients). The report stated that prices in the comparison countries were lower than in the United States, but adjusting for differences in per capita GDP lessened these differences and, in some cases (such as Switzerland), led to a finding that prices in the United States were lower. These lower prices in the comparison countries were attributed to rigorous direct and indirect price controls.[31]

Table 2.1. Comparison of Price Index Methodology Across Five Studies

Study	Data	Comparison Countries	Methodology
U.S. Department of Commerce (2004)	MIDAS, 2004	Australia, Canada, France, Germany, Greece, Japan, Poland, Switzerland, the United Kingdom, and the United States	Active ingredient–level price index using top 60 drugs by U.S. sales, excluding combination drugs; used brand-name and unbranded drugs
Danzon and Furukawa (2006)	MIDAS, 2004–2005	Australia, Canada, France, Germany, Italy, Japan, Mexico, Spain, the United Kingdom, and the United States	Presentation-level price index weighted by U.S. volume; used biologics only
Danzon and Furukawa (2008)	MIDAS, 2005	Australia, Brazil, Canada, Chile, France, Germany, Italy, Japan, Mexico, Spain, the United Kingdom, and the United States	Presentation-level price index weighted by U.S. volume; used brand-name and unbranded drugs
Kanavos and Vandoros (2011)	MIDAS, 2004	Australia, Austria, Belgium, France, Germany, Greece, Italy, Japan, Mexico, Portugal, Slovakia, Spain, Sweden, the United Kingdom, and the United States	Active ingredient–level price index weighted by volume in each country; used only brand-name originator and brand-name non-originator drugs
Kanavos et al. (2013)	MIDAS, 2005, 2007, and 2010	Germany, Italy, Spain, the United Kingdom, and France	Active ingredient–level price indices using country-specific and U.S. volume weights; used only on-patent brand-name originator drugs

SOURCE: U.S. Department of Commerce, International Trade Administration, 2004; Danzon and Furukawa, 2006; Danzon and Furukawa, 2008; Kanavos and Vandoros, 2011; Kanavos et al., 2013.
NOTES: The methods described in the table are often one of several sets of results presented in the source studies. The dates with the MIDAS data refer to the time period of sales used in each study.

Danzon and Furukawa used MIDAS data to calculate price indices for several comparison countries using U.S. volume weights as a main approach.[32] Their 2006 paper used 2004–2005

[30] Danzon and Furukawa, 2008; Kanavos and Vandoros, 2011.

[31] U.S. Department of Commerce, International Trade Administration, 2004.

[32] Danzon and Furukawa, 2006; Danzon and Furukawa, 2008.

data to compare prices for biologic drugs in the United States with those of nine comparison countries.[33] Their 2008 paper used 2005 data to examine prices for a broader set of drugs and compare U.S. prices with prices in 11 other countries (Australia, Brazil, Canada, Chile, France, Germany, Italy, Japan, Mexico, Spain, and the United Kingdom). This later paper adjusted U.S. prices by estimates of rebate amounts from the Medicaid prescription drug rebate program, and it adjusted prices for some drugs in Germany to reflect mandatory rebates on products exempt from reference pricing. In general, U.S. prices were 20–40 percent higher than those in other countries. However, both Japan and Mexico had higher prices than the United States on average. After adjusting for differences in per capita income, U.S. prices were similar to those in other countries and much lower than prices in Brazil, Chile, and Mexico. The 2008 study also found that on a per capita basis, U.S. patients use fewer drugs than patients in most of the comparison countries and use a much larger share of newly launched drugs than all comparison countries.

The reports by **Kanavos and Vandoros and by Kanavos et al.** used MIDAS data to calculate active ingredient-level price indices for 15 OECD countries during 2004 and 2007 and for France, Germany, Italy, Spain, the United Kingdom, and the United States during 2005, 2007, and 2010, respectively.[34] Both studies were limited to brand-name drugs. The 2011 study was broader in scope and included brand-name non-originator drugs, whereas the 2013 study focused more narrowly on the top 68 on-patent brand-name originator drugs with the highest combined sales across countries. Both studies found that prices in the United States were higher than those in comparison countries. The 2011 study tested whether adjusting for differences in regulatory and reimbursement structure, per capita income, and product age explains the observed differences in prices. After adjusting for these characteristics, the differences between U.S. and comparison country prices were not statistically significant, implying that the United States has higher drug prices because of these observable differences. With more-recent data, the 2013 study found that the United States had higher prices for on-patent brand-name originator drugs but that the higher rates of usage of new drugs explained a large portion of the price difference. The authors attributed a portion of this difference to the use of health technology assessment mechanisms that reduce the use of low-value drugs in comparison countries. As Danzon and Furukawa did for their 2008 paper, Kanavos et al. adjusted U.S. prices by an estimate of rebates paid by manufacturers to PBMs and insurers, basing these adjustments on Medicaid prescription drug rebate program discounts.

All five of the studies described here use price index approaches that are similar to the approach that we used for our own analysis, which we will describe later. Although a 2004 report

[33] Danzon and Furukawa note that there is no standard definition of what constitutes a *biologic* versus a *nonbiologic* drug. For the purposes of this report, we use the assignment provided in the MIDAS data. (Danzon and Furukawa, 2006.)

[34] Kanavos and Vandoros, 2011; Kanavos et al., 2013.

by the U.S. Department of Health and Human Services used similar methods,[35] we do not compare results from this study with those from other studies because the report did not present results in tabular form. More recently, the Canadian Patented Medicine Prices Review Board used 2016 MIDAS data to compare prices for patented drugs between Canada and comparison countries, including the United States.[36] We do not compare the Review Board's results with those from other studies because its comparison used Canadian volume weights (unlike other studies, which used U.S. volume weights or blended volume weights). Other sources report price comparisons for individual drugs. In the following sections, we summarize results from the five price index studies identified by our literature review and then turn to a brief summary of results from other sources, such as comparisons of prices for individual drugs.

Price Comparisons by Category of Drugs

The figures in this chapter summarize the reported prices from these studies for all drugs included in the studies (Figure 2.1), for brand-name originator drugs (Figure 2.2), for unbranded generic drugs (Figure 2.3), and for biologics. Specific sources and countries are reported in the figures to the extent that results were available in the source studies. We selected results using U.S. volume weights for presentation. Although we assembled results from these studies into the same figures for ease of comparison, we strongly caution that the studies differ from one another in many ways—such as the time period studied, methodology used (e.g., using presentation-level data versus active ingredient–level data), and countries studied.

Prices for All Drugs Included in Analyses

Figure 2.1 presents aggregate drug prices in each of the comparison countries relative to prices in the United States as listed in three studies.[37] Drug prices are generally higher in the United States when analyzing all drugs together, including brand-name originator and unbranded generic drugs. For example, the first column in the figure indicates that prices in the United States were 143 percent of those in Australia, according to Danzon and Furukawa. As we have noted, the considerable variation in estimates for individual comparison countries across sources is likely the result of differences in measurement approach and time frame. Most importantly, Kanavos and Vandoros analyzed only brand-name drugs, including generics marketed under a brand name.[38]

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[35] U.S. Department of Health and Human Services Task Force on Drug Importation, 2004.

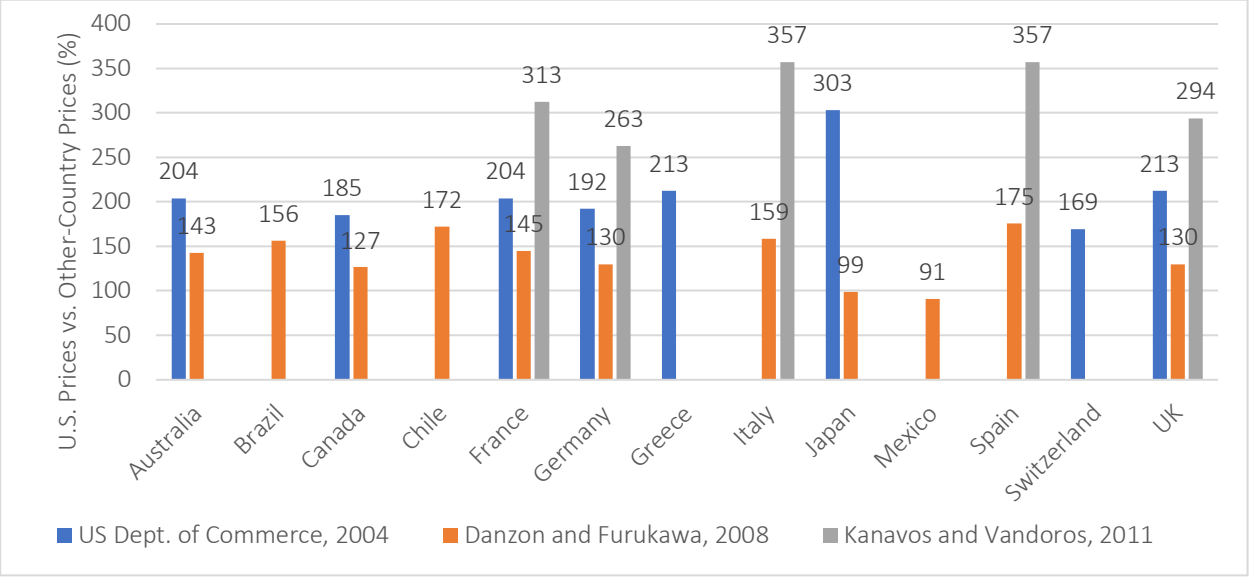
[36] Patented Medicine Prices Review Board, 2018.

[37] U.S. Department of Commerce, International Trade Administration, 2004; Danzon and Furukawa, 2008; Kanavos, and Vandoros, 2011. We present unadjusted results to facilitate comparison across studies. As noted, several studies presented results controlling for differences in per capita GDP and other factors separately.

[38] Kanavos et al., 2013, is omitted from this section because this later study focused more narrowly on on-patent brand-name drugs with high sales.

Although the point estimates vary considerably, there is consistency across studies in the relative ranking of price differences (e.g., all studies, regardless of measurement specifications, indicate that prices in Germany are closer to those in the United States than they are to prices in most other comparison countries). With the exception of Japan and Mexico, U.S. prices were at least 30 percent higher than those in each comparison country across all studies. Prices in Japan were lower than U.S. prices in the 2004 U.S. Department of Commerce study but higher in Danzon and Furukawa's 2008 study. These differences could be because Danzon and Furukawa used presentation-level data and the U.S. Department of Commerce used active ingredient–level data. Presentations in Japan differ significantly from presentations elsewhere particularly because dosages tend to be weaker.[39] The only estimate for Mexico indicates that prescription drug prices are 10 percent higher there than in the United States.

Figure 2.1. U.S. Prescription Drug Prices as a Percentage of Other-Country Prices, All Drugs



SOURCES: Danzon and Furukawa, 2008: Kanavos and Vandoros, 2011; U.S. Department of Commerce, International Trade Administration, 2004.
NOTES: Other-country prices are set to 100. Data are reported only if available in the cited study. The presented results from each study do not make adjustments for per capita GDP PPP or other differences between countries.

Brand-Name Originator Drugs

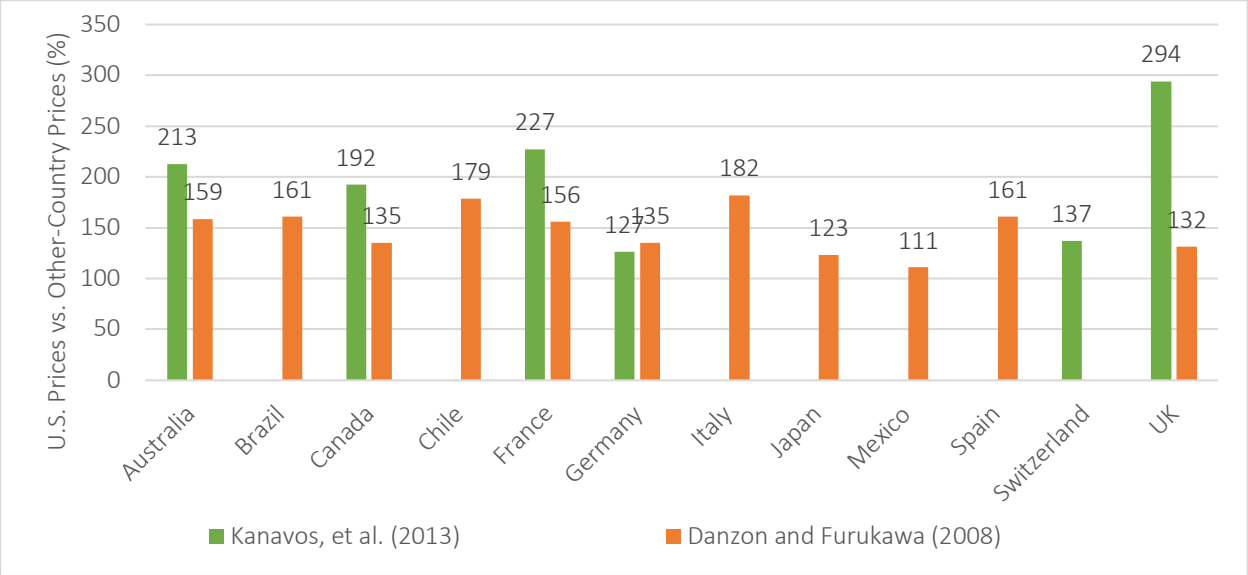
Two studies compared prices for brand-name originator drugs separately, although the studies used different approaches to identify brand-name originator drugs.[40] Compared with

[39] Danzon and Furukawa, 2008.

[40] Danzon and Furukawa, 2008; Kanavos et al., 2013. Danzon and Furukawa analyzed single-source originators. Kanavos et al. used combined sales across countries to analyze the top 68 on-patent brand-name drugs that were sold in each country in 2010, most of which were likely single-source originators.

prices across all drugs, focusing on brand-name originator drugs suggests even higher U.S. prices in most cases than those in other countries (Figure 2.2). Estimated U.S. prices ranged from 111 percent of prices in Mexico to 294 percent of prices in the United Kingdom.

Figure 2.2. U.S. Prescription Drug Prices as a Percentage of Other-Country Prices, Brand-Name Originator Drugs



SOURCES: Kanavos et al., 2013; Danzon and Furukawa, 2008.
NOTES: Other-country prices are set to 100. Data are reported only if available in the cited source.

Generic Drugs

Only one study reported results from a systematic comparison of generic drug prices.[41] U.S. prices for generic drugs ranged from 46 percent of prices in Mexico to 93 percent of prices in France (Figure 2.3).

