**ADBI Working Paper Series**

# International Trade and Determinants of Price Differentials of Insulin Medicine

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No. 551
November 2015

**Asian Development Bank Institute**

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Suggested citation:

Helble, M., and T. Aizawa. 2015. International Trade and Determinants of Price Differentials of Insulin Medicine. ADBI Working Paper 551. Tokyo: Asian Development Bank Institute. Available: http://www.adb.org/publications/international-trade-and-determinants-price-differentials-insulin-medicine/

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**Abstract**

Empirical studies on pharmaceuticals pricing across countries have found evidence that prices vary according to per capita income. These studies are typically based on survey data from a subset of countries and cover only one year. In this paper, we study the international trade and price of insulin by using detailed trade data for 186 importing countries from 1995 to 2013. With almost 12,000 observations, our study constitutes the largest comparative study on pharmaceutical pricing conducted so far. The large dataset allows us to uncover new determinants of price differentials. Our analysis shows that the international trade of insulin increased substantially over this time period, clearly outpacing the increasing prevalence of diabetes. Using the unit values of imports, we also study the determinants of price differentials between countries. Running various panel regressions, we find that the differences in prices across countries can be explained by the following factors: First, corroborating earlier studies, we find that per capita GDP is positively correlated with the unit price of insulin. Second, the price of insulin drugs originating from Organisation for Economic Co-operation and Development countries tends to be substantially higher than for those imported from developing countries. Third, more intense competition among suppliers leads to lower insulin prices. Fourth, higher out-of-pocket payments for health care are associated with higher prices. Finally, higher volumes and tariffs seem to result in lower unit prices.

**JEL Classification:** F14, I11

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"*International trade is vital for access to medicines and other medical technologies, markedly so for smaller and less resourced countries. Trade stimulates competition, which in turn reduces prices and offers a wider range of suppliers, improving security and predictability of supply."* (WHO/WIPO/WTO 2013)

# 1. INTRODUCTION

Non-communicable diseases have become a major public health concern in both developed and developing countries. According the World Health Organization (WHO) (2013a), non-communicable diseases are responsible for almost two-thirds of all deaths. WHO (2013b, 2013c) estimates that 347 million people worldwide currently suffer from diabetes, with more than 80% of diabetes-related deaths occurring in low- and middle-income countries. It is expected that the worldwide number will increase by between 50% and 70% by 2030 (WHO 2013; International Diabetes Federation 2013), and that diabetes will become the fifth-leading cause of death. Among the 10 leading causes of death, no other disease is projected to develop in such a dramatic manner. The surge in diabetes has dramatic consequences for public health finance, with the International Diabetes Federation (2013) estimating that it caused $471 billion of expenditure for 2012, or about 11% of total health care expenditure for adults.

Diabetes occurs either when the pancreas does not produce enough insulin (Type 1) or when the body is unable to process the insulin it does produce (Type 2). Insulin is needed to regulate blood sugar. Due to its similarity to human insulin, animal insulin was first used to treat diabetes. In the 1980s, biosynthetic insulin was developed, replacing animal insulin; today, the overwhelming majority of the insulin sold worldwide is recombinant, biosynthetic "human" insulin.

The global market for insulin interests economists for three reasons. First, biosynthetic insulin products made by different manufacturers can be considered as homogeneous goods. Empirical evidence shows that health outcomes, such as mortality, morbidity, and quality of life, are almost identical across different types of insulin. Some new insulin products are intermediate acting and therefore more convenient; however, their health effect is very similar to the older long-acting ones (e.g., Tricco et al. 2014). Second, the insulin industry can be described as oligopolistic, as three manufacturers dominate the world market. Third, from an international economics perspective, the insulin case is insightful because the same product is needed in all countries around the world, but manufacturing only takes place in a restricted number of countries by a small number of producers. Unrestricted and open trade of insulin is therefore highly important from a public health perspective. In summary, in the insulin market, a small number of producers provide a relatively homogeneous good to the entire world. This case is meaningful to study because similar conditions might apply to other markets. Especially in certain niche markets, market power is concentrated among a few producers that are often concentrated geographically. The findings of our study might therefore be of relevance for other sectors.

Whenever a homogeneous good is provided to different markets, the first question an economist asks concerns the difference in prices. Price differences might be the result of market segmentation, competitive pressure, trade barriers, or other factors. Knowing why prices differ can allow us to better understand the drivers behind prices and possibly design policies to bring prices down. In the case of insulin, lower prices would translate into better access to medicine and lower costs for health systems.

We measured the price of insulin by using trade data and calculating unit prices for each country. The unit price is simply the price in US dollars of one quantity unit (mostly 1 kilogram). Unit prices are a key ingredient of empirical research in international economics. For example, they are used to compute trade price indexes (Broda and Weinstein 2006) and terms of trade, or to identify countries' specializations along a ladder of vertically differentiated varieties (Schott 2008; Fontagné et al. 2008). We calculated unit prices for each bilateral relationship in every year.

The main results of our paper can be summarized as follows. First, all countries in our sample have seen their imports of insulin increase substantially in recent years. Second, unit prices of insulin differ markedly across the countries in our sample. Using an econometric approach, we are able to explain most of the price differences. One key determinant seems to be price discrimination. Pharmaceutical companies charge higher prices for insulin in more affluent markets; however, it seems that market forces attenuate the potential for doing so fully. Most importantly, the greater the number of sources a country uses to import insulin and the larger the volume, the lower the price tends to be. In addition, institutional factors seem to play a role. In countries where most of the expenditure is out-of-pocket, prices seem to be higher, indicating that atomic buyers have less negotiating power. Finally, lower tariffs appear to have a significant effect on lowering prices.

The paper is structured as follows: The next section gives a short background on increase of diabetes and the consequences for public health. The third section discusses the related literature in the field of health economics, as well as international trade. We then briefly explain the data and methodology used. Before concluding, the main section presents the results of our empirical analysis.

## 2. BACKGROUND

Figure 1 shows WHO death estimates for diabetes mellitus for the years 2000, 2015, and 2030. Except for Europe, all regions in the world will see double the number of deaths caused by diabetes mellitus within 30 years. The region with the highest absolute number of deaths is Southeast Asia. For Asia as a whole (Southeast Asia and Western-Pacific Asia taken together), WHO estimates that currently over 200 million people suffer from diabetes, which is again by far the largest number in absolute terms.

The country most affected by the disease is the People's Republic of China (PRC). Based on a comprehensive survey, Xu et al. (2013) estimated the prevalence of diabetes in PRC adults at 11.6% in 2010 (the prevalence of pre-diabetes was estimated at 50.1%), 0.3% higher than in the US. These results suggest that around 114 million PRC adults suffer from diabetes, which shows the disease's seriousness as a PRC public health problem.

