BOSTON UNIVERSITY Global Development Policy Center

GEGI WORKING PAPER 048 • 04/2021

Evaluating the Impact of Data Exclusivity on the Price per Kilogram of Pharmaceutical Imports

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ABSTRACT

Background: Intellectual property provisions in free trade agreements (FTAs) enhance the monopoly power of branded pharmaceutical producers, yet studies that measure their impact on access to medicines or pharmaceutical prices often find small effects. There are at least two possible reasons for this. First, the impacts of TRIPS-Plus provisions appear gradually. These provisions will only apply to new drugs coming onto the market, which means they only affect a handful of drugs each year. Furthermore, FTA provisions will not affect prices of newly approved drugs until the end of their patent terms. Most countries already have TRIPS-*level* patent and data protection in place when FTAs are implemented, so TRIPS-*plus* policies may only effect the length of exclusivity on the margin. The second reason is a focus on FTAs themselves, rather than countries' domestic implementation of FTA obligations. The FTA provisions generally do not change domestic policy until implemented at the domestic level. It is notable that studies of policies often required by FTAs have found substantial impacts on price and/or availability.

This study attempts to overcome the methodological problems noted above. It presents the impact of data exclusivity on the price of pharmaceutical imports. Data exclusivity is a form of intellectual property protection that prevents generic entry by preventing generic firms from relying on the originator's test results to win regulatory approval. It is a TRIPS-Plus provision often required in FTAs.

Methodology: A set of annual price and volume data from the UN Comtrade database covers 42 countries and 8 diagnostic classes between 1996 and 2010. IFPMA and WIPO sources determine the year when these countries implemented data exclusivity in their laws (and which countries did not have data exclusivity during this period). Simple observation shows that the price per kilogram of drug imports grow more quickly in countries that have enacted data exclusivity in their laws than in countries where data exclusivity is not in force. Panel regressions show that the impact on prices is statistically significant and robust to the inclusion of controls. A second set of tests using the IDEAS index, which measures varying levels data exclusivity in countries' laws, yields similar results.

Finding: Between 1996 and 2010, the annual increase in price per kilogram of drug imports for these 42 countries was between 2.4 and 4.5 percentage points higher in countries that had implemented data exclusivity than in countries that had not implemented it.

Discussion: It is difficult to assert a causal relationship between the implementation of data exclusivity and the subsequent pharmaceutical import price inflation. This is partially due to the nature of Comtrade's data and partially due to the imprecision of policy implementation.

Overall study topic: applied economics, health economics, trade policy

INTRODUCTION

Members of the World Trade Organization have ratified nearly 300 regional and bilateral free trade agreements (FTAs) since its founding. Many of these FTAs require countries to enact stronger intellectual property provisions than are required by the World Trade Organization's Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPS Agreement), provisions commonly referred to as "TRIPS-Plus." Specific TRIPS-Plus provisions vary from one FTA to the next. Examples include patent extensions in the event of delays in the patent or regulatory application process, requirements to patent new uses of known products, restrictions on compulsory licenses, and restrictive forms of clinical test data protection.

Many observers have warned that TRIPS-Plus intellectual property provisions will increase the monopoly power of branded pharmaceutical firms, and therefore lead to higher prices for medicines. On the other hand, supporters of the promotion of these provisions abroad have questioned their link to higher prices. Indeed, *ex post* empirical studies that quantify the impact of FTAs on access to medicines or pharmaceutical prices have often found smaller effects than *ex ante* studies predicted (Thrasher, et al. 2019).

Why Have Studies of FTAs Failed to Find a Stronger Effect?

There are at least two reasons why *ex post* studies have not found larger impacts. First, the effect of TRIPS-Plus provisions should become apparent gradually. Most countries already have TRIPS-*level* patent and data protection in place when FTAs are implemented, so any TRIPS-*plus* policies will not affect prices of newly approved drugs until the end of their patent terms. This applies to patent extensions, follow-on patents for new uses, and any market exclusivity that could outlast the term of

the original patent. Furthermore, these provisions will only apply to new drugs approved for marketing after FTA implementation.

The second reason is that many studies focus on trade agreements themselves, rather than countries' domestic implementation of TRIPS-Plus provisions required by the agreements. Examples include Bollyky (2016), finding no impact on drug prices or pharmaceutical spending in 15 countries that have FTAs with the US; and Kyle and Qian (2014), finding that a patents had a smaller impact on drug prices after TRIPS compliance deadlines than before.