Biologic Drugs

Danzon and Furukawa reported prices for biologics in a figure but not in tabular form.[42] When analyzing data at the presentation and therapeutic class levels, they found that prices for biologics in Australia, France, Germany, Italy, Japan, and the United Kingdom were higher than those in the United States and that prices in Canada, Mexico, and Spain were lower.

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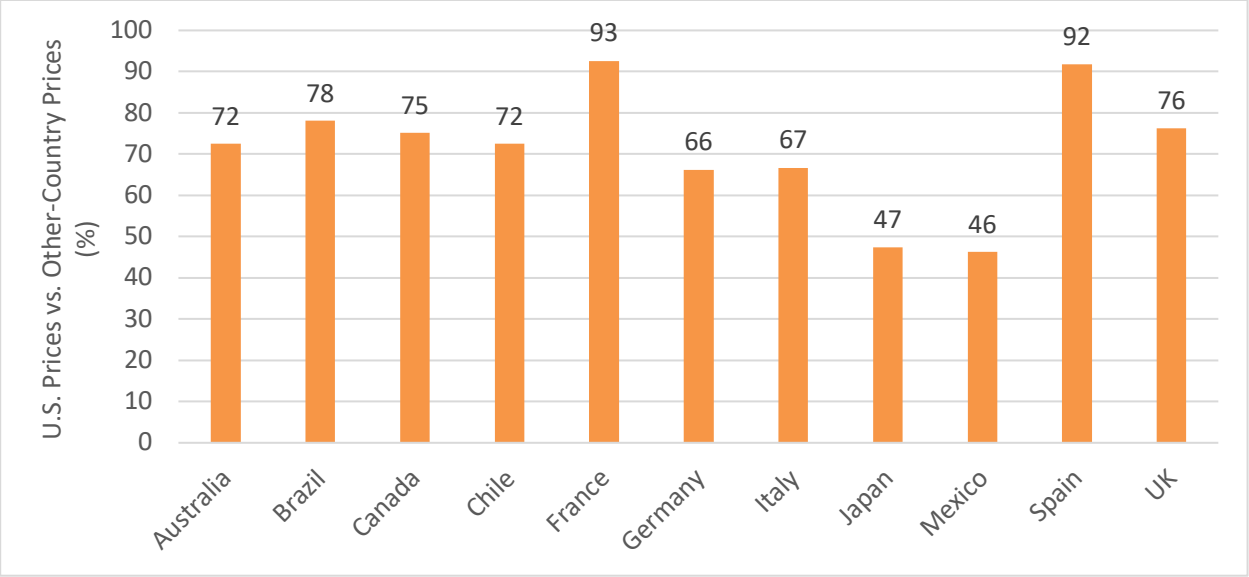
[41] Danzon and Furukawa, 2008, reports price indices calculated for unbranded and branded generics combined. The U.S. Department of Health and Human Services report does not present results from a systematic comparison of generic prices but reports comparisons of generic prices for a narrower set of 29 top-selling generics based on 2002 U.S. sales, and it lists findings of generally lower prices in the United States than in other countries. U.S. Department of Health and Human Services Task Force on Drug Importation, 2004.

[42] Danzon and Furukawa, 2006, exhibit 2.

Figure 2.3. U.S. Generic Drug Prices as a Percentage of Other-Country Prices



SOURCE: Danzon and Furukawa, 2008.
NOTES: Other-country prices are set to 100. Data are reported only if available in the cited source.

Implications of Methodological Changes on Price Comparisons

Each of the studies that reported price index–based differentials was based on decisions regarding which country weights would be used for analysis.[43] Many of the studies presented results using U.S. volume weights, other-country volume weights, and blended volume weights separately. In general, the choice of weighting approach did have a significant impact on the resulting price differential. For example, by using U.S. volume weights rather than other-country weights, Kanavos et al. widened the differential between U.S. and other-country prices in most markets (Australia, Canada, France, and the United Kingdom).[44] This study also presented results using retail and manufacturer prices and found that other-country prices were generally closer to U.S. prices when retail prices were used instead of manufacturer prices. This indicates that wholesale and/or retail markups are typically smaller in the United States than in other countries.

Price Comparisons for Specific Drugs and Small Samples of Drugs

The studies discussed in this chapter so far compare drug prices across a wide set of drugs rather than individual drugs or small numbers of drugs. We reviewed other sources that

[43] U.S. Department of Commerce, International Trade Administration, 2004; Danzon and Furukawa, 2008; Kanavos and Vandoros, 2011; Kanavos et al., 2013.

[44] Kanavos et al., 2013.

presented price comparisons for much smaller sets of drugs (e.g., the top seven drugs by sales in the United States) and sometimes for individual drugs. Comparing prices for specific drugs or narrow sets of drugs might not yield results that are representative of broader price differences because each specific drug represents a small share of total utilization and spending. Furthermore, relevant factors that affect drug prices—such as substitute drugs on market, provider prescribing patterns, and intellectual property—also differ by country. Despite these considerations, we found that the patterns observed are broadly similar when U.S. prices for specific drugs or small sets of drugs are compared with prices in other countries.

Comparing the average monthly prices of seven top-selling drugs in the United States in 2015, one study found that prices after estimated rebates are higher in the United States than in France, Canada, and Germany.[45] Results were similar when comparing prices of cancer drugs; U.S. prices were higher than those observed in Australia, Canada, France, Germany, Japan, and the United Kingdom.[46] Price comparisons of Alzheimer's drugs, in contrast, demonstrated mixed results: U.S. prices are higher than prices in some countries and lower than prices in others.[47]

One recent analysis from ASPE compared prices between the United States and other countries for about 30 drug products that account for a large share of Medicare Part B payments for prescription drugs.[48] We did not categorize this analysis as a systematic comparison of drug prices because of its relatively narrow focus. See Appendix A for a description of this study and a comparison of its methods with the methods we used for this report.

[45] Kesselheim, Avorn, and Sarpatwari, 2016.

[46] Savage et al., 2017; Papanicolas et al., 2018.

[47] Suh et al., 2009.

[48] ASPE, 2018. The number of drug products included in the analysis was 27 when volume was measured in kilograms of active ingredient and 30 when volume was measured in standard units.

3. Price Index–Based Drug Price Comparisons Using 2018 Data

In this chapter, we describe the data and methods for our own comparisons of drug prices between the United States and OECD countries, present results from our main approach, and compare the main results with those from a range of sensitivity analyses using different sets of drugs or approaches.

Data

We used 2018 IQVIA MIDAS data for the United States and the following 32 OECD countries:[49]

Australia	France	Lithuania	Slovakia
Austria	Germany	Luxembourg	Slovenia
Belgium	Greece	Mexico	South Korea
Canada	Hungary	Netherlands	Spain
Chile	Ireland	New Zealand	Sweden
Czech Republic	Italy	Norway	Switzerland
Estonia	Japan	Poland	Turkey
Finland	Latvia	Portugal	United Kingdom

Our IQVIA data extract listed sales for specific drugs in terms of quarterly 2018 manufacturer amounts paid in U.S. dollars converted at quarterly exchange rates and quarterly volume measured in terms of standard units.[50] Each row in the IQVIA extract is defined by a combination of country; manufacturer; sector (retail or hospital); active ingredient;[51] formulation and route of administration of the drug; strength of the drug; over-the-counter indicators; and indicators for whether the drug was a brand-name originator drug, a brand-name non-originator drug, or an unbranded generic drug. Each record at this level lists volume and sales for the four

[49] Author analysis of IQVIA MIDAS sales and volume data for calendar year 2018 (run date October 28, 2019). Data were not available for three OECD countries: Denmark, Iceland, and Israel.

[50] *Manufacturer amounts paid* refers to the sale price paid to manufacturers by wholesalers or distributors. These prices might reflect bulk and other discounts paid at this point in the distribution chain. These prices do not include retail markups or rebates paid from manufacturers to insurers. Note that IQVIA MIDAS data do include other prices, including retail prices, although our extract did not include these prices. Instead, IQVIA provided a set of adjustment factors that can be applied to manufacturer prices as a way to convert them to retail prices. A *standard unit* is a pill for oral solid drug presentations and 5mL for liquid, infused, injected, and other presentations.

[51] The active ingredient of a drug is the molecule that has a biologic impact or effect. Most drugs have a single active ingredient (such as simvastatin). Some drugs have multiple active ingredients (such as ezetimibe and simvastatin). We defined the active ingredient for combination drugs with multiple active ingredients as the full list of active ingredients.

quarters in our data. Our initial data extract consisted of 739,580 records across all drugs and the selected comparison countries. We excluded 154,995 records for over-the-counter drugs because these were out of scope for our analyses and have markedly different prices across countries. We excluded 37,871 records that did not have positive volume or sales.

We aggregated records that shared the same country and presentation (that is, the same active ingredient, formulation and route of administration, and dosage strength) into a single country-presentation-level record by summing sales and volume.[52] We aggregated by presentation rather than by active ingredient to address concerns that differences in the mix of presentations relating to active ingredients could be driving differences in price. We calculated U.S. and other-country unit prices by dividing presentation-level sales by presentation-level volume. After consultation with IQVIA, we excluded 32 country-presentation records with incorrect sales and/or volume data.[53] We also excluded 35 blood factor active ingredients from our analysis because of inconsistencies across country and channel markets in how volume was measured for these drugs in MIDAS.[54]

Descriptive Results on Drug Markets

Table 3.1 compares 2018 prescription drug market size for all OECD countries with data available for analysis in an extract from IQVIA's MIDAS data set (run date October 28, 2019). Across OECD countries in our data, we calculated total sales of $795.2 billion and total volume of 1,016.2 billion standard units. The United States accounted for 58.4 percent of sales but only 24.0 percent of volume. The ratio of sales to volume weight is much higher in the United States than in any other country; without addressing issues around the mix of drugs, this is an initial sign that U.S. prices are much higher than those in other countries. Japan, by comparison, accounted for 9.2 percent of sales and 21.0 percent of volume.[55]

There are also important differences in the mix of drugs between countries, such as the relative contributions of brand and generic drugs to sales and volume totals. Table 3.2 presents the share of drug sales and volume from brand-name originator drugs, brand-name non-originator drugs, and unbranded drugs for each country. Brand-name originator drugs are those marketed by the original developer of the drug (i.e., the originator manufacturer). Brand-name

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[52] As an example, one of the resulting rows of data from this step is U.S. sales and volume in 2018 for atorvastatin 10mg film-coated tablets. There was a separate row for this same presentation in each country and separate rows for different presentations (e.g., 20mg film-coated tablets) in each country.

[53] We excluded pertuzimab presentations in Italy, aclidinium bromide presentations in Canada, ranibizumab presentations in Germany, and gadobenic acid presentations in Hungary.

[54] Blood factors accounted for a total of 0.1 percent of volume and 0.6 percent of sales across all countries.

[55] The OECD countries in the analysis include eight of the ten countries globally with the most spending on prescription drugs in 2018 (the exceptions are China and Brazil). IQVIA Institute for Human Data Science, *The Global Use of Medicine in 2019 and Outlook to 2023*, Durham, N.C., January 29, 2019a.

non-originator drugs are uncommon in the United States and are typically competing "branded generic" versions of off-patent drugs marketed under brand names.[56] Most generic drugs in the United States are unbranded generics.

Table 3.1. Prescription Drug Market Shares by Sales and Volume, 2018

	Sales (billions, U.S. dollars)	Volume (billions, standard units)	Share of Sales (%)	Share of Volume (%)
All countries	**795.2**	**1,016.2**	**100.0**	**100.0**
United States	**464.0**	**243.4**	**58.4**	**24.0**
All countries, excluding United States	**331.2**	**772.7**	**41.6**	**76.0**
Japan	73.2	213.7	9.2	21.0
Germany	39.9	58.4	5.0	5.7
France	31.3	50.0	3.9	4.9
Italy	30.7	43.7	3.9	4.3
United Kingdom	23.7	60.5	3.0	5.9
Spain	23.3	45.2	2.9	4.4
Canada	19.6	28.4	2.5	2.8
Korea	13.6	45.9	1.7	4.5
Australia	8.8	14.3	1.1	1.4
Turkey	6.6	63.9	0.8	6.3
Poland	6.2	27.1	0.8	2.7
Belgium	5.6	8.3	0.7	0.8
Mexico	5.5	14.2	0.7	1.4
Switzerland	5.3	5.2	0.7	0.5
Austria	4.8	6.3	0.6	0.6
Sweden	4.3	8.1	0.5	0.8
Netherlands	3.9	13.0	0.5	1.3
Portugal	3.8	9.6	0.5	0.9
Greece	2.9	9.5	0.4	0.9
Czech Republic	2.8	8.1	0.3	0.8
Finland	2.6	4.9	0.3	0.5
Norway	2.5	4.2	0.3	0.4
Hungary	2.4	7.9	0.3	0.8
Ireland	2.3	4.0	0.3	0.4
Chile	1.4	4.2	0.2	0.4
Slovakia	1.4	4.1	0.2	0.4
New Zealand	1.0	5.0	0.1	0.5
Slovenia	0.7	1.4	0.1	0.1
Lithuania	0.5	1.6	0.1	0.2
Latvia	0.3	1.0	<0.1	0.1
Luxembourg	0.2	0.4	<0.1	<0.1
Estonia	0.2	0.7	<0.1	0.1

SOURCE: Author analysis of IQVIA MIDAS sales and volume data for calendar year 2018 (run date October 28, 2019).
NOTE: The numbers in each column might not sum to totals because of rounding. SU = standard unit.

[56] IQVIA categorizes some brand-name drugs approved in the United States via the 505(b)(2) regulatory approval pathway, such as EpiPen, as brand-name non-originators. Biosimilars are categorized in MIDAS as brand-name originator, brand-name non-originator, or unbranded depending on the product and country. Authorized generics, which are usually generic drugs manufactured and marketed under a license from the originator company, are usually listed in the unbranded generic category rather than the brand-name non-originator category.