**Figure 1: Deaths caused by Diabetes Mellitus (2000, 2015, 2030)**

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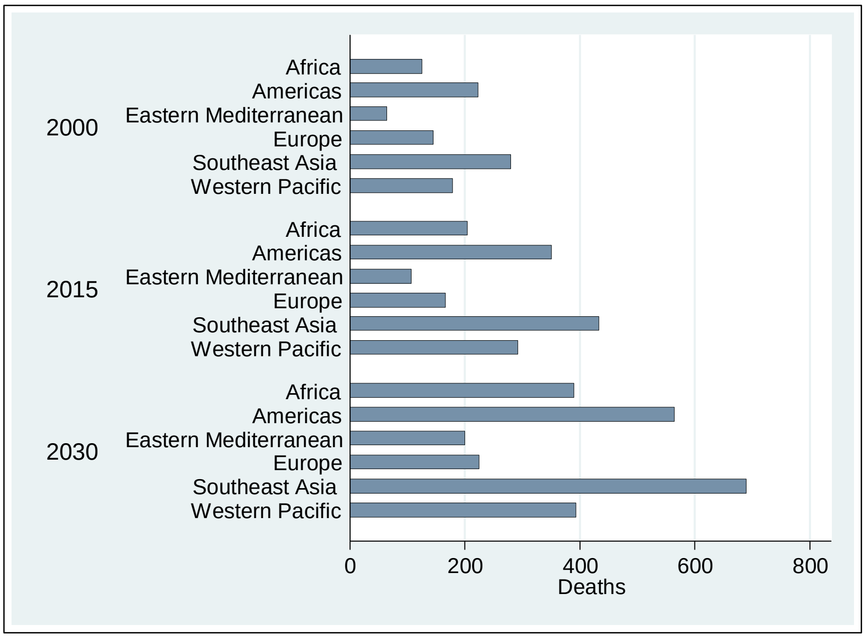
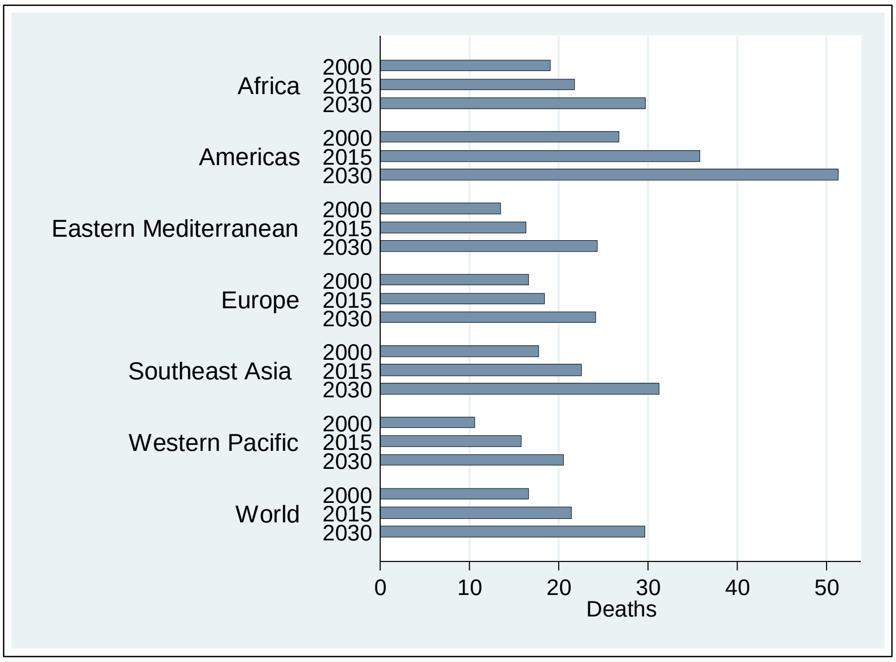



Source: WHO Health Statistics (2013).

Figure 2 shows the deaths per 100,000 people caused by diabetes mellitus. The highest number of deaths was recorded in the Americas in 2000, with Africa and Southeast Asia coming in second and third place, respectively. WHO estimates that in 2015 and 2030 the region with the highest number will remain the Americas, and Southeast Asia will become the region with the second-largest relative number of deaths caused by diabetes mellitus.

**Figure 2: Deaths per 100,000 People Caused by Diabetes Mellitus, by Region**




Source: WHO Health Statistics (2013).

The number of deaths that are directly linked to diabetes mellitus underestimates the health problems caused by the disease. It is well known that over time diabetes mellitus often damages the heart, blood vessels, eyes, kidneys, and nerves, thereby increasing the risk of heart disease and stroke. It has also been identified as the leading cause of renal failure in many developed and developing countries. The burden of the disease on individuals' health and on health systems is therefore substantively higher than the mortality statistics indicate.

Diabetes is an incurable, chronic condition, and patients are typically treated over several decades, which causes high costs for patients and health systems. WHO estimates that people suffering from diabetes require at least two to three times the health care resources compared to people without the disease, accounting for up to 15% of national health care budgets (WHO 2013d). The increased health care costs can be covered by health systems, but in the case of weak health care systems the individuals themselves need to finance most of the additional health care costs. Diabetes and its complications thus have significant economic impacts on individuals, families, health care systems and countries. For example, WHO estimates that in the period 2006–2015, the PRC will lose $558 billion in foregone national income due to heart disease, stroke, and diabetes alone (WHO 2013a).

The rising prevalence of diabetes has led to a surge in drug sales for treatment worldwide. It is estimated that sales of insulin will increase from $12 billion in 2008 to $54 billion in 2030. In the case of the PRC, it is reported that several companies recorded annual increases of 20% over recent years (Bloomberg 2013). Today, three major pharmaceutical companies, namely Novo Nordisk, Eli Lilly, and Sanofi-Aventis, provide the majority of insulin to world markets. However, more and more local manufacturers in off-patent countries have become active in the market, especially in the PRC, India, and the Russian Federation.

Most insulin comes in injectable form, either through syringes, pens, pumps, or needle-free devices. The world insulin market consists mainly of three product classes: recombinant human insulin, as well as fast-acting and slow-acting insulin analogues. The recombinant human segment is gradually being replaced by insulin analogues. Several scientific studies have found that there is currently no evidence of the superiority of insulin analogues over synthetic human insulins in the treatment of adult patients with diabetes.[1] In the following, the word "insulin" encompasses all three product classes.

# 3. RELATED LITERATURE

The health economics literature has repeatedly studied whether pharmaceutical companies apply cross-national price discrimination. The findings have been mixed. For example, Danzon and Chao (2000) show that for seven countries (Canada, France, Germany, Italy, Japan, the UK, and the US), cross-national prices reflect implicit differences in product characteristics. Furthermore, they find that strict price regulation systematically lowers prices for older molecules and globally diffused molecules. In a recent study, Morel et al. (2011) compare average pharmaceutical prices in 14 middle-income countries to those in three high-income countries and a low-income region in western Africa. The authors show that some middle-income countries

[1] For example, the Canadian Agency for Drugs and Technologies in Health found in its 2008 comparison of the effects of insulin analogues and biosynthetic human insulin, that insulin analogues failed to show any clinically relevant differences, both in terms of glycemic control and adverse reaction profile (Banerjee et al. 2007).

pay more for pharmaceuticals than high-income countries; for example, prices in several middle-income countries exceeded those in the UK for some years of the study period.

Another stream of research has gathered strong empirical evidence for price discrimination. Schut and van Bergeijk (1986) test the existence of international price discrimination in the pharmaceutical industry using trade data for 32 countries and conclude that drug prices are highly influenced by purchasing power of a country. Wagner and McCarthy (2004) come to a similar conclusion, finding that price differences exist across countries; however, the differences are rather small. Lichtenberg (2011) finds evidence that pharmaceutical companies charge lower prices in low-income countries than in developed countries. Schweitzer and Comanor (2011) study the prices of 30 drugs in 29 countries and find that many prices are substantially discounted in middle-income and developing countries, compared to prices in developed countries, and do not exceed long-run marginal costs. The empirical literature is thus not conclusive whether price discrimination takes place, but there seems to be consensus that per capita income is a determinant when pharmaceutical companies set prices.