FTAs generally do not change domestic policy until the provisions are implemented at the domestic level. To find the effect of an FTA *provision* on medicine prices, one must identify the point when the relevant domestic law or regulation changed. There may be a delay between the entry of the trade agreement into force and a country's legislative changes needed to comply with it. For instance, the US-Peru FTA was signed in 2006, but Peru implemented its IP provisions in 2009 (USTR 2009). Countries may enact TRIPS-plus intellectual property provisions for reasons unrelated to FTAs, so a policy mandated by an FTA may be in place before an agreement or in the absence of an agreement. An example is Australia's implementation of patent term extensions before it negotiated a trade agreement with the US that mandated such extensions (Australian Government Productivity Commission 2016). In these cases and others, the date that trade agreements took effect differ from the date when TRIPS-Plus intellectual property rules were put in place.

Previous Studies TRIPS-Plus Provisions in Domestic Law

Studies that examine the impact of domestic legal changes often required by FTAs find substantial impacts. One common provision is the expansion of the scope of patentability. FTAs may require countries to grant patents on new uses of already patented medical products, or of common derivatives of known substances. Secondary patents have acted as "effective patent term extensions" in Chile delaying the entry of lower priced generic medicines (Abud, Hall and Helmers 2015). They have extended the patent for the important HIV/AIDS drug Abacavir in the Ukraine, where the originator product is more than twice the cost of an otherwise-available generic (Médecins Sans Frontières 2016). They have added 6.3 to 7.4 years to the effective patent life of drugs in the US (Kapczynski, Park and Sampat 2012). Analysis of the top 12 grossing drugs in 2017 by I-MAK (2018) found that originator firms sought an additional *11-28 years* of additional protection beyond the original 20 year term.

Patent extensions of the type required by trade agreements have been found to have increased prices. The Australian Productivity Commission (2016) estimates that patent extensions cost the government's Pharmaceutical Benefits Scheme approximately AUD 260 million each year in additional medicines costs from 2007 to 2012. Hu et al. (2020) find that Supplementary Protection Certificates in the European Union (which "function identically to a patent extension" within the regional market) have been responsible for higher prices on Sofosbuvir, Trastuzumab and Imatinib. "Linkage" between patent authorities and health regulators in Canada has extended the patent life of "weakly inventive products" in Canada, keeping generics off the market (Bouchard, et al. 2010).

Data Exclusivity: TRIPS-Plus Protection of Test Data

This paper focuses on data exclusivity, a form of protection of test data used to prove a drug is safe and effective. When originator firms invent new medicines, they present clinical trial data to regulators in order to win marketing approval. When generic firms apply for marketing approval, they typically rely on the originator's clinical trial data – allowing them to bring products to the market at a lower cost, which is passed onto the consumer in savings. Data exclusivity is a period of time during

which generic firms cannot obtain marketing approval for their products based on originator firms' clinical data – effectively blocking them from the market. It is a layer of intellectual property protection separate from the patent right. Data exclusivity can block generic competition in the pharmaceutical market after patent expiration or in the absence of patent protection.

Article 39.3 of the TRIPS Agreement requires companies to protect test data submitted to health regulators against "unfair commercial use." The US and most other high-income countries meet this requirement by granting periods of data exclusivity. However, there is no WTO rule mandating this form of test data protection. TRIPS gives countries the policy space to implement article 39.3 in other ways, including through restrictive definitions of "unfair commercial use" and through limiting the scope of new products eligible for data protection (UNCTAD-ICTSD 2005). When TRIPS took effect, most countries other than the US and European nations did not have data exclusivity, but it has become more common as American trade policy has promoted its adoption in other markets (Palmedo 2021).

FTA intellectual property chapters commonly require data exclusivity. In their review of 126 trade agreements signed between 1991 and 2016, Morin and Surbeck (2020) find that 42 required signatories to enact data exclusivity into their laws – including all the comprehensive trade agreements with the United States.

Previous studies of data exclusivity have found that it raises medicine prices and/or reduces access. Data exclusivity requirements have led to higher prices and $396 million additional expenses for Colombia's public health system (Cortés, et. al., 2012). In the US, the price of one particular off-patent drug increased from nine cents to $4.85 per pill after data exclusivity was applied (Kesselheim and Solomon, 2010). Two studies of data exclusivity required by FTAs find a significant impact – data exclusivity blocked generic versions of off-patent medicines from the Guatemalan market (Shaffer and Brenner, 2009) and delayed the introduction of cheaper generics into the Jordanian market for 79 percent of medicines (Malpani, 2009).