Table 3.2. Within-Country Shares of Brand-Name Originator, Brand-Name Non-Originator, and Unbranded Generic Drugs, by Percentage

	Share of Sales: Brand-Name Originator	Share of Sales: Brand-Name Non-Originator	Share of Sales: Unbranded Generic	Share of Volume: Brand-Name Originator	Share of Volume: Brand-Name Non-Originator	Share of Volume: Unbranded Generic
All countries	**78**	**9**	**12**	**27**	**26**	**47**
United States	**82**	**6**	**12**	**11**	**5**	**84**
All countries, excluding the United States	**73**	**13**	**14**	**33**	**32**	**35**
Australia	82	10	8	37	33	30
Austria	76	12	12	47	28	25
Belgium	82	7	11	51	15	34
Canada	75	5	20	22	13	66
Chile	32	60	8	11	43	46
Czech Republic	70	21	8	32	50	18
Estonia	70	19	10	45	33	22
Finland	75	14	11	35	38	27
France	70	9	21	32	19	48
Germany	75	9	16	19	18	63
Greece	73	25	3	55	40	5
Hungary	71	19	9	38	43	19
Ireland	81	9	10	41	36	23
Italy	78	11	11	47	29	25
Japan	78	9	13	36	30	34
Korea	51	43	5	27	66	7
Latvia	68	21	10	36	39	25
Lithuania	71	19	10	42	32	26
Luxembourg	90	7	3	69	22	9
Mexico	45	45	10	18	45	37
Netherlands	67	10	23	18	11	71
New Zealand	76	16	8	23	49	28
Norway	79	11	10	39	20	41
Poland	57	37	6	25	65	11
Portugal	72	14	14	38	27	35
Slovakia	68	24	8	29	54	17
Slovenia	77	19	4	46	50	4
Spain	78	9	14	41	19	40
Sweden	78	12	10	24	29	47
Switzerland	78	9	13	44	29	28
Turkey	52	47	1	32	66	2
United Kingdom	71	9	20	26	12	62

SOURCE: Author analysis of IQVIA MIDAS sales and volume data for calendar year 2018 (run date October 28, 2019).
NOTE: The numbers in each row might not sum to totals because of rounding.

Brand-name originator drugs account for 82 percent of sales but only 11 percent of volume in the United States. Brand-name originator drugs account for a larger share of volume in countries other than the United States (33 percent) but a smaller share of sales (73 percent). The United States has the highest share of volume for unbranded generic drugs (84 percent), and these drugs account for 12 percent of sales compared with 35 percent of volume and 14 percent of sales in

the OECD comparison countries. Brand-name non-originator drugs account for larger shares of both volume (32 percent) and sales (13 percent) in the other OECD countries than in the United States, where they are only 5 percent of volume and 6 percent of sales.

Main Price Index Methodology

We calculated bilateral price indices for the United States versus each other country separately using all of the presentations that had more than 1,000 standard units in volume or $1,000 in sales in both the United States and the individual comparison country.[57] We excluded presentations with low volume or low sales as the first of two steps to prevent outlier presentations from exerting undue influence on our overall results. Less than 0.2 percent of sales and volume across all countries were excluded because of the low volume or sales exclusion criteria (see Appendix Table B.1).

Of the remaining presentations, relatively small shares were present in both the United States and comparison countries to contribute to bilateral comparisons (see Appendix Table B.2). In general, between one-third and two-thirds of presentations above sales and volume thresholds from comparison countries were also above sales and volume thresholds in the United States. Japan is an outlier, with only 18 percent of presentations also sold in the United States. The United States had the largest number of presentations that could contribute to analyses, in part because the United States is the largest market, which increased the likelihood that each presentation was above sales and volume thresholds. Between 10 and 30 percent of presentations above volume and sales thresholds in the United States were also above volume and sales thresholds in other countries. As an example, 6,806 and 4,694 presentation-level records were above volume and sales thresholds for the United States and the United Kingdom, respectively. Of these, only 2,195 matched in both countries.[58]

Presentations that did not contribute to the calculation of a bilateral price index tended to have lower volume and smaller sales in terms of dollars than those that did match. For example, the matched presentations between the United States and United Kingdom (UK) accounted for approximately 56 percent of total volume and 72 percent of total sales in both countries combined. Using active ingredient–level data rather than presentation-level data increased match rates considerably. For example, 51 percent of U.S. active ingredients and 61 percent of UK active ingredients meeting minimum volume and sales thresholds were used for bilateral

[57] This approach allows new drugs launched before or any time during calendar year 2018 to be included in our price indices. There were 33 new drugs first sold in any of our OECD countries in 2018; of these, 16 were sold in the United States in 2019. We excluded presentations with fewer than 1,000 standard units in volume or less than $1,000 in sales because these records tended to have outlier prices.

[58] This represents 31 percent of U.S. presentations and 45 percent of UK presentations meeting volume and sales thresholds.

comparison between the two countries, and these active ingredients accounted for 90 percent of volume and 92 percent of sales in both countries combined.

As a final step, we excluded any remaining presentations where the ratio of prices between the United States and the comparison country was less than 0.01 or greater than 100. This step excluded a small number of presentations from each bilateral comparison and about 1 percent of sales and volume in most countries (see Appendix Table B.3). In exploratory analyses, we found that the most common scenario leading to outlier prices involved presentations with both (a) extremely low volume and relatively high sales in a non-U.S. country and (b) relatively high volume and very low prices in the United States. Some outliers could be the results of inconsistencies in the measurement of sales or volume across markets. It is also possible that the high prices in non-U.S. countries reflect high private-pay amounts outside of a public health care system and price controls. We cannot definitively distinguish between these cases. The differences in prices reported in the MIDAS data might be more relevant to policymakers in the second case. We varied the price ratio exclusion thresholds in a set of sensitivity analyses that we will describe later in this chapter.

These steps resulted in a different number of presentations being analyzed for each pairwise comparison between countries. Table 3.3 compares the starting number of presentations in each country with the final number of presentations used for bilateral comparisons with the United States and the share of starting U.S. and other-country volume and sales that contributed to bilateral comparisons. Appendix Table B.4 replicates Table 3.3 at the active ingredient level rather than the presentation level. Using active ingredient–level data rather than presentation-level data results in larger shares of sales and volume contributing to each comparison. These gains come at the cost of a less-precise overlap with the specific presentations sold. Appendix Table B.5 reports the distribution of volume and sales from presentations contributing to bilateral comparisons across brand-name originator, brand-name non-originator, and unbranded categories (similar to Table 3.2). In general, the presentations contributing to bilateral comparisons accounted for smaller shares of brand-name originator and brand-name non-originator sales and volume than all presentations sold in comparison countries did.

We used U.S. volume weights (i.e., the share of total U.S. volume accounted for by each presentation) to calculate price indices because of our interest in price differences from a U.S. policy perspective. For each bilateral comparison, we calculated a U.S. volume-weighted price equal to the sum of the products of the U.S. volume weights and U.S. prices. Similarly, we calculated an other-country volume-weighted price equal to the sum of the products of the U.S. volume weights and other-country prices. Our reported price indices are the ratio of the U.S. volume-weighted price to the other-country volume-weighted price scaled by 100. We did not adjust price indices by per capita GDP PPP or for other differences across markets. To compare U.S. prices with those in other countries broadly, we calculated a separate "all non-U.S. countries" price index using prices calculated by aggregating sales and volume across all non-U.S. countries in our data. The price indices were calculated as described earlier.

Table 3.3. Number of Presentations Used to Calculate Price Indices

	Total Presentations in the MIDAS Extract	Total Presentations Contributing to Bilateral Comparisons	Other-Country Shares Contributing to Bilateral Comparisons (%)		United States Shares Contributing to Bilateral Comparisons (%)	
			Volume	Sales	Volume	Sales
Australia	3,106	1,765	67.4	76.7	51.8	64.2
Austria	3,913	1,851	51.8	75.2	53.9	69.5
Belgium	3,491	1,736	61.4	74.7	49.1	65.3
Canada	3,571	2,417	75.0	86.0	65.6	72.6
Chile	2,884	1,151	42.5	45.2	45.4	48.2
Czech Republic	2,972	1,436	55.6	69.3	50.3	61.0
Estonia	1,755	898	55.9	68.0	42.6	32.1
Finland	2,926	1,597	59.6	75.0	51.2	67.4
France	4,083	1,884	51.9	73.3	48.0	66.4
Germany	5,804	2,354	60.0	76.3	61.1	73.3
Greece	2,648	1,286	55.1	67.1	48.5	41.6
Hungary	2,624	1,350	55.5	67.4	47.7	53.7
Ireland	3,011	1,664	51.3	81.4	52.9	66.0
Italy	4,964	1,964	52.8	71.5	50.6	69.0
Japan	5,780	1,266	18.0	51.6	31.4	49.2
Korea	4,113	1,607	38.0	58.2	51.6	60.8
Latvia	2,304	1,104	52.5	65.0	44.2	43.9
Lithuania	2,375	1,191	51.1	64.0	47.1	45.0
Luxembourg	2,145	1,110	61.0	73.5	46.4	44.1
Mexico	4,517	1,491	39.3	47.8	51.5	60.0
Netherlands	3,423	1,706	59.8	71.0	56.0	49.4
New Zealand	2,326	1,182	42.9	66.1	44.2	44.9
Norway	2,886	1,621	51.9	74.6	48.7	62.4
Poland	3,646	1,572	55.8	63.7	56.1	52.8
Portugal	4,277	1,794	53.1	70.4	51.8	65.9
Slovakia	2,676	1,354	51.0	66.6	49.2	54.4
Slovenia	2,169	1,210	56.6	73.4	44.3	59.4
Spain	4,596	2,053	54.1	77.1	54.6	70.0
Sweden	3,370	1,822	59.5	76.4	55.4	70.4
Switzerland	3,636	1,773	53.5	79.3	52.7	69.2
Turkey	3,265	1,378	36.4	61.7	50.8	58.6
United Kingdom	6,344	2,484	54.7	75.9	59.1	74.1
United States	7,390	N/A	N/A	N/A	N/A	N/A
All countries, excluding the United States	**30,905**	**4,550**	**42.9**	**68.4**	**85.8**	**89.1**
All countries	**34,021**	**N/A**	**N/A**	**N/A**	**N/A**	**N/A**

SOURCE: Author analysis of 2018 IQVIA MIDAS sales and volume data (run date October 28, 2019).
NOTE: N/A = not applicable.

Additional Analyses

Replicating our main approach using subgroups of presentations by type, we conducted the following additional analyses:

- We compared prices separately for all brand-name originator drugs and for unbranded generic drugs.[59] The latter analysis focuses on drugs typically thought of as generic drugs in the United States. Prior studies found that the United States had relatively low prices for generics and relatively high prices for brand-name originator drugs.[60] We also compared prices for brand-name non-originator and unbranded generic drugs combined (i.e., combining unbranded generics and brand-name non-originator drugs). We did not separately compare prices for biosimilars because of the small number of biosimilars marketed in the United States in 2018.
- Following the approach taken in the U.S. Department of Commerce report,[61] we compared prices for the top 60 drugs by U.S. sales at the active ingredient level, excluding combination products.
- We compared prices for biologics and nonbiologic drugs separately because manufacturer prices might be different across countries for these categories of drugs.
- We compared prices for presentations of active ingredients that were paid for in 2018 by Medicare Part B, Medicare Part D, or both Medicare Part B and Part D.[62] We used Medicare Part B and Part D dashboard data to assign active ingredients to these three categories. We restricted the Part B category to presentations with infused, injected, and ophthalmic formulations, and we excluded presentations with parenteral formulations from the Part D category.[63]
- We compared prices for presentations of active ingredients of different "vintages" based on when they were first sold. We used the "new active substance" field in the MIDAS data to assign active ingredients to five-year launch cohorts. We excluded combination products from this analysis because of the lack of launch timing information for these drugs.
- We also changed individual steps in our main methodology as a series of sensitivity analyses.
- We aggregated sales and volume to the active ingredient level rather than the presentation level to test whether the mix of drugs within active ingredient is driving price differences.

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[59] We excluded a small number of presentations categorized as "unbranded biologics" in MIDAS when we calculated unbranded generic price indices. These presentations tended to be older biologics and not biosimilars (which are usually marketed under a brand name).

[60] Danzon and Furukawa, 2008.

[61] U.S. Department of Commerce, International Trade Administration, 2004.

[62] The Medicare Part B medical benefit covers drugs, including many infused and some injected drugs, administered in physician offices and outpatient facility settings. Medicare Part D covers outpatient drugs dispensed via pharmacies.

[63] The Part B formulation restriction excluded certain oral antineoplastic drugs covered under Part B. The Part D formulation restriction excluded infused or injected presentations covered by Part D plans or erroneously included in the Part D category.

- We calculated price indices using volume weights from comparison countries rather than from the United States. Relatedly, we calculated Fisher indexes using the geometric mean of U.S.-weighted and comparison country–weighted price indices.
- We used retail instead of manufacturer prices to test whether higher wholesale and retail markups in other countries narrow price differences between them and the United States.
- In two separate sensitivity analyses to address the difference between U.S. manufacturer and net prices due to rebates and other discounts, we (1) decreased all U.S. prices by 26 percent and (2) decreased U.S. brand-name originator prices by 33 percent.[64] Although rebates and other discounts that are not reflected in manufacturer and retail sales and prices are increasingly common in other countries, our sensitivity analysis focuses on adjusting just U.S. prices, recognizing that the resulting prices will understate the gap between U.S. prices and other-country prices.
- We used the following alternative price ratio exclusion criteria:
  - no exclusions regardless of low volume, low sales, or extreme price ratios
  - excluding low volume and/or sales presentations only
  - excluding low volume and/or sales presentations and using less-stringent price ratio thresholds (0.1 percent and 1,000x)
  - excluding low volume and/or sales presentations and using more-stringent price ratio thresholds (10 percent and 10x).

Presentation of Results

We illustrate our main results and results from some subsets of drugs and sensitivity analyses in bar charts in which the price index calculated from each bilateral comparison is reported to compare U.S. prices with prices in individual comparison countries (where other-country prices equal 100). The bar charts present results for Canada, France, Germany, Italy, Japan, and the United Kingdom (the Group of Seven [G7] countries, excluding the United States) as well as for Mexico. Results for all analyses, including price indices for other countries and from sensitivity analyses not presented as figures, are in Appendix C.