In this study, we use unit price data to determine whether, in the case of insulin, price discrimination is applied or not. However, our paper goes one step further: we not only look at income, but also at various other market conditions as possible price determinants. Broadening the explanatory scope of price discrimination is the key contribution of this paper. Most specifically, we test whether market size, competition, trade policy, institutional arrangement, and regulation matter for prices. We are able to do so because we study a very narrow product that is provided by a small number of producers. Our paper is therefore not only a contribution to the health economics literature, but also to the international trade literature. The trade models that constitute the best fit with our set-up are those based on monopolistic competition. In these models, gains from trade are typically derived from changes in the number of available varieties in each country, as well as the market size (Krugman 1980). Even though we do not apply firm-level trade data, our paper is related to the recent empirical literature on heterogeneous firm-level trade models, pioneered by Melitz (2003) and Bernard et al. (2003). The reason is that our empirical findings indicate that the number of foreign suppliers is another important determinant of prices.

# 4. DATA AND DESCRIPTION

## 4.1 Data

Most international trade data is recorded according to the Harmonized Commodity Description and Coding System (HS), which classifies all trade flows into around 6,000 product groups, or subheadings. The majority of finished pharmaceutical products can be found in the headings HS 3003 (bulk medicines) or HS 3004 (dosified medicines). Insulin products are contained in two subheadings: HS 300331 “medicaments containing insulin (not in measured doses or put up for retail sale) and HS 300431 medicaments containing insulin (put in packings for retail sale). International trade of bulk medicines containing insulin is very small compared to international trade of HS 300431 (less than 0.01% in 2010). For our study, we will therefore only take into account trade flows and tariffs for HS 300431.

In comparison to other medicines included in the HS 3004 heading, HS 300431 covers a relatively small range of drugs, namely biosynthetic recombinants of human insulin and its analogues. Describing a relatively narrow group of drugs constitutes an important advantage. First, all insulin drugs serve the same purpose and have very similar degrees of efficacy. In addition, almost all insulin to treat diabetes is sold in liquid form. As a consequence, the volume (measured in kilograms [kg]) becomes an additional indicator of the magnitude of trade, next to the value. And most importantly, having a reliable volume measurement allows us to calculate the unit value, which is simply the price in US dollars of one quantity unit (usually 1 kg). Unit values serve as an estimate of the prices at which a commodity is imported from each trading partner for every year.

Working with unit values can sometimes be challenging because the products that are recorded under a specific subheading can be very heterogeneous in terms of their characteristics, including their volume. For example, in the subheading HS 300440 “medicaments containing alkaloids or derivatives thereof,” different drugs are lumped together, and it therefore becomes almost meaningless to calculate unit prices. However, we argue that HS 300431 is particularly well suited to working with unit values as the pharmaceuticals contained in this subheading are relatively homogeneous.

Furthermore, in the empirical research in international economics, unit values are chosen for price estimates. For example, unit values are used to compute trade price indexes (Broda and Weinstein 2006) or terms of trade, or to identify countries’ specialization along a ladder of vertically differentiated varieties (Schott 2008; Fontagné et al. 2008).

For this research, we downloaded the trade (imports) and tariff data for 1995–2013 from the World Integrated Trade Solution database. Our sample holds 11,817 non-zero bilateral trade flows between the 186 importing countries and 161 exporting countries. Before our analysis, we dropped several observations that appeared to be outliers, likely due to measurement error. The observations dropped by us are shown in Appendix, Table A.1. Furthermore, we dropped observations with zero volumes and those with unit prices greater than 3,[2] accounting for about 2.35% of the original samples.

In order to enrich the analysis, we downloaded additional country- and year-specific data from the World Bank’s World Development Indicators database,[3] namely GDP per capita, population size, health expenditure per capita (absolute and adjusted for purchasing power), the percentage of out-of-pocket payment of total health expenditure, and the percentage of external resources in total health expenditure.

## 4.2 Data Description

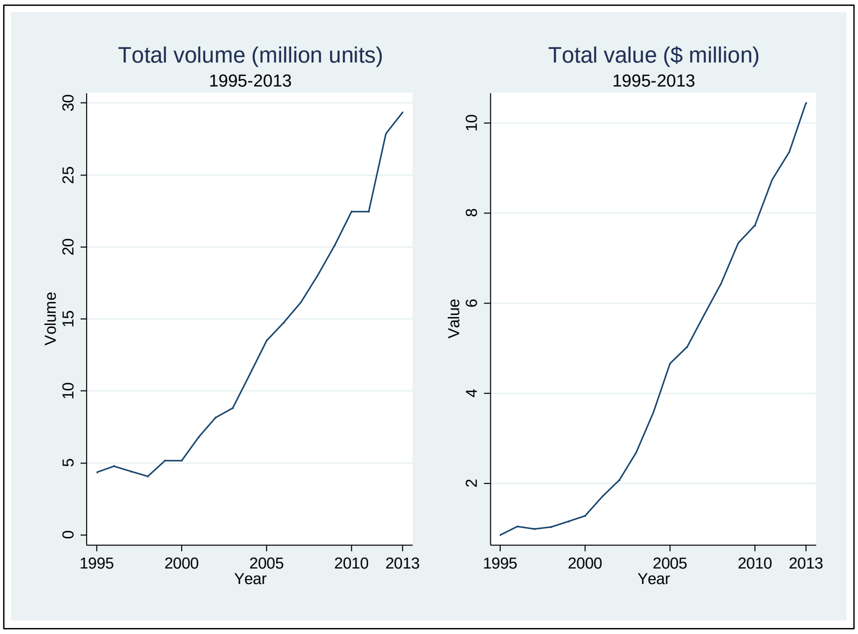
### 4.2.1 Evolution of Imports of Medicaments Containing Insulin

We start our analysis by looking at the evolution of worldwide imports in values and volumes of HS 300431 from 1995 to 2013. Figure 3 depicts that the volumes and values of HS 300431 have increased steeply, especially since 2000.

[2] This figure as a threshold is approximately 10 times larger than the sample mean of the unit price.

[3] http://data.worldbank.org/indicator

**Figure 3: Evolution of Volumes and Values of HS 300431, 1995–2015**

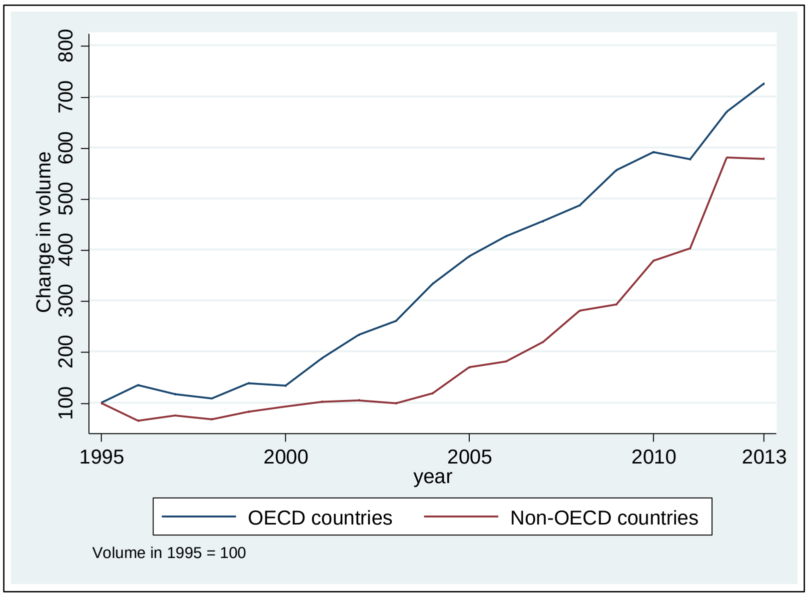



Source: UN COMTRADE.