HYPOTHESIS

Most studies examining the impact of TRIPS-Plus provisions to date have focused on particular drugs in particular countries. In this paper, I take another approach - evaluating the impact of a TRIPS-Plus intellectual property rule across many countries. Specifically, I examine the impact of test data exclusivity on prices of pharmaceutical imports using trade data from the UN Comtrade database. I hypothesize that countries that have enacted data exclusivity will face more rapid increases in the cost of drug imports. The relative price increases will be gradual, but it will build over time and one will be able to see a distinct medium-to-long run effect.

DATA

The Year When Countries Enacted Data Exclusivity

A report by the International Federation of Pharmaceutical Manufacturers Associations identifies the laws that protect test data in a set of 42 countries[1] and indicates whether they include a period of exclusivity (IFPMA 2011). The World Intellectual Property Organization's Lex database provides

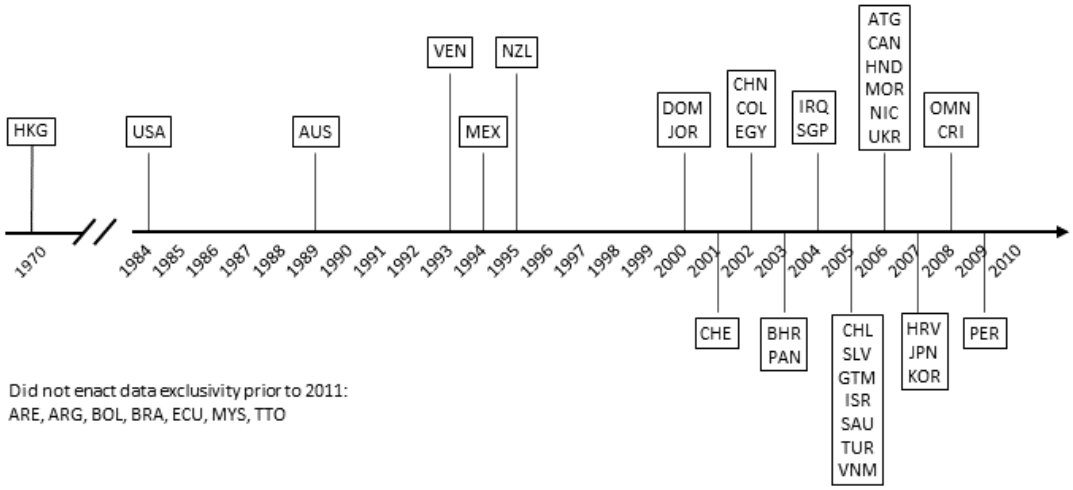
[1] The IFPMA report also includes the date when the EU enacted a regional requirement for Member countries to enact a term of data exclusivity, but it does not include information on how each individual country enacted data exclusivity.

the year in which most of the laws took effect. In some cases, neither the IFPMA nor WIPO source indicate the year a law took effect, so secondary sources were utilized.[2]

Sixteen of the countries in the set are currently classified as high income countries by the World Bank, and the rest are classified as middle income. The set does not include any countries from sub-Saharan Africa, but does include countries from the Americas, Europe, Asia and North Africa.

Figure 1 shows the growing prevalence of data exclusivity in the set of countries over time. Hong Kong has had a de facto data exclusivity in place since its 1970 Pharmacy and Poisons Regulations required all applicants to submit clinical data (it has since been revised to allow abbreviated generic applications after a period of data exclusivity). The US implemented data exclusivity early with the passage of the Hatch-Waxman Act in 1984. Initially, there were few other countries protecting test data with terms of exclusivity – only four other countries in the set enacted data exclusivity prior to 2000. Many other countries adopted data exclusivity in the 2000s. In all, 35 of the 42 countries in the set had data exclusivity in their laws prior to the publication of the IFPMA report.

Figure 1. Timeline of Data Exclusivity Laws



Differing Levels of Data Exclusivity Conferred by Law

The data on the timeline above overlooks the heterogeneous nature of data exclusivity laws. There are many differences in the level or strength of data exclusivity provided in various countries.

The most obvious difference is the length of the term of protection. Another is the scope of medicinal products subject to data exclusivity – some laws require exclusivity for all new pharmaceutical products while others require it for new chemical entities (NCEs), and the definition of an NCE varies from one country to the next. Furthermore, some laws may allow generic producers to rely on clinical test data submitted to foreign governments. Still others may allow a public interest concerns to override data exclusivity in some situations, or allow potential generic registrants to oppose data exclusivity.