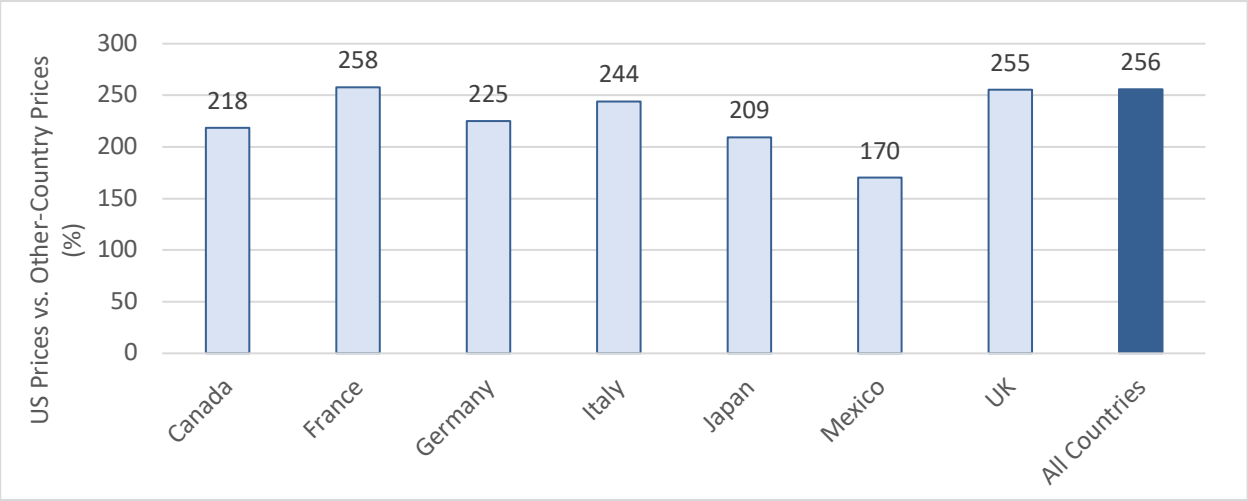
Main Results

Our main results present 2018 price differentials for pairwise comparisons of the United States with a set of other countries (or all 32 OECD comparison countries combined) using presentation-level prices, U.S. volume weights, and all presentations that are sold in both the United States and the comparison market. Other-country prices are equal to 100 for each comparison. Prices in the United States are higher than those in all comparison countries (see

[64] IQVIA Institute for Human Data Science, 2019b. This IQVIA report provided an estimate of U.S. total invoice (i.e., wholesale) spending and net spending on prescription drug products and noted that net spending was 28 percent lower than wholesale spending. Separately, the report noted that net spending was 35 percent lower than wholesale spending for "protected brands" that we considered a close analog to brand-name originators. Using additional adjustment factors provided by IQVIA as part of the MIDAS data documentation, we adjusted both the 28 and 35 percent figures downward to account for the fact that ex-manufacturer prices are lower than wholesale prices. The resulting reductions to U.S. ex-manufacturer prices were 26 percent for all drugs and 33 percent for brand-name originator drugs.

Figure 3.1 for comparisons of U.S. prices with those in Mexico and the G7 countries, and see Appendix C for comparisons with other OECD countries). Each result illustrated in Figure 3.1 reports U.S. prices relative to a comparison country. For example, U.S. prices were 218 percent of prices in Canada (or, alternatively, Canadian prices were 46 percent of U.S. prices). U.S. prices were 256 percent of those in the 32 OECD comparison countries combined. In comparisons with individual countries, U.S. prices ranged from 170 percent of prices in Mexico to 779 percent of prices in Turkey. Among comparisons with individual G7 countries, U.S. prices ranged from 209 percent of prices in Japan to 258 percent of prices in the France.

Figure 3.1. U.S. Prescription Drug Prices as a Percentage of Prices in Selected Other Countries, All Drugs, 2018



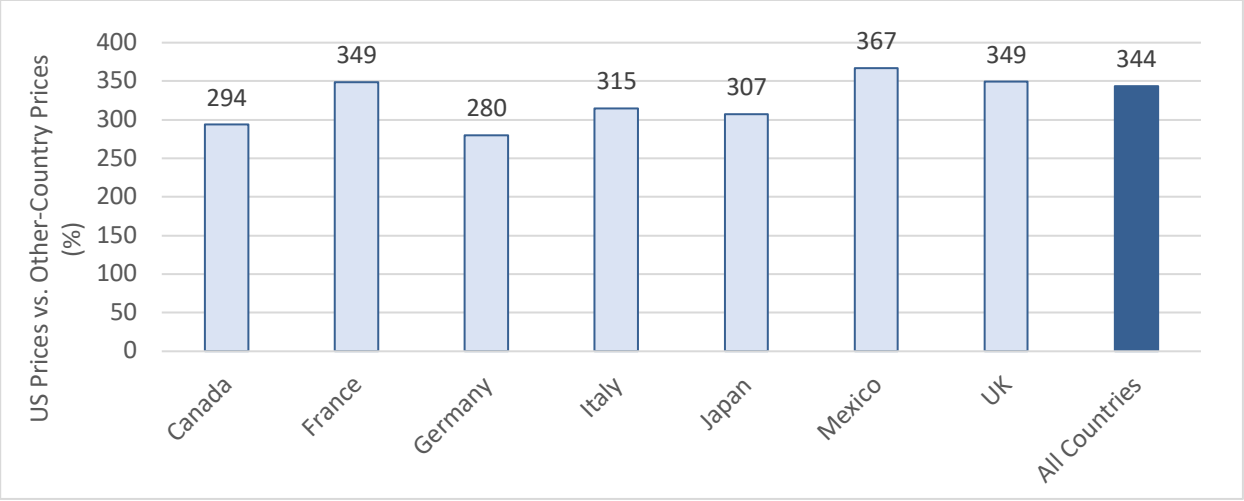
SOURCE: Author analysis of IQVIA MIDAS sales and volume data for calendar year 2018 (run date October 28, 2019).
NOTE: "All countries" refers to all 32 OECD comparison countries combined. Other-country prices are set to 100. Only some presentations sold in each country contribute to bilateral comparisons.

Results for Subsets of Drugs

Figure 3.2 illustrates compared prices for brand-name originator drugs. In aggregate, prices in the United States were 344 percent of those in other countries. U.S. prices were even higher (395 percent of those in other countries) for the top 60 drugs by U.S. sales excluding combination products, all of which are primarily brand-name originator drugs, to mirror the approach in the Department of Commerce study.[65] See Appendix Table C.1 for price indices for the top drugs by U.S. sales.

[65] U.S. Department of Commerce, International Trade Administration, 2004.

Figure 3.2. U.S. Brand-Name Originator Drug Prices as a Percentage of Other-Country Prices, 2018



SOURCE: Author analysis of IQVIA MIDAS sales and volume data for calendar year 2018 (run date October 28, 2019).
NOTE: "All countries" refers to all 32 OECD comparison countries combined. Other-country prices are set to 100. Only some presentations sold in each country contribute to bilateral comparisons.

Figure 3.3 illustrates compared prices for unbranded generic drugs. Overall, U.S. unbranded generic drug prices are 84 percent of those in other countries, and most individual comparison countries have higher prices for unbranded generics than the United States does.[66] Prices in the United States are 43 percent of those in Japan and 68 percent of those in the United Kingdom. Combining brand-name non-originator drugs and unbranded generic drugs does substantively affect results, with many countries showing lower prices than the United States (see Appendix Table C.1).[67] This reversal could be the result of some drugs categorized by IQVIA as brand-name non-originator drugs having high U.S. prices.

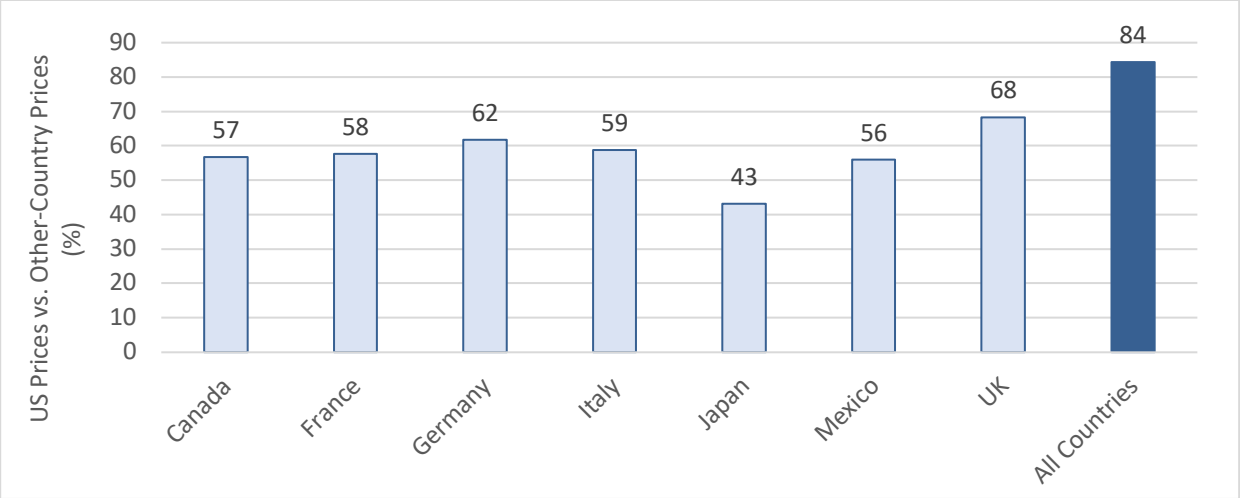
Figures 3.4 and 3.5 illustrate compared prices for biologics and nonbiologics, respectively.[68] U.S. prices are higher than prices in all comparison countries for both biologics and nonbiologics, at 295 percent and 234 percent of prices in all other countries combined, respectively; these higher prices are likely driven by brand-name originator drugs.

[66] These results do not change substantively when unbranded biologics are included with other unbranded generic drugs.

[67] Prices in the United States were 121 percent of those in all other countries combined when unbranded generics and brand-name non-originator drugs were combined.

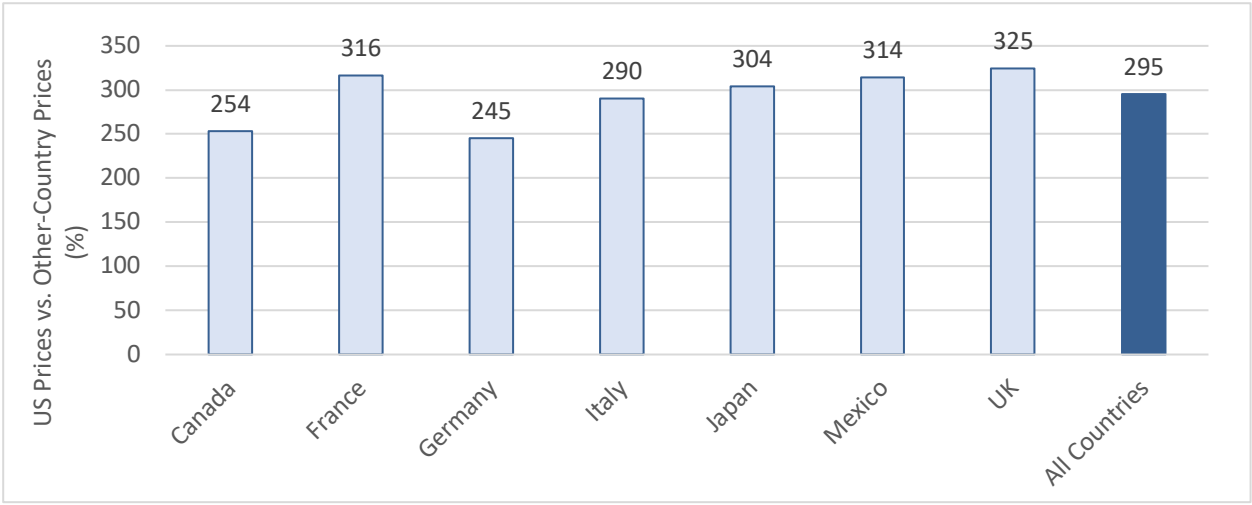
[68] We rely on the assignment of each active ingredient to a biologic and nonbiologic category in MIDAS. Biosimilars are categorized as biologics. Small-molecule brand and generic drugs that are not biologics are categorized as nonbiologics.

Figure 3.3. U.S. Unbranded Generic Drug Prices as a Percentage of Other-Country Prices, 2018



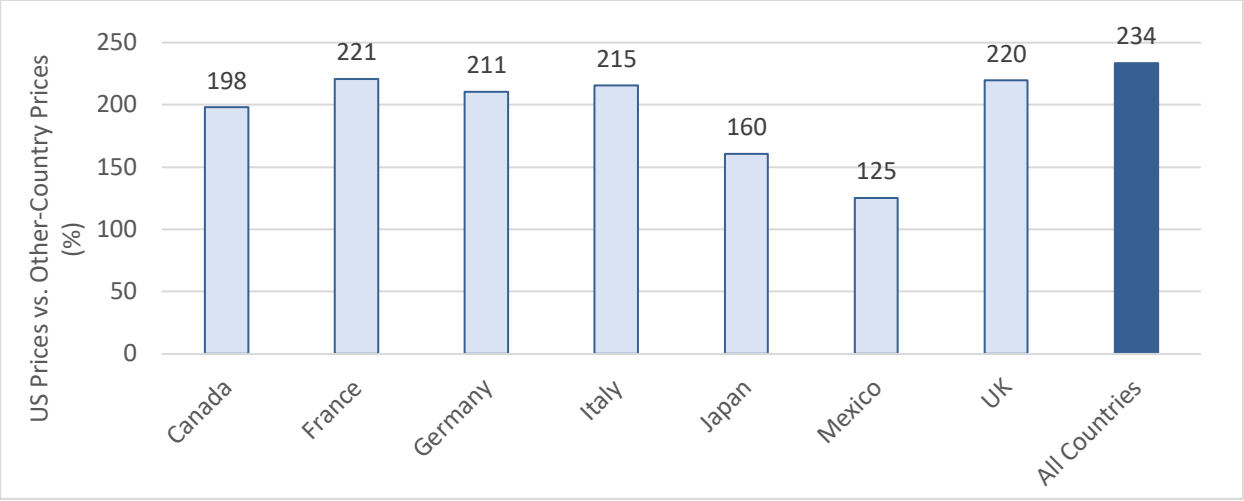
SOURCE: Author analysis of IQVIA MIDAS sales and volume data for calendar year 2018 (run date October 28, 2019).
NOTE: "All countries" refers to all 32 OECD comparison countries combined. Biologics are excluded. Other-country prices are set to 100. Only some presentations sold in each country contribute to bilateral comparisons.

Figure 3.4. U.S. Biologic Prices as a Percentage of Other-Country Prices, 2018



SOURCE: Author analysis of IQVIA MIDAS sales and volume data for calendar year 2018 (run date October 28, 2019).
NOTE: "All countries" refers to all 32 OECD comparison countries combined. Other-country prices are set to 100. Only some presentations sold in each country contribute to bilateral comparisons.