Figure 4 illustrates the change in the trade volumes of medicaments containing insulin among Organisation for Economic Co-operation and Development (OECD) countries and non-OECD countries, setting the volume in 1995 as 100. The need for insulin appears to be growing in both developed countries and developing countries. Whereas OECD countries started to import much more from 2000 onwards, non-OECD countries followed only a few years later. From 2000 to 2013, the volume of insulin imported in value terms by OECD countries grew by 13.96% annually; in non-OECD countries by 15.05%.

**Figure 4: Evolution of Imports of HS 300431**

($, indexed to 1995=100)



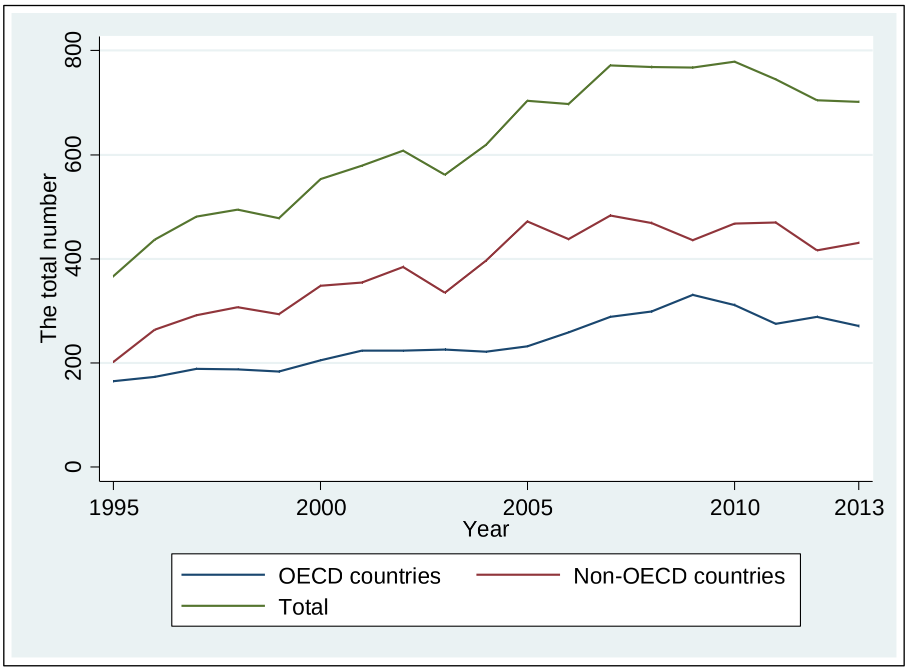

OECD = Organisation for Economic Co-operation and Development.

Source: UN COMTRADE.

#### 4.2.2 Market Competition

Another interesting question to ask is how the number of exporting countries has changed over the period. A higher number would indicate that countries import their insulin from an increasing number of sources, which could lead to more competition and potentially lower prices.[4] A higher number of suppliers might also go hand in hand with greater supply security. Figure 5 illustrates the number of countries from which countries import insulin; in other words, all trade relations for HS 300431. The total number grew steadily among both OECD countries and the other countries until the late 2000s. Since 2010, we observe a slight decline.

**Figure 5: Evolution of the Number of International Trade Relations for HS 300431, 1995–2013**




OECD = Organisation for Economic Co-operation and Development.

Source: UN COMTRADE.

#### 4.2.3 The Unit Price

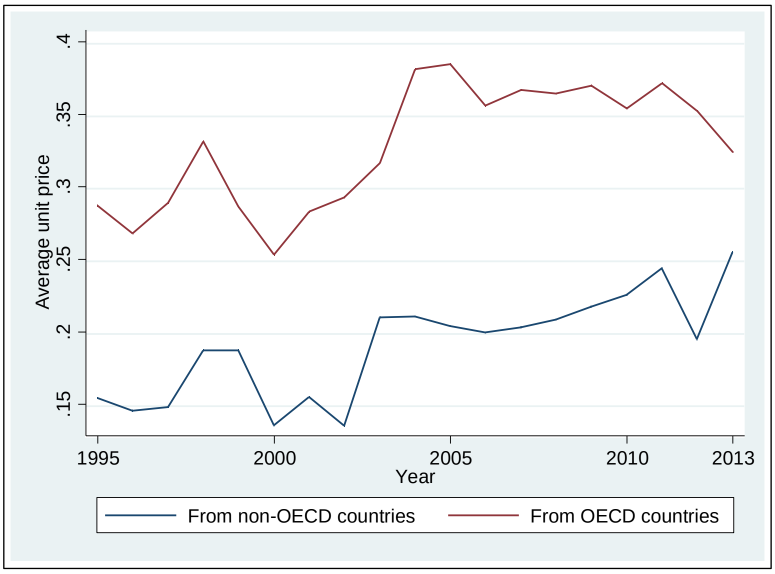
As explained above, the key advantage of studying international trade in HS 300431 is that we are able to calculate unit prices for each source; for example, one can calculate the unit price of 1 kg of HS 300431 that Chile imports from Denmark. In order to assess whether developed country exporters charge similar prices compared to developing country exporters, we have calculated the unit price for each source country. Averaging among developed and developing countries, we obtain the result depicted in Figure 6. The red and blue lines show the evolution of the average landed unit price for HS 300431 coming from developed countries and developing countries, respectively. It is interesting that the unit price of imports coming from developed countries has been constantly and significantly higher than those originating from developing countries. The gap between the two price measures has increased from 2003 to 2008 and has only narrowed very recently. Trade data alone cannot reveal why this price difference

[4] Price competition in a country has been well researched. For example, see Wang (2006) for the PRC's pharmaceutical market and Wiggins and Maness (2004) for the US market.

exists. In the next section, we will therefore study determinants explaining these differences.

**Figure 6: Evolution of Average Import Unit Prices of HS 300431, 1995–2009**

(simple average)




OECD = Organisation for Economic Co-operation and Development.

Source: UN COMTRADE.

# 5. METHODOLOGY

## 5.1 Factors Explaining Differential Pricing

Our research objective is to identify the main determinants of price differences across countries. We look at three variations of insulin prices:

i. unit price, i.e., value (in US dollars) divided by volume (in kg);

ii. unit price difference from the average price across all countries in each year; and

iii. unit price difference from the average price charged by an exporting country in each year.