[2] This report relies on Lekhan, et al. (2015) to define the year data exclusivity entered into force in Ukraine. It relies on Moeller IP Advisors (2008) to define the year data exclusivity entered into force in Panama.

Table 1. Inverse I.D.E.A.S. Scores after Enacting Data Exclusivity

Country	Inverse IDEAS Score
Peru	0.40
Chile	0.46
Mexico	0.50
Egypt	0.54
Canada	0.55
Costa Rica	0.58
Dominican Republic	0.59
Colombia	0.59
Jordan	0.65
Panama	0.65
El Salvador	0.66
Guatemala	0.66
Ukraine	0.66
Honduras	0.74
Nicaragua	0.83
Bahrain	0.85
Oman	1.19
Australia	1.41
Singapore	1.41
Korea	1.56
Hong Kong	2.00

Shaikh (2016) gives a detailed account of different ways countries have enacted data exclusivity, and introduces an Index of Data Exclusivity and Access (IDEAS), which quantifies the differences. IDEAS was constructed to evaluate national laws "based on their orientation towards access to medicine with regard to test data exclusivity." The index is derived from 25 questions within four categories – the compliance with TRIPS Article 39, the strength of data protection conferred by the law, the duration of protection, and the inclusion of exceptions or enabling provisions. Its values range from 0 to a possible high score of 4, with higher values indicating greater policy space for allowing generic registrations based on original data.

IDEAS analyzes data exclusivity in 23 countries, 21 of which are in my original dataset. After my initial econometric tests (described below) using a binary indicator of data exclusivity from the full set of 42 countries, I run a second set of tests using the IDEAS data from these 21 countries. For ease of interpretation, my tests utilizing IDEAS use the *inverse* of the original IDEAS score – so a higher score indicates a higher level of data exclusivity.

The inverse IDEAS scores range from 0.4 in Peru after 2008, after it implemented its FTA with the US; to 2.0 for Hong Kong, which has never allowed the registration of generic pharmaceuticals based on originator data. Table 1 shows the level of data exclusivity provided by each country after implementation.

Price Per Kilogram of Imported Pharmaceuticals

The UN Comtrade database reports the annual value (in US dollars) and volume (in kilograms) of commercial pharmaceutical imports as recorded by border authorities. Unlike published prices, which may be subject to further discounts or markups, Comtrade reports the actual amounts of money paid at the wholesale level. Annual data for both value and volume is available for imports into many countries from the mid-1990s through the present. The amount of data over time makes Comtrade data well suited to demonstrate the impact of TRIPS-Plus provisions on medicine prices.

Comtrade data is disaggregated by product class using the international Harmonized Commodity Description and Coding System, commonly referred to as the Harmonized System, or HS. This allows one to see changes in the price per kilogram of pharmaceuticals trade in certain classes of drugs over time. The data is available at the two-, four- and six-digit level of the HS – the more digits, the more precise the product class.

Comtrade could be used to identify trends in trade between specific exporter-importer pairs. However, international value chains complicate the analysis of imports of finished pharmaceutical products. Differing tariff rates for FTA partners and exporters who receive other types of preferential treatment may further distort trade flows (Urata and Okabe 2014), which could bias a dataset utilizing exporter-importer pairs. On the other hand, data on imports from the entire world reflects what countries are able to import given their domestic IP and regulatory system. The ability to import generic rather than branded drugs is not affected by the country of origin, but by the intellectual property law of the importer. If data exclusivity protects the originator product in an importing country, then the originator version must be purchased, regardless of the exporting country.

This study's pricing indicator is the annual price per kilogram paid by each country for each six-digit HS class of drug imports from 1996 through 2010. This covers the period when most of the countries in my set adopted data exclusivity. During this time, Comtrade has data on imports of eight different classes of retail medicines classified at the 6-digit HS level, which are shown in Table 2. All of these are shipments of packaged medicines for human consumption, rather than active pharmaceutical ingredients or other unmixed pharmaceutical products, which fall under a different HS classification.

Table 2 also shows descriptive statistics for the price per kilogram in each of the HS classes in the dataset. The mean varied significantly over the period from one class to the next, ranging from $29.70 for imports in HS 300450 (medicines containing vitamins) to $268.49 for those classified as HS 300439 (medicines containing certain types of hormones and antibiotics). There was also a lot of variation within each class, with the standard deviation exceeding the mean for half of the HS groups. Though skewed when taken as a whole and when disaggregated by HS class, the data on price per kilogram logs normal.