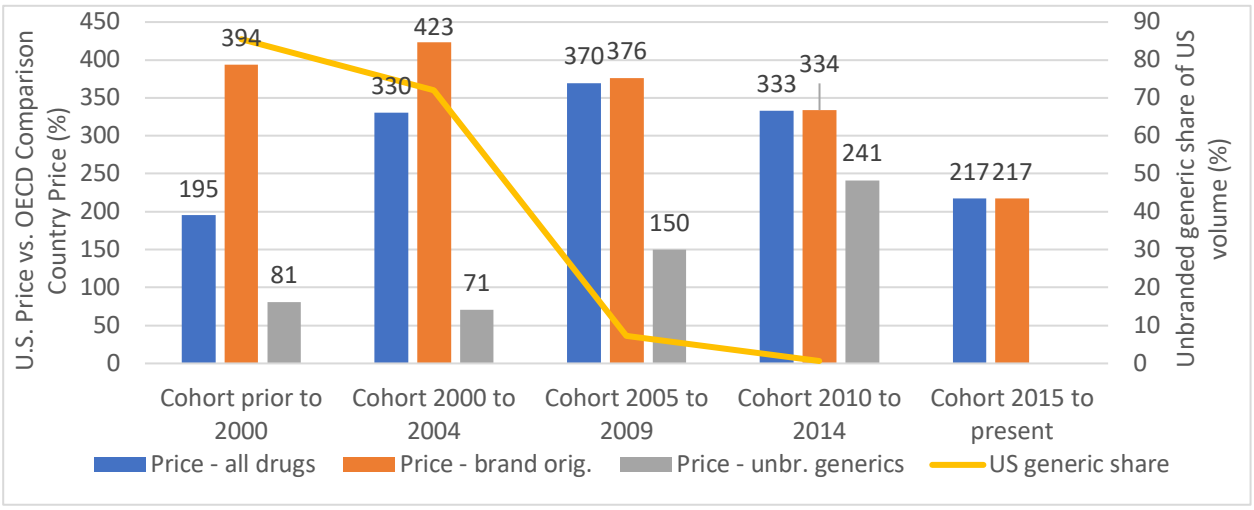
Figure 3.5. U.S. Nonbiologic Drug Prices as a Percentage of Other-Country Prices, 2018



SOURCE: Author analysis of IQVIA MIDAS sales and volume data for calendar year 2018 (run date October 28, 2019).
NOTE: "All countries" refers to all 32 OECD comparison countries combined. Other-country prices are set to 100. Only some presentations sold in each country contribute to bilateral comparisons.

As a final subgroup result, Figure 3.6 compares U.S. prices with the price in OECD comparison countries combined for different cohorts of presentations by the launch date for their active ingredient. For both all drugs and brand-name originator drug cohorts, U.S. prices are higher than prices in comparison countries even for the oldest drugs (i.e., the cohort approved prior to 2000). U.S. prices were much higher for drugs launched more recently, with the exception of the cohort of drugs launched from 2015 to the present. The relatively closer U.S. and comparison country prices for the most recent cohort could be due to several factors, such as compositional changes in the drugs launched each year and the implications of manufacturer launch strategy in comparison countries. Mirroring earlier results, U.S. prices for unbranded generics were lower than prices in comparison countries for earlier launch cohorts. U.S. prices for unbranded generics were higher than those in OECD comparison countries for drugs in more-recent cohorts. This could be partly the result of the 180 days of marketing exclusivity granted to first-to-launch generic manufacturers in the United States. No generic equivalents were available in the United States for drugs launched from 2015 to the present because the originator brands would still have exclusivity.

Figure 3.6. U.S. Prices as a Percentage of OECD Comparison Country Prices by Drug Launch Cohort, 2018



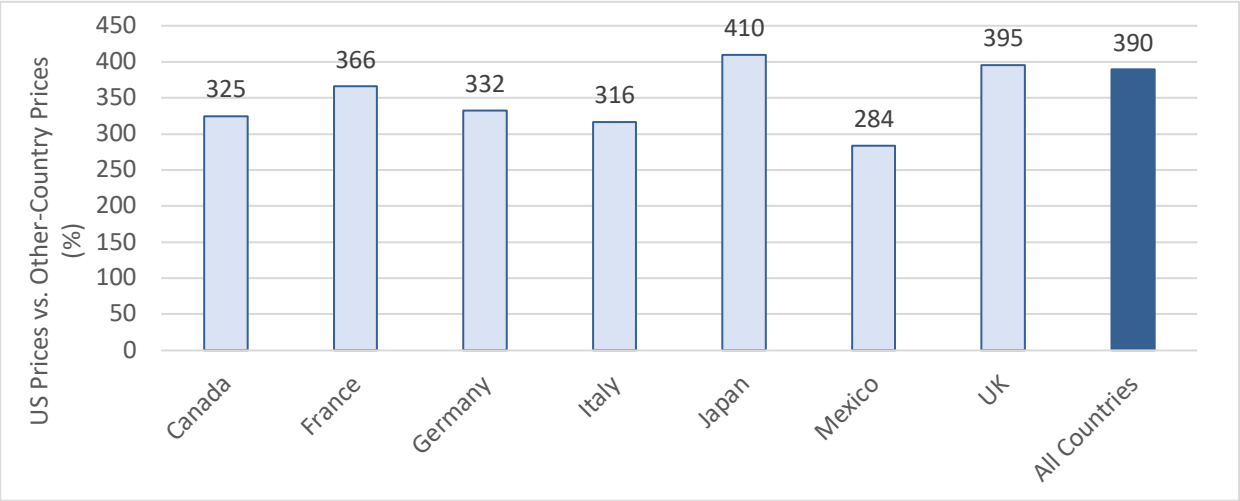
SOURCE: Author analysis of IQVIA MIDAS sales and volume data for calendar year 2018 (run date October 28, 2019).
NOTE: Other-country prices are set to 100. Only some presentations sold in each country contribute to bilateral comparisons. "Brand orig." is the brand-name originator. "Unbr. generics" is the unbranded generic. Combination products are excluded. There were no unbranded generics sold in 2018 for drugs in the 2015 to present cohort. This is likely due to ongoing patent protection and regulatory exclusivity for these drugs.

The United Kingdom, France, and Italy generally have the lowest prices among the comparison countries listed in the figures for all drugs and for brand-name originator, biologic, and nonbiologic drugs separately; Canada, Germany, and Japan tend to have higher prices across each subset of drugs. Other countries—such as Mexico—are less consistent in the relationship of their prices to U.S. prices between figures (with the exception that prices for unbranded generic drugs in Mexico are always lower than U.S. prices). In the case of Mexico, the role of relatively expensive brand-name non-originator drugs compared with U.S. unbranded generics results in prices for all drugs and nonbiologic drugs that are closer to U.S. prices than other comparator countries.

Results from Sensitivity Analyses

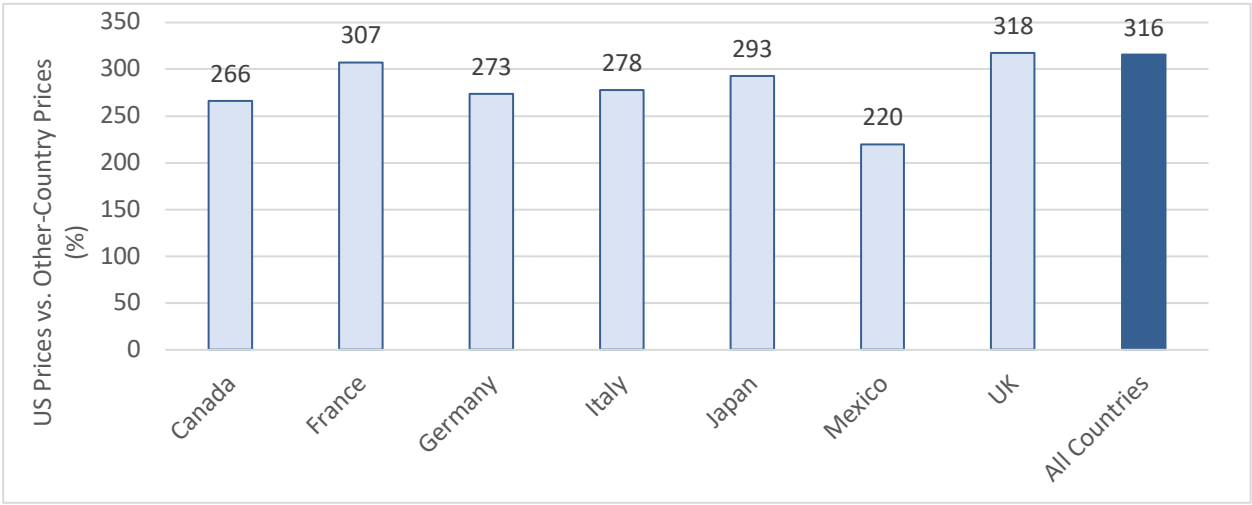
Figures 3.7 and 3.8 present results from a sensitivity analysis using other-country volume weights (Figure 3.7) and blended volume weights (Figure 3.8) rather than U.S. volume weights. Compared with the main results, U.S. prices are even higher than other-country prices in these sensitivity analyses. U.S. prices were 390 percent of those in other countries when using other-country weights and 316 percent of those in other countries when using a blended rate (the geometric mean), compared with 256 percent in our main results. Higher U.S. prices when using other-country weights are expected if prescribing patterns outside the United States are skewed toward drugs with favorable prices in individual countries because of price controls and/or volume purchasing.

Figure 3.7. U.S. Prescription Drug Prices as a Percentage of Other-Country Prices, Other-Country Volume Weights, 2018



SOURCE: Author analysis of IQVIA MIDAS sales and volume data for calendar year 2018 (run date October 28, 2019).
NOTE: "All countries" refers to all 32 OECD comparison countries combined. Other-country prices are set to 100. Only some presentations sold in each country contribute to bilateral comparisons.

Figure 3.8. U.S. Prescription Drug Prices as a Percentage of Other-Country Prices, Blended Volume Weights (Fisher Index), 2018



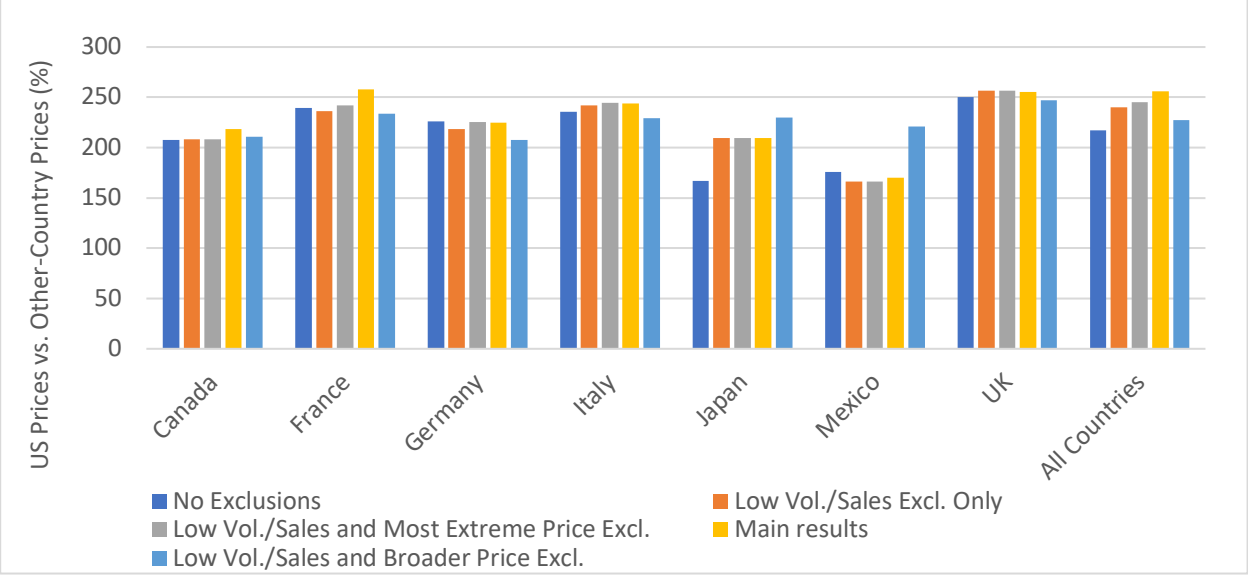
SOURCE: Author analysis of IQVIA MIDAS sales and volume data for calendar year 2018 (run date October 28, 2019).
NOTE: "All countries" refers to all 32 OECD comparison countries combined. Other-country prices are set to 100. Only some presentations sold in each country contribute to bilateral comparisons.

We calculated price indices using four different approaches to excluding presentations with extremely high or low U.S. prices compared with prices in other countries. The first scenario does not contain any exclusions based on volume, sales, or price ratios; the second leaves out presentations in countries with volume less than 1,000 standard units or sales less than $1,000; the third contains an additional exclusion for presentations in countries with prices less than

0.1 percent or 1,000 times greater than that of the U.S. price; the fourth replicates our main results with price ratio thresholds of 1 percent and 100 times; and the last one features a more restrictive price ratio exclusion criteria of 10 percent and 10 times.

Results were generally consistent across these sensitivity analyses (Figure 3.9). Results for each bilateral comparison are in Appendix Table C.2. Omitting all exclusion steps resulted in a larger gap between other-country and U.S. prices than we found in our main results for six countries and a smaller gap between other-country and U.S. prices for 26 countries. The largest relative difference in results was in Hungary, where U.S. prices with and without exclusions were 274 and 210 percent of prices in Hungary, respectively. More aggressive treatment of outlier presentations in terms of price did have relatively large effects on results in some countries (e.g., Japan and Mexico). These additional exclusions might be unnecessarily removing presentations from the analysis in which other-country prices are significantly lower or higher than U.S. prices.

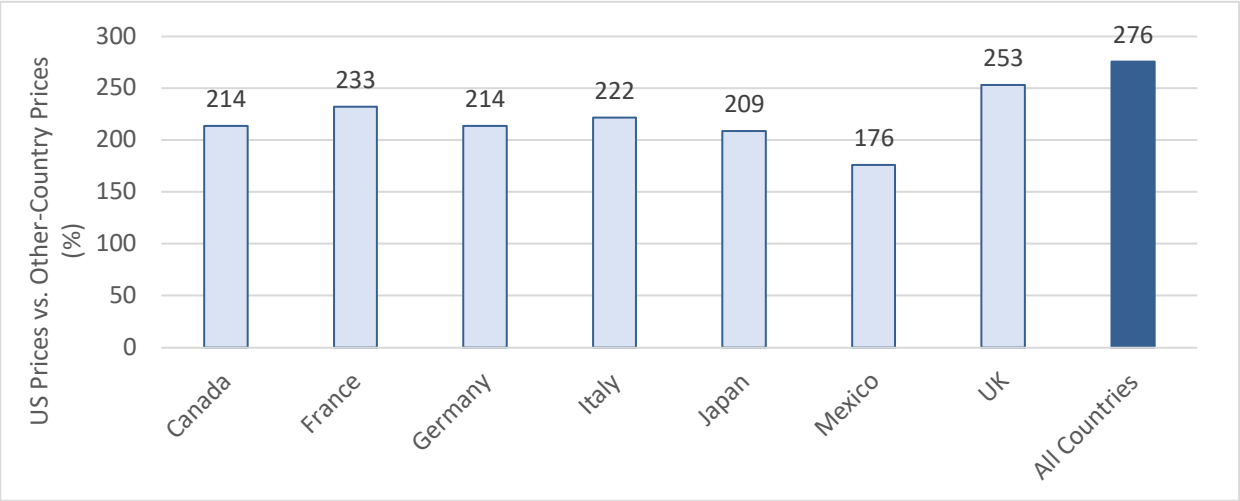
Figure 3.9. U.S. Prescription Drug Prices as a Percentage of Other-Country Prices, Price Outlier Exclusion Sensitivity Analysis Results, 2018



SOURCE: Author analysis of IQVIA MIDAS sales and volume data for calendar year 2018 (run date October 28, 2019).
NOTE: "All countries" refers to all 32 OECD comparison countries combined. Other-country prices are set to 100. Only some presentations sold in each country contribute to bilateral comparisons.