### 5.1.1 Unit Price

The unit price is calculated as follows:

$$(Unit\ price)_{ikt} = \frac{value_{ikt}}{volume_{ikt}} \quad (1)$$

*i*: importing country, *k*: exporting country, *t*: year

### 5.1.2 Unit Price Difference from the Average Price across All Countries

Variations (ii) and (iii) are based on the idea of so-called "reference pricing."[5] Reference pricing means that prices are set by comparing pharmaceutical prices for the same product across countries. Authorities in many countries around the world (WHO and HAI 2011) apply the reference pricing method when regulating the price of medicines. Research by the OECD shows that various methods are used, including applying different country baskets (OECD 2008). The simplest way to determine the reference price for country *i* is to use the simple average price across all countries. In (ii), we calculate the simple average price across all countries and then calculate the difference between the average price and the price in each importing country.[6] The equation takes the following form:

$$(Price\ difference)_{ikt} = (Unit\ price)_{i\,k\,t} - (Reference\ price)_t \quad (2)$$

where $(reference\ price)_t = \frac{1}{\#\ of\ observations}\{\sum_i \sum_k (unit\ price)_{ikt}\}$

### 5.1.3 Unit Price Difference from the Average Price Charged by an Exporting Country

Though variations (ii) and (iii) look similar, the two are rather different. The reference price of (ii) is the average of all the prices charged in year *t* by all insulin-exporting countries. By contrast, the reference price of (iii) is the average of all the prices charged by a company in country *k* in year *t*. The reference price, therefore, varies depending on the exporting country. The price difference, defined as the discrepancy between a unit price and this reference price, could clearly reflect evidence of price "discrimination" by the same exporting country.

$$(Price\ difference\ 2)_{ikt} = (unit\ price)_{ikt} - (Reference\ price\ 2)_{kt} \quad (3)$$

where $(Reference\ price\ 2)_{kt} = \frac{1}{\#\ of\ observations}\{\sum_i (unit\ price_{ikt})\}$

Applying (ii) and (iii), the differences can be both positive and negative, which requires special caution when we interpret the result. We therefore use the value of price difference without transforming it to a logarithmic form, because the price difference can be positive or negative by definition.[7]

As explanatory variables, we use those summarized in Table 1. Descriptive statistics of each variable are shown in Table 2. GDP per capita reflects the purchasing power of the importing country. The market size and potential demand in country *i* are measured by that country's population. The dummy variable is used to control for the origins of the drug: We conjecture that the drug coming from an OECD country has a higher price due to a quality premium.

[5] Usually, the reference price is defined as the price patients pay for the drug. In our case, the unit value measures the price of a drug when being imported. Due to the intermediation of wholesalers and distributors, the final price might be substantially higher.

[6] For computational simplicity, we used the average price of all countries, including the price that country *i* is facing.

[7] To restrict the use of positive values in the logarithmic form would cause serious selection bias to the estimation.

Furthermore, in our regression model, market structure difference is carefully controlled for. The market competition is measured by the number of foreign countries exporting the drug to country *i*. We conjecture that the presence of more suppliers heightens the price competition, which should lower unit prices. Health care financing is measured by the percentage of out-of-pocket expenditure in total health care expenditure. High out-of-pocket expenditures typically indicate that large parts of the population are not covered by any health insurance. As a consequence, health insurance companies cannot lobby for lower prices and regulators are often weak, which eventually leads to higher drug prices. Furthermore, we include the total volume of insulin imported and assume that countries that import more should be able to negotiate lower prices with pharmaceutical companies. Finally, we introduce the applied Most Favored Nation tariffs in our regression. Higher tariffs could provide incentives for pharmaceutical companies to ask for lower landed prices. A higher import duty could be viewed as a tax that is probably borne by both the producer and patient.

**Table 1: Determinants of the Unit Price and the Price Difference**

| Variable | Definition | Expected Effect on Price |
|---|---|---|
| **ln(GDP per cap)** | The logarithmic amount of GDP per capita | + |
| **ln(population)** | The logarithmic size of the population | +/- |
| **Developed** | The dummy variable, which is 1 if the partner county is an OECD country | + |
| **ln(competitors)** | The logarithmic number of foreign countries exporting the medicaments containing insulin to country *i* | - |
| **ln(O-O-P)** | The log-transformed proportion of out-of-pocket expenditure in total health expenditure (%) | + |
| **ln(volume)** | The logarithmic amount of imported volume of insulin | - |
| **ln(tariff)** | The log-transformed rate of tariff | - |

GDP = gross domestic product.

Source: Authors.

**Table 2: Descriptive Statistics**

| | Observations | Mean | Std. dev. | Min. | Max. |
|---|---|---|---|---|---|
| **Unit price** ($'000) | 11,817 | 0.3066723 | 0.3561625 | $5.21*10^{-6}$ | 2.99925 |
| **GDP per capita** | 11,674 | 18356.73 | 16169.49 | 421.5877 | 136727.3 |
| **Population** | 11,627 | $1.97*10^{8}$ | $7.17*10^{8}$ | 27450 | $5.74*10^{9}$ |
| **Developed** | 11,817 | 0.7946179 | 0.4039976 | 0 | 1 |
| **Competitors** | 11,817 | 7.419227 | 4.865569 | 1 | 34 |
| **O-O-P** | 11,665 | 30.31856 | 17.15235 | 2.975975 | 88.32974 |
| **Tariff** | 5,516 | 3.027348 | 5.175675 | 0 | 42 |

GDP = gross domestic product, O-O-P = the percentage of out-of-pocket expenditure in total health care expenditure.

Source: Authors.

## 5.2 Estimation Strategy

The equations that we will estimate take the following simple forms:

- $(Unit\ price)_{ikt} = X'_{ikt}\beta + \varepsilon_{ikt}$
- $(Price\ difference)_{ikt} = X'_{ikt}\beta + \varepsilon_{ikt}$
- $(Price\ difference\ 2)_{ikt} = X'_{ikt}\beta + \varepsilon_{ikt}$

We first introduce GDP per capita, the partner country development dummy, and the market structure, as well as institutional variables, as independent variables. We add the volume of imports in a separate regression, as they potentially influence the unit price. Finally, we add the applied tariff rates as explanatory variables. We do this last because we only have tariff information for about one-quarter of the observations; thus, this sample is reduced substantially.

We analyze our panel data using fixed effect ordinary least squares (OLS) regressions.[8] We run our fixed effect OLS estimations including two types of fixed effect separately: (I) a country-specific fixed effect and (II) a country-pair-specific fixed effect. The differences are described in the following subsections.

### 5.2.1 Country-Specific Fixed Effect

Suppose the error term can be divided into two parts:

$$\varepsilon_{ikt} = \alpha_i + \eta_{ikt}$$

where a country-specific error, $\alpha_i$ , captures observable and unobservable heterogeneity that is constant over time (such as institutions, culture, and historical backgrounds), and $\eta_{itk}$ is an idiosyncratic error. Eliminating a country-specific effect by the within transformation[9] allows us to estimate the coefficients of interest.

$$Y_{ikt} = X'_{ikt}\beta + \alpha_i + \eta_{ikt}$$

Taking the within transformation, the equation becomes:

$$(Y_{ikt} - \overline{Y_i}) = (X_{ikt} - \overline{X_i})'\beta + (\alpha_i - \overline{\alpha_i}) + (\eta_{ikt} - \overline{\eta_i})$$

where $\overline{A_i} = \frac{1}{\#\ of\ observations}\sum_k \sum_t A_{ikt}$.

Rewriting this, we get:

$$\widetilde{Y_{ikt}} = \widetilde{X_{ikt}}'\beta + \widetilde{\eta_{ikt}}$$

which allows us to estimate the fixed effects estimators, $\beta$.