Figure 2 compares the annual average price per kilogram paid by importing countries each year by countries with and without data exclusivity from 1996 to 2010. The price increased at a higher rate in the countries that had enacted data exclusivity. Average prices in each group tended to be similar until the early 2000s, and began to diverge after 2004.

Figure 3 compares the average price per kilogram separately for each HS classification. While import price inflation was higher in countries with data exclusivity for all of the HS groups, the difference was most pronounced in HS 300431 (medicines containing insulin) and HS 300439.

The following section tests the significance of the difference in pharmaceutical import price inflation in countries with and without data exclusivity.

Table 2. HS Classifications and Descriptive Statistics

HS Code	Product Description	Mean	St. Dev.	N
300410	Medicaments, containing penicillins, streptomycins or their derivatives	43.92	27.26	549
300420	Medicaments; containing antibiotics (other than penicillins, streptomycins or their derivatives)	86.74	119.20	515
300431	Medicaments; containing insulin	231.55	178.69	524
300432	Medicaments; containing corticosteroid hormones, their derivatives or structural analogues (but not containing antibiotics)	119.68	285.54	529
300439	Medicaments; containing hormones (but not insulin), adrenal cortex hormones or antibiotics	268.49	558.99	521
300440	Medicaments; containing alkaloids or their derivatives, containing ephedrine or its salts	107.45	148.18	524
300450	Medicaments; containing vitamins or their derivatives	29.70	46.38	543
300490	Medicaments; consisting of mixed or unmixed products n.e.c. in heading no. 3004	51.33	50.38	524

Figure 2. Average Price per Kilogram of Pharmaceutical Imports (USD)

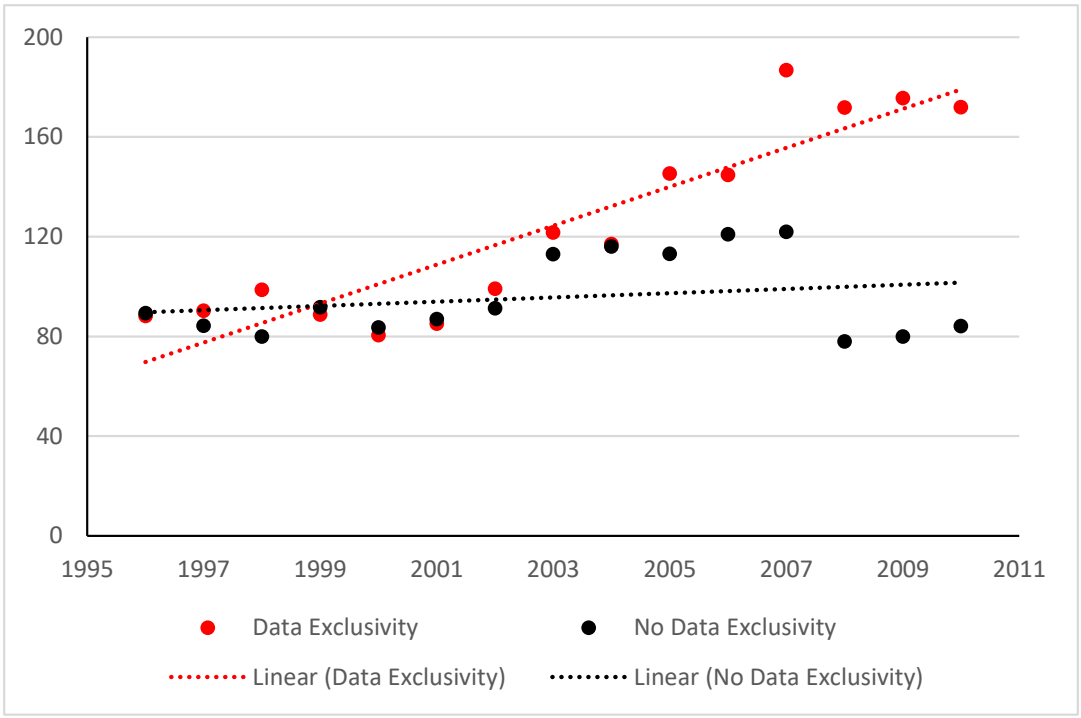


Figure 3. Average Price per Kilogram of Pharmaceutical Imports (USD), disaggregated by HS Class