Figure 3.10 presents results from the sensitivity test that compares prices calculated at the active ingredient level instead of at the presentation level. The differences between U.S. and other-country prices are typically slightly larger at the active ingredient level than at the presentation level, but the difference is small. U.S. prices were 276 percent of those in other countries when price indices were calculated using active ingredient–level data; they were 256 percent of other-country prices when using presentation-level data.

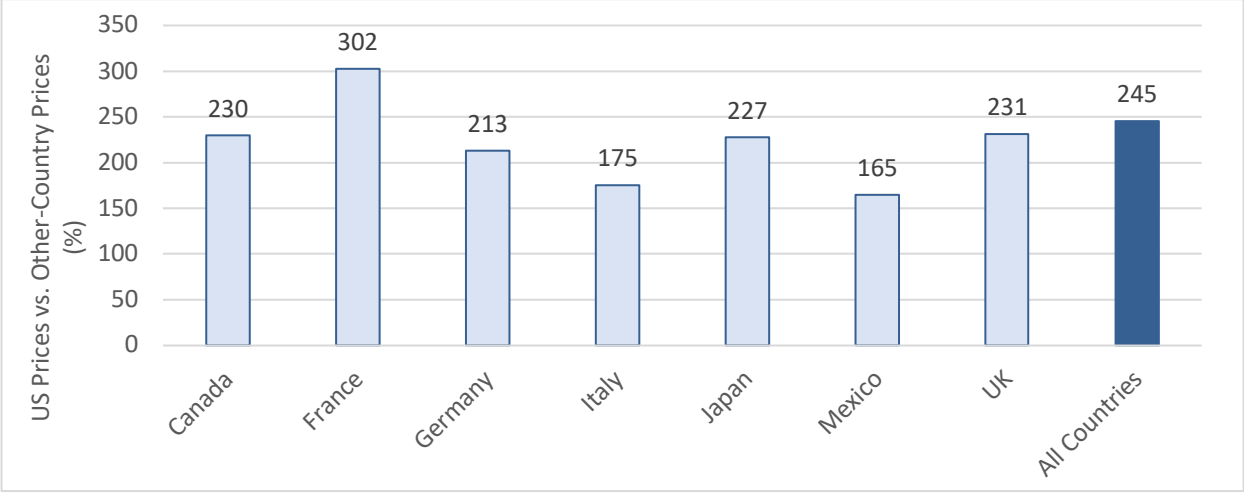
Figure 3.10. U.S. Prescription Drug Prices as a Percentage of Other-Country Prices, Active Ingredient Level, 2018



SOURCE: Author analysis of IQVIA MIDAS sales and volume data for calendar year 2018 (run date October 28, 2019).
NOTE: "All countries" refers to all 32 OECD comparison countries combined. Other-country prices are set to 100. Only some presentations sold in each country contribute to bilateral comparisons.

Figure 3.11 presents price comparisons using retail prices rather than manufacturer prices. U.S. prices are still notably higher than those in other countries (245 percent, compared with 256 percent in our main results using manufacturer prices). Other-country prices increase when using retail prices rather than manufacturer prices in some bilateral comparisons (e.g., Germany, Italy, Mexico, and the United Kingdom), likely because of higher wholesale and retail markups in these countries.

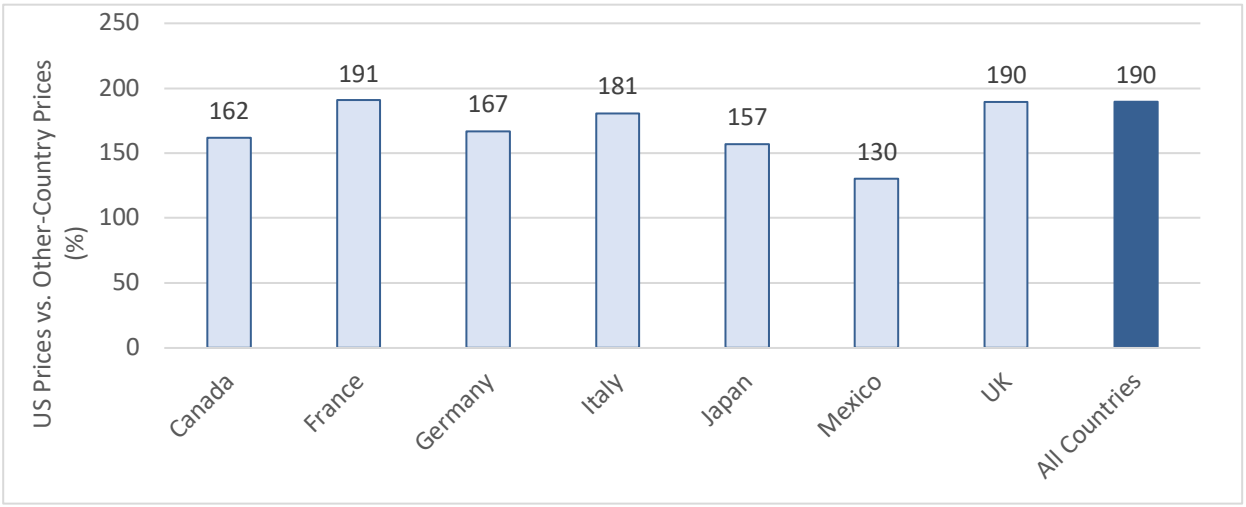
Figure 3.11. U.S. Prescription Drug Retail Prices as a Percentage of Other-Country Prices, 2018



SOURCE: Author analysis of IQVIA MIDAS sales and volume data for calendar year 2018 (run date October 28, 2019).
NOTE: "All countries" refers to all 32 OECD comparison countries combined. Other-country prices are set to 100. Only some presentations sold in each country contribute to bilateral comparisons.

In a final pair of sensitivity analyses, we reduced U.S. prices based on estimates of the relative difference between U.S. manufacturer and net prices due to rebates and other discounts, first for all drugs and then for brand-name originators only.[69] A 26-percent reduction in all U.S. prices yielded U.S. prices that were 190 percent of those in other countries, compared with 256 percent in our main results (Figure 3.12). More narrowly, with a 33-percent reduction to U.S. prices for brand-name originator drugs, U.S. prices for brand-name originator drugs were 230 percent of those in other countries, compared with 344 percent without the adjustment (Figure 3.13). As we have noted, the results from these sensitivity analyses understate differences between prices in the United States and other countries because we have not applied similar adjustments to prices in other countries to reflect rebates and other discounts on manufacturer prices, such as statutory rebates to German sickness funds or patient access scheme discounts in the United Kingdom.[70]

Figure 3.12. U.S. Prescription Drug Prices as a Percentage of Other-Country Prices, U.S. Net Price Adjustment, 2018

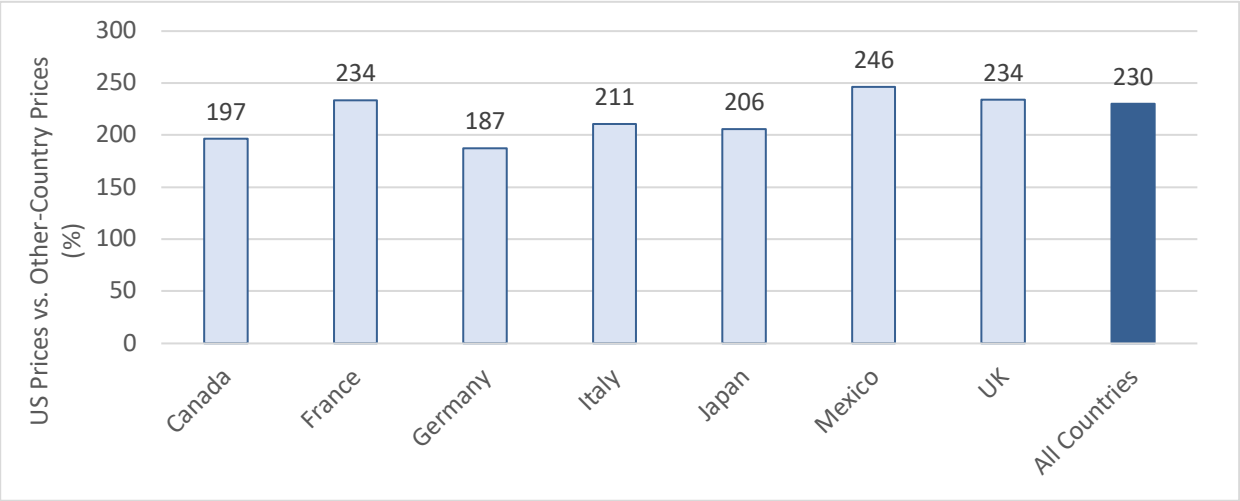


SOURCE: Author analysis of IQVIA MIDAS sales and volume data for calendar year 2018 (run date October 28, 2019).
NOTE: "All countries" refers to all 32 OECD comparison countries combined. Other-country prices are set to 100. Only some presentations sold in each country contribute to bilateral comparisons.

[69] IQVIA (2019b) provides an estimate of U.S. total invoice (i.e., wholesale) spending and net spending on prescription drug products and noted that net spending was 28 percent lower than wholesale spending. Separately, the IQVIA report noted that net spending was 35 percent lower than wholesale spending for "protected brands" that we considered a close analog to brand-name originators. Using additional adjustment factors provided by IQVIA as part of the MIDAS data documentation, we adjusted both the 28 and 35 percent figures downward to account for the fact that ex-manufacturer prices are lower than wholesale prices. The resulting reductions to U.S. ex-manufacturer prices were 26 percent for all drugs and 33 percent for brand-name originator drugs.

[70] Persson and Jonsson, 2016.

Figure 3.13. Brand-Name Originator Drug Prices as a Percentage of Other-Country Prices, U.S. Net Price Adjustment, 2018

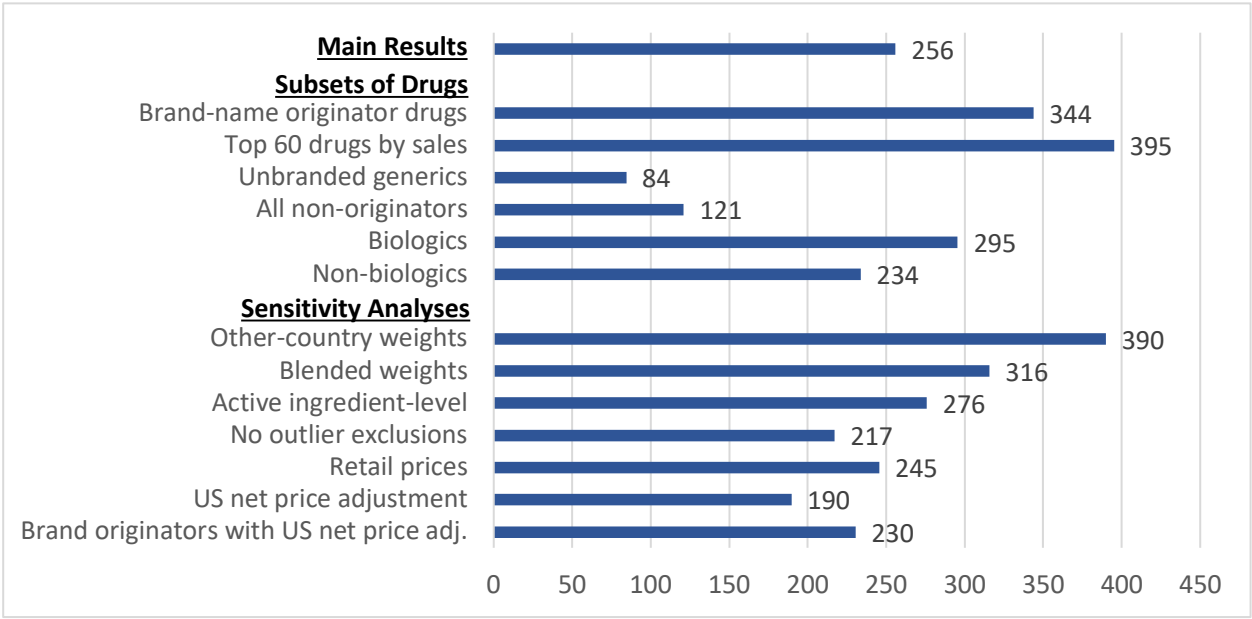


SOURCE: Author analysis of IQVIA MIDAS sales and volume data for calendar year 2018 (run date October 28, 2019).
NOTE: "All countries" refers to all 32 OECD comparison countries combined. Other-country prices are set to 100. Only some presentations sold in each country contribute to bilateral comparisons.

4. Discussion

We found that 2018 drug prices in the United States were substantially higher than those in other countries. The magnitude of the difference between prices in the United States and other countries was substantial. For all drugs, U.S. prices were 256 percent of prices in other countries. U.S. prices for brand-name originator drugs were 344 percent of prices in other countries. Of the subsets of drugs that we looked at, only unbranded generics had lower prices in the United States than in most comparator countries. Different methodological decisions generally did not change the overall pattern of higher drug prices in the United States. All G7 comparator countries had lower prices than the United States, but France, Italy, and the United Kingdom had particularly low prices across drug categories regardless of methodological decisions. Our results broadly align with findings from prior studies that reported higher overall and brand-name originator prescription drug prices and lower unbranded generic drug prices in the United States. Our main findings—that U.S. prices are higher than those in comparison countries for all drugs and for brand-name originator drugs but lower for unbranded generic drugs—held through several additional sensitivity analyses, such as results calculated with and without outlier presentations in terms of price and results calculated using different volume weights. Figure 4.1 compares our main result with results from subsets of drugs and with results from these sensitivity analyses.