[8] In this paper, we do not discuss the results from a random effects model because the Hausman test significantly preferred the fixed effect model over other models (p<0.01).

[9] The subtraction of the group time means from each variable is used in the traditional fixed effect estimation model.

### 5.2.2 Country-Pair Fixed Effect

Next, we assume instead that the error term can be divided into country-pair-specific error, $\alpha_{ik}$ and an idiosyncratic error, $\eta_{itk}$.

$$\varepsilon_{ikt} = \alpha_{ik} + \eta_{ikt}$$

The justification for this assumption is very simple and intuitive. The price between country *i* and country *k* should be different from the price between country *i* and country *j≠k*, because country pairs *ik* and *ij* probably have different transaction costs due to different geographical distance, different languages, distinct business customs, and different religions; $\alpha_{ik}$ captures these differences. This country-pair fixed effect OLS estimation would provide even clearer evidence for the existence of price differentiation by controlling for transaction costs between *i* and *k*.

The equation to be estimated then becomes:

$Y_{ikt} = X'_{ikt}\beta + \alpha_{ik} + \eta_{itk}$.

Taking the within transformation, the equation becomes:

$$(Y_{ikt} - \overline{Y_{ik}}) = (X_{itk} - \overline{X_{ik}})'\beta + (\alpha_{ik} - \overline{\alpha_{ik}}) + (\eta_{ikt} - \overline{\eta_{ik}})$$

where $\overline{B_{ik}} = \frac{1}{\#\ of\ observations}\sum_t B_{ikt}$.

This can be rewritten as:

$$\ddot{Y_{ikt}} = \ddot{X_{ikt}}'\beta + \ddot{\eta_{ikt}}$$

In our country-pair fixed effects regression, we estimate the fixed effects estimators, $\beta$.

When we regress price difference with the country-pair fixed effects, the developed-country dummy variable (Table 1) cannot be included because the price difference defined in equation (3) already implicitly controls for the partner country difference. It is thus misleading to include the developed country dummy in the regression model in this subsection.

# 6. ESTIMATION RESULTS

## 6.1 Country Fixed Effect

Table 3 summarizes the estimation results for the three different types of dependent variables: unit prices (columns 1–3); price difference 1 (columns 4–6); and price difference 2 (columns 7–9). We first notice that the GDP per capita is highly significant for all the three dependent variables. The first column shows that a 10% higher GDP per capita implies a 6.8% higher price. This means that as GDP increases, the price of insulin tends to increase less. This result corroborates several earlier studies (Danzon et al. 2011) that also found that the poorest countries pay the highest prices for medicine relative to their per capita income. Insulin does not seem to be an exception.

The effect on the price difference needs to be interpreted carefully. As the absolute value shows the degree of price differentiation, the closer to zero the difference approaches, the less likely that discrimination is happening. As the difference takes both positive and negative values, the interpretation is not straightforward. The qualitative interpretation differs depending on whether the initial difference is positive or negative. For example, the positive significance for the per capita GDP price difference implies that the price gap from the reference price becomes larger if the original gap is positive.

The coefficient for the population size comes out negative, as expected, but it is insignificant in all regressions. One reason might be that the population size is not an adequate proxy for the market size of insulin products. Developing countries with large populations might have not the financial means to treat diabetes adequately; therefore, the volume might be lower and prices rather high.

With OECD exporting countries, the unit prices are systematically higher. The same observation holds when we look at price differences. The main reason for the higher prices charged by OECD countries is that their insulin mainly belongs to the latest generation and is often still under patent protection.

Furthermore, our estimations show that competition is an important determinant of insulin prices. We find that the higher the number of competitors (measured by the number of source countries), the lower the unit price becomes and the price difference shrinks if a positive gap exists. In other words, competition among insulin producers significantly reduces prices.

Our results further indicate that the proportion of out-of-pocket expenditures relative to total health care expenditure is positively correlated with the unit value. The result is statistically significant across all specifications, and suggests that in markets with less-developed health financing systems, pharmaceutical companies tend to exploit their market power towards innumerable atomic buyers. Strengthening health financing has thus not only the already well-established positive effects, such as providing safeguards against catastrophic health expenditures, but it might be an important element in bringing down prices for pharmaceuticals.

Next, we added the logarithm of the volume of insulin imported. Interestingly, we observe a negative and statistically significant effect in all specifications. In other words, higher volumes bring prices down and reduce price differentials. The result implies that a 10% increase in the volume lowers the unit price of insulin by 0.47%. We also note that when we add volume as a variable, the significance of all the variables remains.

Finally, we add the tariff rate as an explanatory variable. The sample size becomes significantly smaller as yearly data on tariffs are rather sparse. A higher tariff seems to have a negative effect on unit prices, as well as on price differentials. We know from trade theory that a tariff drives a wedge between consumer and producer prices. Due to higher prices for consumers, producers need to lower their price.[10] We observed again that when we add both the trade volumes and the tariff rate, the results remain fairly stable in all three relevant columns, that is, (3), (6), and (9). The only exception is the significance of the proportion of out-of-pocket expenditure in (6) and (9), which disappears.

Table A.2 in the Appendix has another result of regressions of the unit price, and the price ratio on the same sets of explanatory variables that are used in the main regressions. Significance levels of variables are very similar to the results in Table 3.

[10] Our unit values are based on cost, insurance, and freight (CIF) import data and therefore reflect the landed price.

**Table 3: Estimation Results, Country Fixed Effect**

| | (1) ln(Unit price) | (2) ln(Unit price) | (3) ln(Unit price) | (4) Price difference | (5) Price difference | (6) Price difference | (7) Price difference2 | (8) Price difference2 | (9) Price difference2 |
|---|---|---|---|---|---|---|---|---|---|
| ln(GDP per cap) | 0.681*** | 0.742*** | 0.437*** | 0.0939*** | 0.120*** | 0.0670** | 0.0767*** | 0.0978*** | 0.0847*** |
| | (0.0547) | (0.0546) | (0.103) | (0.0151) | (0.0150) | (0.0270) | (0.0143) | (0.0142) | (0.0257) |
| ln(population) | 0.0408 | 0.0952 | -0.180 | -0.0244 | -0.000836 | -0.0790 | -0.0459 | -0.0249 | -0.0968 |
| | (0.173) | (0.172) | (0.302) | (0.0478) | (0.0471) | (0.0792) | (0.0450) | (0.0446) | (0.0753) |
| Developed | 0.684*** | 0.740*** | 0.763*** | 0.0820*** | 0.106*** | 0.101*** | | | |
| | (0.0298) | (0.0300) | (0.0444) | (0.00825) | (0.00824) | (0.0117) | | | |
| ln(competitors) | -0.103*** | -0.134*** | -0.116** | -0.0477*** | -0.0609*** | -0.0770*** | -0.0433*** | -0.0562*** | -0.0752*** |
| | (0.0308) | (0.0307) | (0.0490) | (0.00853) | (0.00844) | (0.0129) | (0.00800) | (0.00795) | (0.0122) |
| ln(O-O-P) | 0.414*** | 0.396*** | 0.265** | 0.124*** | 0.116*** | 0.0425 | 0.0910*** | 0.0853*** | 0.0479 |
| | (0.0705) | (0.0701) | (0.123) | (0.0195) | (0.0193) | (0.0322) | (0.0184) | (0.0182) | (0.0306) |
| ln(volume) | | -0.0470*** | -0.0664*** | | -0.0204*** | -0.0249*** | | -0.0169*** | -0.0200*** |
| | | (0.00412) | (0.00638) | | (0.00113) | (0.00168) | | (0.00106) | (0.00158) |
| ln(tariff) | | | -0.212*** | | | -0.0462*** | | | -0.0396*** |
| | | | (0.0435) | | | (0.0114) | | | (0.0109) |
| Observations | 11,337 | 11,337 | 5,292 | 11,337 | 11,337 | 5,292 | 11,337 | 11,337 | 5,292 |

Notes: Standard errors in parentheses; fixed effects OLS; * $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$

Source: Authors.