ECONOMETRIC TESTS

Econometric Methodology

To test the relationship between data exclusivity and the growth of import prices, I run panel regressions based on two econometric models. Both use HS class imports to a particular country as the panel variable. The difference between the two models is how they capture time – Model (1) uses the variable $Year_t$ *to* account for the upward trend, and Model (2) drops $Year_t$ and adds fixed effects for time *t*.

$$(Log)Price_{hs\text{-}c,t} = \alpha_{hs,c} + \beta_1 Year_t{}^{*}DataExclusivity_{c,t} + \beta_2 Year_t + \beta_3 DataExclusivity_{c,t} + \beta_4 (Log)Kg_{hs\text{-}c,t} + \beta_n \boldsymbol{X}_{c,t} + FE_{hs\text{-}c} + \varepsilon \quad (1)$$

$$(Log)Price_{hs\text{-}c,t} = \alpha_{hs\text{-}c} + \beta_1 Year_t{}^{*}DataExclusivity_{c,t} + \beta_2 DataExclusivity_{c,t} + \beta_3 (Log)Kg_{hs\text{-}c,t} + \beta_n \boldsymbol{X}_{c,t} + FE_{hs\text{-}c,t} + \varepsilon \quad (2)$$

I first run regressions using the full dataset of 42 countries for which I have binary data on data exclusivity implementation. In these tests, $DataExlusivity_{c,t}$ is a dummy variable equal to 1 for observations in years after a country has enacted exclusivity in its law. The independent variable of interest is the interaction variable $Year_t{}^{*}DataExclusivity_{c,t}$, which shows the difference in the rate at which pharmaceutical prices per kilogram change in countries that have data exclusivity, relative to those that do not.

In the following subsection, I run the same regressions on the subset of 21 countries for which I have IDEAS data on levels of data exclusivity protection. In these regressions, the variable *IDEASi* – the inverted IDEAS score – is used in place of the dummy variable and *Year*IDEASi* is used in place of the interaction variable.

In each model, the dependent variable, $(Log)Price_{hs\text{-}c,t}$ is the logged price per kilogram of pharmaceutical imports by HS class, country and year. The quantity of medicines purchased per country per class each year is included as the control variable $(Log)Kg_{hs\text{-}c,t}$ and a vector of country- and time-specific controls is included as $\boldsymbol{X}_{c,t}$. These include logged GDP per capita, health expenditure as a percentage of GDP, and the proportion of health spending that occurs out-of-pocket. $FE_{hs\text{-}c}$ are the fixed effects for HS-country groups, and ε is a robust error term clustered by the HS-country groups.

Results

TESTS WITH A BINARY INDICATOR OF DATA EXCLUSIVITY

Table 3 shows the results of four regressions based on the binary indicator of data exclusivity. Each indicates that the relationship between data exclusivity and higher prices for pharmaceutical imports is statistically significant and robust to the inclusion of controls. The coefficient on *Year*DataExclusivity* is positive and significant in all specifications. The overall models fit the data well – all the right hand side variables have significant coefficients with the expected signs, the adjusted R-squared are all above 0.80 and the within-entity R-squareds range from 0.39 to 0.49.

Column (1) shows the results with the overall time trend as a variable for the period 1996-2010. The annual growth rate for pharmaceutical imports in countries without data exclusivity was 3.9 percent, but the corresponding growth rate in countries with data exclusivity was 7.6 percent. Though the difference is small year to year, it compounds. Over 15 years at these rates of growth, a price in a theoretical country without data exclusivity would increase 78 percent and the corresponding price in a theoretical country *with* data exclusivity would increase 200 percent.

The control variables in this specification behave as expected. Logged GDP per capita in US dollars, taken from the World Bank, is positive, indicating the expected relationship between a country's wealth and prices. Logged total kilograms is negative, supporting previous findings that larger pharmaceutical purchases are associated with lower prices (Helbe and Aizawa 2017).

The next column reports a specification including controls describing a country's health sector; out-of-pocket spending as a percentage of total health spending, and health expenditure as a percentage of GDP. Both are taken from the World Bank development indicator database, which has data on these variables from 2000 forward, so these specifications have a smaller sample size and encompass the last eleven years of the original dataset. Out-of-pocket spending as a percentage of total spending is included because it is has been shown that prices tend to be lower in countries where more spending is out of pocket (Pavenik 2002). Health spending as a percentage of GDP has been shown to be associated with higher prices among OECD countries (Anderson, et al. 2005). Both of these relationships are supported by the coefficients on these variables, though they are only weakly significant in this specification. When these controls are added and the period is restricted, the model predicts faster price growth in countries without data exclusivity. The difference in the rate of price growth in countries with and without data exclusivity is smaller, but still significant.