Figure 4.1. Summary of Results: U.S. Prices as a Percentage of Other-Country Prices, 2018



SOURCE: Author analysis of IQVIA MIDAS sales and volume data for calendar year 2018 (run date October 28, 2019).
NOTE: "Other-Country Prices" refers to all 32 OECD comparison countries combined. For "Top 60," we compared prices for the top 60 drugs by U.S. sales at the active ingredient level, excluding combination products. "Adj." is adjustment. Only some presentations sold in each country contribute to bilateral comparisons.

The Role of Methodological Decisions

The magnitudes of estimated price differentials varied with our measurement approach. For our main results, we opted to use presentation-level data because these more-granular price and volume weights allow comparisons that reflect the mix of drugs in each market. The differences between U.S. prices and prices in other countries was slightly wider when we used active ingredient–level data instead. This suggests that, on average, the U.S. mix of drugs within an active ingredient tended toward higher-priced presentations.

Our comparison of price indices using data from presentations above volume and sales thresholds in the United States and individual comparison countries resulted in relatively small shares of presentations sold in individual countries contributing to each comparison. This leads to concerns regarding the generalizability of our findings. However, as discussed earlier, the presentations and active ingredients available for comparison tended to account for larger shares of volume and sales compared with presentations and active ingredients that did not contribute to our analysis.

Excluding U.S. and other-country presentations for which the other-country price was very high or low compared with the U.S. price had generally modest implications on the magnitude of results. U.S. prices relative to other-country prices without these outlier exclusion steps were almost always within 10 percent of those from our main results. We opted to implement these outlier exclusion steps because presentations with extreme differences between U.S. and other-country prices have the potential to exert significant leverage over volume-weighted price calculations. Although our main concern was that inconsistencies in how sales or volumes are measured across markets could lead to outliers, there is the possibility that some of the excluded presentations with very high U.S. or other-country prices could have reflected an actual price difference, and in this case their exclusion would bias our results. For example, high prices in non-U.S. countries could reflect high private-pay amounts outside of a public health care system and price controls.

We chose to use data from all of 2018 to calculate price indices. Other studies noted the relatively quicker approval and uptake of newer, typically more-expensive drugs and presentations in the United States compared with other countries.[71] Our bilateral comparisons omit new drugs and presentations released in the United States in 2018 but not yet in other countries. Access to innovative treatment likely has important benefits to patients. Our study does not address the trade-offs between higher prices and earlier access to new drugs.

We opted to use U.S. volume weights because of the U.S. policy focus of the analysis. This choice had important implications for our results. Using other-country volume weights yielded U.S. prices that were 390 percent of those in other countries (compared with 256 percent when using U.S. volume weights). Prescribing patterns outside the United States might be skewed

[71] Danzon and Furukawa, 2008.

toward drugs with favorable prices in individual countries as a result of price controls and/or volume purchasing. As a result, it is unsurprising that other-country volume weights result in findings of relatively higher U.S. drug prices.

General Limitations

There are important limitations that apply to all of the prior studies that we describe in this report and to our own analysis. First, although drug prices to payers net of rebates and all discounts are particularly relevant to policymakers and other stakeholder groups, there is no comprehensive source of prices at this level in the United States or in other countries. We expect a significant difference between manufacturer prices and prices to payers net of rebates in the United States and in other countries (such as Germany and the United Kingdom) where similar rebates and discounts are increasingly common. We used manufacturer prices because they are the best available comparable data for all countries.

Although we applied an estimated adjustment to U.S. prices to approximate rebates and other discounts applied to manufacturer prices as one of our sensitivity analyses, we recognize that the resulting prices will almost certainly differ from the actual net prices to payers for individual presentations. We also recognize that resulting price indices might understate differences between prices in the United States and other countries because they adjust only U.S. prices downward even though rebates and similar discounts are increasingly common in other countries. U.S. prices would appear relatively higher—i.e., more in line with our main results—if we were able to also adjust for rebates and other discounts applied to manufacturer prices in other countries.

None of the other studies that we reviewed had a reliable estimate of discounts to manufacturer prices, but all of the studies recognized this as a key limitation. Two studies applied assumptions on discounts—based on analyst estimates or the Medicaid drug rebate program—to approximate these discounts.[72]

The lack of reliable U.S. net drug prices to payers is a major limitation when comparing U.S. prices with those in other markets. The price differentials between the United States and other countries presented here and in other studies could be biased upward if actual negotiated discounts are larger than the factor applied to brand-name originator drugs as an ad hoc adjustment.

Second, manufacturer prices (i.e., the prices paid to manufacturers net of discounts at the time of purchase), such as those available from IQVIA's MIDAS data, are calculated in some countries by applying a set of assumed adjustment factors on observed local-level prices. In other words, IQVIA obtains a list price or average invoice price at the local level and then calculates manufacturer prices where necessary by applying a set of country-specific average margin

[72] Danzon and Furukawa, 2008; Kanavos et al., 2013.

factors. These average margin country-specific factors are generated and updated by local industry experts. The MIDAS data set is the standard for use in industry to compare manufacturer prices.

Finally, we use standard units as reported by IQVIA in the MIDAS data as our unit of volume. Although standard units are designed to improve comparability in volume measurement between different drugs, there are remaining concerns, particularly when the number of units used in practice differs from country to country. As an example, lower-dosage presentations are more common in some other countries (e.g., Japan) than in the United States, and volume could be higher. We address this, in part, by using presentation-level (rather than active ingredient–level) data. We did not have data available to further adjust the volumes reported in MIDAS by a defined daily dose or other conversion factor to improve comparability.

Potential Further Analyses

Several prior studies have noted that adjusting for differences in per capita income explains a portion of the difference in prescription drug prices across countries, particularly for drugs sold to middle- and low-income countries.[73] However, the differences in income are not large enough to explain the entire difference in prices between the United States and other OECD countries. Other studies assess whether variations in health care system and regulatory characteristics between countries explain variation in prices.[74] The current analyses did not test these associations, and we recommend that future analyses do so. An improved understanding of the drivers of drug price differences between countries is an important input into U.S. policy discussions on drug prices.

In our results focusing on specific subsets of drugs, we found that U.S. brand-name originator drugs are the primary driver of higher prices in the United States in aggregate across all drugs. We found significant variation between biologic prices in the United States and those of other countries, with some countries having higher prices or significantly lower prices for biologics than the United States does but with most having slightly lower prices. This variation in the price differentials—and the range of biologic price differentials identified in prior studies—likely reflects the rapid pace of change in biologic markets in different countries, the range of drugs that are flagged as biologics in the IQVIA data, and possibly the different treatment of biologics compared with small-molecule drugs in the United States in terms of manufacturer and list prices. Future analyses should explore the effects of decisions related to the categorization and treatment of biologics in price index calculations.

[73] Patricia Danzon, Andrew W. Mulcahy, and Adrian K. Towse, "Pharmaceutical Pricing in Emerging Markets: Effects of Income, Competition, and Procurement," *Health Economics*, Vol. 24, No. 2, February 2015.

[74] For example, see Kanavos et al., 2013.

Finally, although there are many biosimilars in development and an increasing number of biosimilars approved by the U.S. Food and Drug Administration, only a handful of biosimilars were marketed in the United States in 2018, and, as a result, we did not separately compare prices for them. Once the U.S. biosimilar market is more established, comparisons of biosimilar prices between the United States and other countries—particularly European countries with robust biosimilar markets—will be helpful to understand the degree of competition in U.S. biosimilar markets and the degree to which biosimilars could lower U.S. spending on biologics.

Appendix A. Comparison of Part B Drug Brief and RAND Methodology

A recent policy brief from ASPE compared prices between countries for a limited number of drug products that accounted for a large share of Medicare Part B payments.[75] The ASPE analysis uses a price index approach similar to the one we used in this report. Both analyses calculated volume-weighted price indices to compare prices in the United States with those in other countries.

There are, however, important differences in terms of the scope of the ASPE analysis and the analyses described in this report. The ASPE analysis covered drug products that were most relevant to the Part B policy context addressed by the policy brief. Most of these drug products are expensive biologic specialty drugs. Many of these drugs are injected or infused. The main results in our report draw on data for all drugs, including biologic and nonbiologic ones. Although our report shows results for biologics separately, our results for biologics draw on data for a mix of higher-priced specialty drugs (similar to those considered in the ASPE analysis) as well as lower-cost biologics, such as insulins.

There are also important methodological differences, such as the following:

- The ASPE analysis used data from the first quarter of 2018; the analyses in our report use data from all of calendar year 2018. The narrower time frame for the ASPE analysis was designed to align international prices to Medicare Part B prices, which are updated quarterly.
- The ASPE analysis measured utilization in terms of kilograms of active ingredients and calculated prices as the ratio of sales to kilograms. The current report uses standard units to measure volume and to calculate prices. Kilograms might be the more appropriate unit to measure volume for Part B biologics. Medicare prices for Part B drugs are usually based on the amount of active ingredient extracted from a standard package size accounting for overflow. We used standard units because it is a common denominator for measuring utilization across a broad range of drug types.
- The ASPE analysis calculates prices and volume weights at the drug-product-per-country level. In many cases, a drug product in the ASPE analysis maps to what we define as an active ingredient in the current report.[76]
- The ASPE analysis used data from fewer countries than we considered in our analyses.

[75] ASPE, 2018.

[76] We calculate results using active ingredient-level data as a sensitivity analysis. Active ingredient-level data are aggregated more than the presentation-level data that we used in our main results.

Appendix B. Counts and Shares by Exclusion Step

Tables B.1–B.3 provide detailed information on how the number of presentations and the share of volume and sales that contributed to our analysis changed as we implemented exclusion criteria. Table B.1 lists all data available in our MIDAS extract and describes the number of presentations and the shares of volume and sales in each country excluded when we omit presentations with very low sales and/or volume. Table B.2 describes the share of the remaining presentations, sales, and volume that contribute to bilateral comparisons between the United States and each other country. Table B.3 describes how the extreme price outlier exclusion criteria results in the number of presentations that contribute to our final results.

Table B.4 replicates Table 3.3 from the main report but at the active ingredient rather than presentation level.

Similar to Table 3.2, Table B.5 reports the share of sales and volume across brand-name originator, brand-name non-originator, and unbranded generic categories after all restrictions and exclusions are applied.

Table B.1. Initial Pool of Presentations and First Exclusion Step

	Total Presentations with Sales > 0 and Volume > 0, No Other Exclusions (A)	Total Presentations with ≥ 1,000 Sales and ≥ 1,000 Volume (B)	Share of Volume (B/A) (%)	Share of Sales (B/A) (%)
Australia	3,106	2,829	>99.9	99.3
Austria	3,913	3,329	>99.9	98.1
Belgium	3,491	2,888	>99.9	99.5
Canada	3,571	3,313	>99.9	99.8
Chile	2,884	2,327	>99.9	99.2
Czech Republic	2,972	2,603	>99.9	97.6
Estonia	1,755	1,325	>99.9	98.3
Finland	2,926	2,557	>99.9	97.6
France	4,083	3,659	>99.9	99.7
Germany	5,804	5,305	>99.9	99.7
Greece	2,648	2,265	>99.9	99.8
Hungary	2,624	2,344	>99.9	98.0
Ireland	3,011	2,537	99.8	98.4
Italy	4,964	4,506	>99.9	99.7
Japan	5,780	5,615	>99.9	>99.9
Korea	4,113	3,841	>99.9	99.8
Latvia	2,304	1,701	>99.9	96.8
Lithuania	2,375	1,803	>99.9	95.9
Luxembourg	2,145	1,592	99.7	94.5
Mexico	4,517	3,632	>99.9	99.6
Netherlands	3,423	3,011	>99.9	99.2
New Zealand	2,326	1,861	>99.9	97.6
Norway	2,886	2,486	>99.9	97.3
Poland	3,646	3,133	>99.9	99.5
Portugal	4,277	3,537	>99.9	98.5
Slovakia	2,676	2,294	>99.9	96.6
Slovenia	2,169	1,750	>99.9	92.7
Spain	4,596	4,140	>99.9	99.5
Sweden	3,370	2,979	>99.9	98.2
Switzerland	3,636	3,206	>99.9	98.8
Turkey	3,265	3,043	>99.9	>99.9
United Kingdom	6,344	4,694	>99.9	99.7
United States	7,390	6,806	>99.9	>99.9
All countries, excluding the United States	**30,905**	**26,484**	**>99.9**	**>99.9**
All countries	**34,021**	**29,254**	**>99.9**	**99.8**

SOURCE: Author analysis of IQVIA MIDAS sales and volume data for calendar year 2018 (run date October 28, 2019).

Table B.2. Total Presentations Potentially Contributing to Bilateral Comparisons

	Total Presentations with ≥ 1,000 Sales and ≥ 1,000 Volume (A)	Total Presentations Potentially Contributing to Bilateral Comparisons with United States, Before Price Ratio Exclusion (B)	Share of Volume (B/A) (%)	Share of Sales (B/A) (%)
Australia	2,829	1,668	67.4	76.7
Austria	3,329	1,638	51.8	75.2
Belgium	2,888	1,518	61.4	74.7
Canada	3,313	2,275	75.0	86.1
Chile	2,327	899	42.5	45.0
Czech Republic	2,603	1,279	55.6	68.8
Estonia	1,325	723	55.9	67.8
Finland	2,557	1,415	59.6	74.9
France	3,659	1,756	51.9	73.3
Germany	5,305	2,240	60.0	76.4
Greece	2,265	1,134	55.1	67.1
Hungary	2,344	1,201	55.5	67.1
Ireland	2,537	1,459	51.3	81.4
Italy	4,506	1,836	52.8	71.5
Japan	5,615	1,229	18.0	51.6
Korea	3,841	1,523	38.0	58.2
Latvia	1,701	847	52.5	65.0
Lithuania	1,803	923	51.1	63.4
Luxembourg	1,592	874	61.0	73.2
Mexico	3,632	1,246	39.3	47.7
Netherlands	3,011	1,559	59.8	70.9
New Zealand	1,861	975	42.9	66.1
Norway	2,486	1,425	51.9	74.2
Poland	3,133	1,375	55.8	63.6
Portugal	3,537	1,578	53.1	70.4
Slovakia	2,294	1,164	51.0	66.0
Slovenia	1,750	996	56.6	72.8
Spain	4,140	1,919	54.1	77.1
Sweden	2,979	1,642	59.5	76.2
Switzerland	3,206	1,628	53.5	79.5
Turkey	3,043	1,308	36.4	61.7
United Kingdom	4,694	2,195	54.7	76.0
United States	6,806	N/A	N/A	N/A
All countries, excluding the United States	**26,484**	**4,320**	**42.9**	**68.5**

SOURCE: Author analysis of IQVIA MIDAS sales and volume data for calendar year 2018 (run date October 28, 2019).