## 6.2 Country-Pair Fixed Effects

In Table 4, the estimation results are presented when using country-pair fixed effects. The coefficient of GDP per capita is statistically significant in all columns, indicating the strong presence of price discrimination for insulin around the world. The coefficient for population size shows a negative value, but it is insignificant, as we saw in the previous estimation.

The coefficient for the number of competitors remains negative, except for (2) and (3). It turns insignificant for the unit price, but remains significant for both types of price differences. In other words, competition does not seem to significantly reduce the unit price charged, but shrinks the price gap when the unit price is higher than the reference price.

The results for the ratio of out-of-pocket expenditures are very similar to Table 3. They show a significant and positive correlation with unit price and price differences.

Next, as we did in the previous subsection, we add the volume information as an explanatory variable. This a negative significant effect on unit price, which implies again that the larger the volume of insulin traded, the lower the price charged by a partner exporting country and the smaller the positive gap from the reference price. The inclusion of trade volume information does not change the significance of the other variables, such as the log of population size. However, the size of the coefficient of GDP per capita for the unit price and the price differences becomes larger and its standard error becomes smaller (columns (2), (5) and (8)).

Once we control for the tariff rate as well as the volume, the estimation results are very similar, demonstrating the robustness of our findings. The only significance that we lose is for the relationship between the proportion of out-of-pocket expenditure and the price difference in columns (6) and (9). On the other hand, the coefficient of the population size turns significant now (p<0.05). The correlation between the unit price and GDP per capita weakens, but its statistical significance remains. The tariff rate shows a negative significant correlation with the unit price (p<0.10) and has a significant effect to reduce the positive price gap (p<0.01).

Table A.3 in the Appendix has another result of regressions of the unit price, and the price ratio on the same sets of explanatory variables that are used in the main regressions. Significance levels of variables are very similar to the results in Table 3.

**Table 4: Estimation Results, Country-Pair Fixed Effect**

| | (1) ln(Unit price) | (2) ln(Unit price) | (3) ln(Unit price) | (4) Price difference | (5) Price difference | (6) Price difference | (7) Price difference2 | (8) Price difference2 | (9) Price difference2 |
|---|---|---|---|---|---|---|---|---|---|
| ln(GDP per cap) | 0.638*** | 0.846*** | 0.645*** | 0.104*** | 0.158*** | 0.117*** | 0.0775*** | 0.127*** | 0.120*** |
| | (0.0556) | (0.0544) | (0.102) | (0.0171) | (0.0169) | (0.0304) | (0.0164) | (0.0162) | (0.0293) |
| ln(population) | -0.154 | -0.0465 | -0.188 | -0.0928* | -0.0648 | -0.174** | -0.0843 | -0.0587 | -0.180** |
| | (0.174) | (0.168) | (0.299) | (0.0535) | (0.0522) | (0.0890) | (0.0513) | (0.0502) | (0.0857) |
| ln(competitors) | -0.0173 | 0.0275 | 0.000853 | -0.0525*** | -0.0409*** | -0.0553*** | -0.0466*** | -0.0360*** | -0.0492*** |
| | (0.0300) | (0.0290) | (0.0456) | (0.00922) | (0.00901) | (0.0136) | (0.00884) | (0.00866) | (0.0131) |
| ln(O-O-P) | 0.462*** | 0.385*** | 0.234** | 0.132*** | 0.112*** | 0.0380 | 0.101*** | 0.0832*** | 0.0264 |
| | (0.0670) | (0.0648) | (0.114) | (0.0206) | (0.0201) | (0.0340) | (0.0198) | (0.0193) | (0.0327) |
| ln(volume) | | -0.139*** | -0.163*** | | -0.0362*** | -0.0418*** | | -0.0330*** | -0.0385*** |
| | | (0.00551) | (0.00865) | | (0.00171) | (0.00258) | | (0.00165) | (0.00248) |
| ln(tariff) | | | -0.0789* | | | -0.0455*** | | | -0.0478*** |
| | | | (0.0437) | | | (0.0130) | | | (0.0125) |
| Observations | 11,337 | 11,337 | 5,292 | 11,337 | 11,337 | 5,292 | 11,337 | 11,337 | 5,292 |

Notes: Standard errors in parentheses; country-pair fixed effects OLS; * $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$

Source: Authors.

# 7. CONCLUSION AND DISCUSSION

The objective of this paper has been twofold: First, we aimed at demonstrating the importance of international trade for the supply of medicaments containing insulin. Taking a sample of 186 countries over the period 1995 to 2013, our results indicate that insulin imports increased substantially over the last 20-year period (1995–2013), clearly outpacing the increasing prevalence of diabetes in the world. International trade is thus vital for providing insulin to patients across the world.

In the second part of the paper, we used the unit values of imports of insulin products (HS 300431) to analyze the difference in prices between countries. Our study constitutes the largest empirical assessment of pharmaceutical pricing in terms of number of countries included. Running various panel data regressions, we have been able to uncover new insights explaining the price differences across countries:

- First, GDP per capita is positively correlated with the unit price, which confirms earlier findings (e.g., Schweitzer and Comanor 2011) that price discrimination is a common practice applied by pharmaceutical companies.
- Second, manufacturers from OECD countries systematically charge higher prices for their insulin medicine compared to insulin drugs originating from developing countries.
- Third, market conditions play another important role in determining insulin prices. The higher the number of competitors (measured by the number of source countries) and the larger the market (measured by the size of trade volume), the lower the price becomes.
- Fourth, when faced with a dispersed buyers' market (measured as the percentage of out-of-pocket payments for health care), prices tend to be higher.
- Finally, we find evidence that the higher the volume imported by a country and the higher the imposed tariff, the lower the price.

Our results corroborate earlier studies that evidenced international price discrimination. In every market economy, price discrimination is widely used to extract consumer surplus. However, price discrimination for pharmaceuticals is often restricted in domestic markets due to the particular nature of public health, health system financing, and of the pharmaceutical products themselves. By contrast, international price discrimination for pharmaceuticals appears to be common practice. International price discrimination can improve access to pharmaceuticals for patients in developing countries, as it allows for offering of lower prices. However, the degree of price discrimination for pharmaceuticals remains debatable. In line with earlier studies (e.g., Schweitzer and Comanor 2011), we find that the price elasticity is below unity. In other words, lower-income countries pay relatively more for the same drug compared to higher-income countries. A price elasticity of one would be more equitable when assessed against affordability relative to income. A price elasticity of larger than one would mean that as income per capita grows, the price of drugs increases even more. Such a relationship would mean that drugs are cheaper in poorer countries due to higher prices in more affluent markets. However, a higher elasticity also translates into larger price differences, which then increases the incentives for parallel trade.