Table 3. Regressions on Logged Price per Kilogram
(Data Exclusivity Indicated by Binary Variable)

VARIABLES	(1) Time Trend RHS	(2) Time Trend RHS	(3) Year Fixed Effects	(4) Year Fixed Effects
Year * Data Exclusivity	0.037*** (0.010)	0.024** (0.011)	0.045*** (0.011)	0.038*** (0.012)
Year	0.039*** (0.006)	0.054*** (0.011)		
Data Exclusivity	-0.324*** (0.119)	-0.227* (0.123)	-0.391*** (0.128)	-0.366*** (0.136)
(Log) GDP Per Capita	0.409*** (0.069)	0.325*** (0.072)	0.427*** (0.087)	0.315*** (0.080)
(Log) Kilograms	-0.467*** (0.032)	-0.523*** (0.038)	-0.468*** (0.032)	-0.523*** (0.038)
OOP Spending as % of Total		-0.008* (0.005)		-0.010** (0.005)
Health Expenditure as % GDP		0.059* (0.031)		0.078** (0.033)
Constant	8.856*** (0.644)	7.039*** (0.666)	6.018*** (0.799)	7.589*** (0761)
Observations	4229	3150	4229	3150
# of HS-Country Groups	328	312	328	312
Adjusted R^2	0.810	0.838	0.811	0.839
Within-Entity R^2	0.431	0.488	0.389	0.448
Subject-Country F.E.	YES	YES	YES	YES
Year F.E.	NO	NO	YES	YES

Standard errors in parentheses * p<0.10, ** p<0.05, *** p<0.01

The specifications reported in Columns (3) and (4) apply time fixed effects instead of including *Year* as a right hand variable. The coefficients on *Year*DataExclusivity* are slightly higher in these specifications than in the corresponding ones with the linear time trend. The significance of the health sector control variables raises to 95 percent, and the adjusted- and within-entity R squareds fall slightly. Overall, the results are similar when fixed effects are substituted for the time trend.

TESTS BASED ON THE IDEAS MEASUREMENT OF THE LEVEL OF DATA EXCLUSIVITY

In this subsection, I present the empirical tests using an inverse of the IDEAS scores to account for differing levels of data exclusivity provided in different countries. The results resemble those in the previous section using a dummy variable. The overall fit is similar despite the smaller sample size, though the controls describing countries' health sectors have different coefficients. Out-of-pocket spending as a percentage of total health spending remains negative, but is now significant at the 99 percent level. On the other hand, the coefficient on health expenditures as a percentage of GDP becomes insignificant.

The coefficients on *Year*IDEAS* in Columns (1) and (3) are 0.005 and 0.004 lower than the corresponding coefficient on *Year* DataExclusivity* in Table 3. The coefficient on this interaction term is insignificant in Column (2), which is unexpected, but is likely explained by the shortened period and smaller sample size. The largest difference is found in Column (4), where the coefficient on *Year*IDEAS* is 0.008 higher than the corresponding coefficient on *Year* DataExclusivity* in Table 3. This result – based on the model utilizing time fixed effects rather than a linear time control, and controlling for health sector variables – suggests that the difference between prices in countries with and without data exclusivity may be larger in countries with stronger data exclusivity laws.

Table 4. Regressions on Logged Price per Kilogram
Data exclusivity indicated by inverse IDEAS index

VARIABLES	(1) Time Trend RHS	(2) Time Trend RHS	(3) Year Fixed Effects	(4) Year Fixed Effects
Year * IDEASi	0.032*** (0.012)	0.024 (0.018)	0.041*** (0.015)	0.046*** (0.022)
Year	0.034*** (0.008)	0.039*** (0.014)		
IDEASi	-0.323** (0.153)	-0.230 (0.214)	-0.403** (0.172)	-0.449* (0.249)
(Log) GDP Per Capita	0.518*** (0.086)	0.428*** (0.099)	0.554*** (0.108)	0.425*** (0.103)
(Log) Kilograms	-0.431*** (0.040)	-0.459*** (0.047)	-0.429*** (0.040)	-0.458*** (0.046)
OOP Spending as % of Total		-0.018*** (0.006)		-0.020*** (0.006)
Health Expenditure as % GDP		0.046 (0.046)		0.055 (0.048)
Constant	4.376*** (0.659)	5.800*** (0.870)	4.325*** (0.823)	6.190*** (0.945)
Observations	2154	1640	2154	1640
# of HS-Country Groups	168	160	168	160