Table B.3. Presentations Contributing to Bilateral Comparisons After Price Ratio Exclusion

	Total Presentations Potentially Contributing to Bilateral Comparisons with United States, Before Price Ratio Exclusion (A)	Total Presentations Contributing to Bilateral Comparisons, After Price Ratio Exclusion[a] (B)	Share of Volume (B/A) (%)	Share of Sales (B/A) (%)
Australia	1,668	1,630	99.6	99.4
Austria	1,638	1,606	99.7	98.4
Belgium	1,518	1,480	99.1	98.7
Canada	2,275	2,213	99.4	98.2
Chile	899	879	99.3	98.9
Czech Republic	1,279	1,239	99.0	98.6
Estonia	723	707	98.2	98.0
Finland	1,415	1,383	99.5	98.9
France	1,756	1,700	99.0	97.2
Germany	2,240	2,169	98.4	98.2
Greece	1,134	1,102	99.3	98.6
Hungary	1,201	1,168	99.7	98.1
Ireland	1,459	1,432	99.7	98.7
Italy	1,836	1,771	98.7	98.6
Japan	1,229	1,191	97.1	99.2
Korea	1,523	1,472	98.7	98.5
Latvia	847	829	98.9	98.7
Lithuania	923	897	98.4	98.6
Luxembourg	874	854	99.3	98.6
Mexico	1,246	1,203	90.8	97.3
Netherlands	1,559	1,516	98.5	98.1
New Zealand	975	950	99.2	96.6
Norway	1,425	1,389	98.2	98.5
Poland	1,375	1,329	98.5	97.5
Portugal	1,578	1,523	98.8	96.9
Slovakia	1,164	1,126	98.9	98.8
Slovenia	996	978	99.2	99.3
Spain	1,919	1,854	98.9	98.8
Sweden	1,642	1,604	99.0	98.4
Switzerland	1,628	1,592	99.0	98.9
Turkey	1,308	1,273	99.0	99.2
United Kingdom	2,195	2,127	99.7	97.9
United States	6,806	N/A	N/A	N/A
All countries, excluding the United States	**4,320**	**4,078**	**98.6**	**98.3**

SOURCE: Author analysis of IQVIA MIDAS sales and volume data for calendar year 2018 (run date October 28, 2019).

[a] Excluded presentations with price ratio less than 1 percent of U.S. price or greater than 100x U.S. price.

Table B.4. Number of Active Ingredients Used to Calculate Price Indices

	Total Active Ingredients with Sales > 0 and Volume > 0, No Other Exclusions (A)	Total Active Ingredients Contributing to Bilateral Comparisons, After Price Ratio Exclusion[a] (B)	Share of Volume (B/A) (%)	Share of Sales (B/A) (%)
Australia	1,140	886	86.7	94.4
Austria	1,534	942	77.1	89.2
Belgium	1,379	878	82.4	91.0
Canada	1,247	1,018	92.9	96.9
Chile	1,173	568	74.7	74.5
Czech Republic	1,288	815	77.2	83.9
Estonia	817	476	78.9	84.0
Finland	1,178	808	83.8	90.6
France	1,526	967	80.9	90.5
Germany	1,801	1,093	83.2	90.6
Greece	1,091	678	81.1	85.7
Hungary	1,189	766	77.3	84.9
Ireland	1,158	806	83.0	93.6
Italy	1,801	1,062	82.7	90.3
Japan	2,101	967	40.6	76.0
Korea	1,711	942	55.4	74.7
Latvia	1,151	602	70.9	78.7
Lithuania	1,174	655	73.6	78.9
Luxembourg	910	532	80.2	86.2
Mexico	1,879	773	57.9	67.7
Netherlands	1,196	815	85.0	89.2
New Zealand	1,066	684	73.1	92.1
Norway	1,182	838	83.4	90.8
Poland	1,435	830	77.8	83.3
Portugal	1,732	966	74.3	83.5
Slovakia	1,230	767	70.4	79.8
Slovenia	1,017	668	83.8	86.0
Spain	1,719	1,019	78.6	90.2
Sweden	1,261	889	85.1	90.7
Switzerland	1,345	884	82.7	91.7
Turkey	1,387	794	58.6	79.3
United Kingdom	1,818	1,113	85.1	92.9
United States	2,184	2,032	N/A	N/A
All countries excluding the United States	5,901	1,388	66.7	86.2
All countries	**6,393**	**N/A**	**N/A**	**N/A**

SOURCE: Author analysis of IQVIA MIDAS sales and volume data for calendar year 2018 (run date October 28, 2019).

[a] Excluding active ingredients below sales and volume thresholds and/or with ratios of less than 1 percent of U.S. price or greater than 100x U.S. price.

Table B.5. Within-Country Shares of Brand-Name Originator, Brand-Name Non-Originator, and Unbranded Generic Drugs, Presentations Contributing to Bilateral Comparisons, by Percentage

	Share of Sales: Brand-Name Originator	Share of Sales: Brand-Name Non-Originator	Share of Sales: Unbranded Generic	Share of Volume: Brand-Name Originator	Share of Volume: Brand-Name Non-Originator	Share of Volume: Unbranded Generic
United States	82	6	12	11	5	84
All countries, excluding the United States	84	4	12	37	9	55
Australia	91	3	6	48	11	41
Austria	85	4	11	41	14	45
Belgium	85	4	10	46	4	50
Canada	78	3	19	18	7	74
Chile	60	25	15	15	13	73
Czech Republic	86	5	9	41	17	42
Estonia	84	3	12	50	8	42
Finland	84	5	11	43	8	49
France	79	3	18	25	7	68
Germany	82	4	14	17	7	76
Greece	94	3	3	78	11	11
Hungary	87	3	10	48	8	45
Ireland	89	2	9	45	10	44
Italy	87	3	10	52	10	38
Japan	90	2	8	60	7	33
Korea	89	4	7	66	14	19
Latvia	87	3	10	45	11	45
Lithuania	86	4	10	48	8	43
Luxembourg	94	2	3	74	13	13
Mexico	75	10	15	28	13	59
Netherlands	74	5	20	14	4	82
New Zealand	87	5	8	29	11	60
Norway	86	5	9	43	10	47
Poland	86	6	8	44	26	30
Portugal	82	4	15	36	8	56
Slovakia	87	6	7	45	14	41
Slovenia	95	2	3	74	17	9
Spain	84	3	13	39	8	53
Sweden	85	6	8	19	12	69
Switzerland	84	3	13	42	9	49
Turkey	80	19	1	72	24	4
United Kingdom	80	4	16	19	1	80

SOURCE: Author analysis of IQVIA MIDAS sales and volume data for calendar year 2018 (run date October 28, 2019).
NOTE: The numbers in each row might not sum to totals because of rounding.

Appendix C. Price Index Results by Country

Tables C.1 and C.2 report calculated price indices for each bilateral comparison (i.e., the United States versus each comparison country individually and all comparison countries combined). The tables cover each set of results summarized in the body of the report. Table C.2 focuses on different sensitivity analyses around the extreme price outlier exclusion criteria.

Table C.1. Calculated U.S. Versus Other-Country Price Indices, 2018

	Main Results	Brand-Name Originator Drugs	Top 60 Drugs by U.S. Sales	Unbranded Generics Without Biologics	Unbranded Generics and Brand-Name Non-Originators	Biologics	Non-biologics	Other-Country Weights	Fisher Index	Active Ingredient Level	Retail Prices	U.S. Net Price Adjustment	Brand-Name Originators w/ Net Price Adjustment
Australia	299.93	392.77	432.07	69.79	88.58	332.29	280.18	432.80	360.29	286.90	339.13	221.98	263.16
Austria	226.42	294.09	354.16	42.57	78.67	273.14	198.98	328.90	272.89	193.83	124.41	167.84	197.04
Belgium	251.63	323.91	399.60	61.32	101.71	299.99	225.47	337.30	291.33	231.79	195.96	186.34	217.02
Canada	218.49	293.70	329.30	56.70	83.40	253.57	198.00	324.69	266.35	214.02	229.54	161.94	196.78
Chile	177.07	460.85	427.78	68.59	41.50	387.00	138.47	300.12	230.53	191.42	150.13	131.05	308.77
Czech Republic	284.67	350.33	437.90	59.52	117.52	339.58	251.93	446.89	356.68	275.69	282.18	210.66	234.72
Estonia	351.92	684.40	732.04	55.64	98.25	634.48	297.60	617.52	466.17	354.50	367.18	261.79	458.55
Finland	236.85	313.98	357.48	62.49	88.61	264.44	220.90	409.20	311.32	207.85	211.05	175.61	210.37
France	257.75	348.70	425.43	57.75	90.61	316.27	220.92	365.84	307.07	232.51	302.36	190.74	233.63
Germany	225.05	279.75	324.58	61.66	94.80	245.35	210.62	332.11	273.39	213.95	213.33	166.91	187.43
Greece	343.40	717.67	719.09	60.24	108.64	524.27	292.21	482.26	406.95	321.87	326.55	254.14	480.84
Hungary	273.95	353.64	370.92	71.99	122.37	298.37	258.71	414.84	337.12	274.99	320.27	203.02	236.94
Ireland	228.56	298.16	352.96	43.18	77.00	277.20	205.32	359.14	286.50	225.58	206.80	169.48	199.77
Italy	243.98	315.00	367.23	58.77	104.13	290.22	215.44	316.41	277.84	222.01	175.41	180.69	211.05
Japan	209.25	307.41	363.35	43.14	72.25	303.97	160.49	409.66	292.78	209.08	227.45	157.07	205.96
Korea	305.43	532.83	578.65	31.92	57.20	453.20	238.93	427.67	361.42	314.78	370.91	226.27	357.00
Latvia	316.77	484.91	527.83	72.62	94.30	452.43	270.58	457.25	380.58	313.97	332.35	234.41	324.89
Lithuania	348.09	552.16	607.95	77.94	123.20	516.10	296.50	554.21	439.22	320.52	378.80	259.58	369.95
Luxembourg	283.02	446.66	609.18	63.03	91.93	515.20	232.85	447.17	355.75	258.59	224.71	210.41	299.26
Mexico	170.31	367.32	363.04	55.96	51.72	314.25	125.10	283.92	219.90	176.28	164.86	130.27	246.10
Netherlands	251.22	377.22	472.01	103.68	117.96	250.44	251.56	519.63	361.30	239.86	217.11	186.91	252.74
New Zealand	285.31	340.52	331.86	118.00	170.48	290.07	282.04	475.12	368.18	279.72	329.56	213.09	228.15
Norway	274.09	352.05	402.03	74.48	117.18	311.86	251.77	410.11	335.27	213.59	243.74	203.23	235.88
Poland	289.04	356.15	394.93	84.78	146.34	321.48	270.17	465.98	367.00	332.18	339.28	213.92	238.62
Portugal	304.00	373.32	403.52	89.55	138.93	312.69	298.15	437.39	364.65	282.95	358.32	225.59	250.13
Slovakia	341.11	428.73	459.88	96.51	151.10	372.43	321.13	489.44	408.60	298.66	346.62	252.43	287.25
Slovenia	291.40	399.42	450.77	63.18	108.01	370.97	252.60	442.61	359.13	276.98	303.67	215.67	267.61
Spain	244.90	297.26	362.96	57.81	100.03	274.56	225.55	343.85	290.19	241.15	215.97	181.74	199.17
Sweden	272.17	332.23	355.03	88.22	121.45	279.14	267.48	400.18	330.03	240.02	317.36	201.79	222.59
Switzerland	181.87	283.45	300.82	24.32	47.64	225.91	159.60	270.76	221.91	176.48	134.53	134.90	189.91
Turkey	779.44	1050.93	978.03	164.96	291.36	758.34	800.01	1203.50	968.53	619.02	792.31	578.10	704.12
United Kingdom	255.43	349.36	414.31	68.22	101.77	324.60	219.53	395.20	317.72	253.23	231.21	189.51	234.07
United States	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00
All countries, excluding the United States	255.83	343.61	394.85	84.35	121.00	295.36	233.53	389.62	315.72	275.75	245.40	189.61	230.22

Table C.2. Calculated Price Indices, U.S. Versus Other-Country Drugs, Exclusion Criteria Sensitivity Analyses

	Scenario 1: No Cleaning Steps	Scenario 2: Volume or Sales > 1,000; No Other Exclusions	Scenario 3: Volume or Sales > 1,000; 0.1%–1,000x Price Ratio Exclusion	Scenario 4: Main Results	Scenario 5: Volume or Sales > 1,000; 10%–10x Price Ratio Exclusion
Australia	304.12	302.08	300.24	299.93	257.64
Austria	220.34	225.48	227.61	226.42	208.95
Belgium	257.03	248.64	251.85	251.63	222.35
Canada	207.85	208.46	208.46	218.49	210.68
Chile	186.46	177.21	177.11	177.07	219.79
Czech Republic	276.17	281.19	285.30	284.67	254.13
Estonia	407.92	353.82	353.82	351.92	251.66
Finland	239.22	238.30	238.30	236.85	217.30
France	239.21	236.37	242.27	257.75	233.79
Germany	225.92	218.54	225.14	225.05	207.75
Greece	387.15	345.74	345.74	343.40	249.94
Hungary	210.15	274.59	274.59	273.95	245.36
Ireland	248.08	229.86	229.51	228.56	214.94
Italy	235.41	241.68	244.49	243.98	229.09
Japan	166.78	209.44	209.44	209.25	229.87
Korea	314.55	306.23	306.22	305.43	264.54
Latvia	351.41	318.01	317.54	316.77	254.52
Lithuania	382.33	350.84	350.84	348.09	277.76
Luxembourg	324.05	284.37	284.37	283.02	248.28
Mexico	175.92	166.03	166.03	170.31	220.96
Netherlands	255.74	249.52	253.10	251.22	223.11
New Zealand	302.22	288.73	288.73	285.31	266.07
Norway	290.75	274.86	274.86	274.09	242.39
Poland	316.47	289.67	289.67	289.04	245.50
Portugal	310.78	301.67	305.55	304.00	273.96
Slovakia	355.03	341.72	341.72	341.11	285.42
Slovenia	305.89	291.46	291.46	291.40	246.48
Spain	204.70	244.21	246.45	244.90	220.91
Sweden	276.77	273.07	273.07	272.17	250.19
Switzerland	187.87	180.86	182.37	181.87	193.02
Turkey	766.96	787.50	786.82	779.44	354.16
United Kingdom	250.41	256.66	256.62	255.43	247.07
United States	100.00	100.00	100.00	100.00	100.00
All countries, excluding the United States	216.95	240.13	245.13	255.83	227.18

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