Given pharmaceutical companies' attempts to charge different prices according to the income per capita, what policy options are available to governments? Our results hint at several strategies that might lead to lower prices for insulin. First, increasing the number of source countries provides a simple, yet effective, tool to foster price competition. Second, building up health financing systems that reduce out-of-pocket payments seems another suitable strategy to bring down insulin prices. Part of these efforts could be to pool the purchase of insulin.[11] Third, our results show that imposing higher tariffs lowers the unit price. However, imposing tariffs comes at a cost. We know from basic trade policy theory that both consumers and producers suffer from welfare loss due to the introduction of a tariff. If the demand curve is rather inelastic, as it is in the case of life-saving drugs such as insulin, producers are able to transfer most of the cost to the patients. Imposing tariffs on insulin drugs is therefore a risky policy, as most of the burden is borne by the patients, not the pharmaceutical companies. Eliminating tariffs would therefore be the more efficient policy from the point of view of both public health and economic efficiency.

Finally, a word of caution is important. Final drug prices can be very different from the prices reported to customs when entering the country. The final price paid by the patient is determined by wide array of determinants, such as national health regulations and standards, the market power of national retailers and health insurance companies, and domestic transportation cost. In order to improve the affordability of insulin for all patients, much more is needed than the measures identified above. However, the three measures are low-hanging fruits with potentially large benefits for diabetes patients.

[11] The PRC government, for example, is trying to limit the increase in medical expenditures by buying more medicines in bulk at lower costs (Bloomberg 2013).

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* The Asian Development Bank refers to China by the name People's Republic of China.

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# APPENDIX

The following observations were dropped from the samples estimated because they were likely to suffer some measurement/reporting errors.

**Table A.1: Dropped Samples**

| Country | Partner Country | Year |
|---|---|---|
| Germany | Denmark | 1999 |
| Germany | France | 1999 |
| Croatia | Germany | 2013 |
| Croatia | Hungary | 2013 |
| Croatia | Denmark | 2013 |
| Albania | India | 2004 |
| Honduras | Panama | 2000 |
| Maldives | Singapore | 1998 |
| Mali | France | 2007 |
| Mauritania | PRC | 2006 |
| Mongolia | Denmark | 1996 |
| Mozambique | India | 2011 |

PRC= People's Republic of China.

Source: Authors.

**Table A.2: Estimation Results, Country Fixed Effect Estimator**

| | (1)<br>Unit price | (2)<br>Unit price | (3)<br>Unit price | (4)<br>Price ratio | (5)<br>Price ratio | (6)<br>Price ratio | (7)<br>Price ratio2 | (8)<br>Price ratio2 | (9)<br>Price ratio2 |
|---|---|---|---|---|---|---|---|---|---|
| ln(GDP per cap) | 0.169*** | 0.196*** | 0.147*** | 0.293*** | 0.381*** | 0.207** | 0.200*** | 0.267*** | 0.275*** |
| | (0.0152) | (0.0150) | (0.0271) | (0.0498) | (0.0493) | (0.0883) | (0.0423) | (0.0419) | (0.0774) |
| ln(population) | -0.0000251 | 0.0237 | -0.0623 | -0.0695 | 0.00985 | -0.210 | -0.112 | -0.0452 | -0.220 |
| | (0.0479) | (0.0472) | (0.0793) | (0.157) | (0.155) | (0.259) | (0.133) | (0.132) | (0.227) |
| Developed | 0.0821*** | 0.107*** | 0.100*** | 0.267*** | 0.349*** | 0.324*** | | | |
| | (0.00827) | (0.00826) | (0.0117) | (0.0271) | (0.0271) | (0.0381) | | | |
| ln(competitors) | -0.0415*** | -0.0548*** | -0.0724*** | -0.155*** | -0.199*** | -0.244*** | -0.107*** | -0.148*** | -0.206*** |
| | (0.00855) | (0.00846) | (0.0129) | (0.0280) | (0.0277) | (0.0420) | (0.0237) | (0.0235) | (0.0367) |
| ln(O-O-P) | 0.123*** | 0.115*** | 0.0493 | 0.401*** | 0.375*** | 0.189* | 0.241*** | 0.223*** | 0.171* |
| | (0.0196) | (0.0193) | (0.0322) | (0.0642) | (0.0632) | (0.105) | (0.0545) | (0.0538) | (0.0921) |
| ln(volume) | | -0.0205*** | -0.0251*** | | -0.0686*** | -0.0825*** | | -0.0535*** | -0.0681*** |
| | | (0.00114) | (0.00168) | | (0.00372) | (0.00548) | | (0.00312) | (0.00476) |
| ln(tariff) | | | -0.0464*** | | | -0.155*** | | | -0.105*** |
| | | | (0.0114) | | | (0.0373) | | | (0.0327) |
| Observations | 11,337 | 11,337 | 5,292 | 11,337 | 11,337 | 5,292 | 11,337 | 11,337 | 5,292 |

Note: Standard errors in parentheses; fixed effect OLS; * $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$

Source: Authors.

## Table A.3: Estimation Results, Country-Pair Fixed Effect Estimator

| | (1) Unit price | (2) Unit price | (3) Unit price | (4) Price ratio | (5) Price ratio | (6) Price ratio | (7) Price ratio2 | (8) Price ratio2 | (9) Price ratio2 |
|---|---|---|---|---|---|---|---|---|---|
| ln(GDP per cap) | 0.180*** | 0.234*** | 0.197*** | 0.304*** | 0.487*** | 0.363*** | 0.184*** | 0.336*** | 0.374*** |
| | (0.0172) | (0.0169) | (0.0305) | (0.0565) | (0.0557) | (0.100) | (0.0484) | (0.0478) | (0.0879) |
| ln(population) | -0.0695 | -0.0413 | -0.156* | -0.271 | -0.176 | -0.491* | -0.202 | -0.123 | -0.432* |
| | (0.0537) | (0.0524) | (0.0891) | (0.177) | (0.172) | (0.293) | (0.151) | (0.148) | (0.257) |
| ln(competitors) | -0.0467*** | -0.0350*** | -0.0499*** | -0.170*** | -0.131*** | -0.172*** | -0.118*** | -0.0855*** | -0.134*** |
| | (0.00925) | (0.00904) | (0.0136) | (0.0305) | (0.0298) | (0.0447) | (0.0261) | (0.0255) | (0.0392) |
| ln(O-O-P) | 0.130*** | 0.110*** | 0.0433 | 0.425*** | 0.357*** | 0.165 | 0.277*** | 0.221*** | 0.119 |
| | (0.0207) | (0.0202) | (0.0340) | (0.0681) | (0.0664) | (0.112) | (0.0583) | (0.0570) | (0.0983) |
| ln(volume) | | -0.0365*** | -0.0423*** | | -0.123*** | -0.140*** | | -0.101*** | -0.119*** |
| | | (0.00172) | (0.00258) | | (0.00565) | (0.00849) | | (0.00485) | (0.00745) |
| ln(tariff) | | | -0.0468*** | | | -0.151*** | | | -0.121*** |
| | | | (0.0130) | | | (0.0429) | | | (0.0376) |
| Observations | 11,337 | 11,337 | 5,292 | 11,337 | 11,337 | 5,292 | 11,337 | 11,337 | 5,292 |

Note: Standard errors in parentheses; fixed effect OLS; * $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$

Source: Authors.