VARIABLES	(1) Time Trend RHS	(2) Time Trend RHS	(3) Year Fixed Effects	(4) Year Fixed Effects
Adjusted R^2	0.768	0.776	0.770	0.78
Within-Entity R^2	0.429	0.448	0.392	0.420
Subject-Country F.E.	YES	YES	YES	YES
Year F.E.	NO	NO	YES	YES

Standard errors in parentheses * p<0.10, ** p<0.05, *** p<0.01

BARRIERS TO ESTABLISHING CAUSALITY USING TRADE DATA AND THE TIMING OF LEGAL CHANGE

The previous section used Comtrade data to illustrate a correlation between data exclusivity and higher prices of imports. It is difficult to find a causal relationship between the two due to the nature of the data, and to issues related to the timing and execution of legal change.

Data Issues

Comtrade's strength as a source of information for the analysis of pharmaceutical prices is that it covers many countries over many years. However, use of Comtrade for this purpose has its shortcomings as well.

Changes to intellectual property law will delay generic entry for individual drugs as they reach the market, rather than affecting entire classes of drugs at once, but Comtrade does not allow one to see the impact on any particular drug. Nor does it have data on imports of branded versus generic medicines. One cannot observe whether a change to intellectual property law is followed by a change in the proportion of generics, which would be useful when estimating the effect of legal changes on the supply of pharmaceuticals. Furthermore, Comrade's reliance on the categories defined by the harmonized system of tariffs is not well suited to evaluating health impacts. With the exception of insulin products, the Harmonized System of categorization is not linked to treatment of certain conditions or diseases. For instance, it does not have data on anticancer drugs, or antiretrovirals for HIV/AIDS.

Since Comtrade is a source of trade data, it does not provide any information on the prices and quantities of locally produced pharmaceuticals. The proportion of imports in total pharmaceutical supply varies from one country to the next, so the price of imports will have an inconsistent impact on overall price levels.

Legal Issues

Two particular issues complicate establishing causality when examining price changes following the establishment of data exclusivity.

First, countries may implement data exclusivity while making simultaneous changes to other potentially impactful intellectual property or healthcare laws. This may be especially relevant when countries add data exclusivity as part of a law specifically intended to implement FTA obligations. For instance, Guatemala issued decrees in 2006 that introduced data exclusivity, extended patent terms, established linkage between health and patent authorities, and expanded the scope of patentability (Biadgleng and Maur 2011). It is difficult to tease out the impact of data exclusivity as opposed to other changes when multiple legal changes happen at once.

Second, laws passed to grant data exclusivity may not always be implemented completely, leaving data protection incomplete or missing entirely. The US pharmaceutical industry has regularly complained in annual Special 301 Reviews that countries have not enforced their laws related to data exclusivity, or have implemented them in ways that renders protection inadequate (Pharmaceutical Research and Manufacturers of America 2020). Deere (2008) notes that – for a variety of intellectual property obligations in trade agreements – governments may recognize the value of agreeing to changes at the negotiating table regardless of their intentions to make changes on the ground.

CONCLUSION

Data exclusivity requirements have been included in all bilateral and regional trade agreements the US has negotiated since the creation of the WTO. The European Commission and the European Free Trade Association have required data exclusivity in many of their agreements as well. Though the expansion of data exclusivity is tied to trade agreements, its impact is based on domestic implementation of trade obligations, rather on the agreements themselves.

This paper has demonstrated that enactment of data exclusivity in a country's law was associated with a higher rate of pharmaceutical import price inflation in a heterogeneous set of 42 countries. Tests on a subset of 21 countries using a measurement of different levels of data exclusivity support this finding. A more thorough mapping of data protection laws over more countries and over a longer period would further reinforce it. Nonetheless, econometric tests demonstrate the association of a common TRIPS-Plus provision mandated by numerous FTAs with accelerated price inflation for pharmaceuticals.

The analysis of pharmaceutical import prices relied on Comtrade data, which may be well suited to study gradual changes in prices that occur over the medium to long term. It contains data over a long time horizon for many countries and is freely available. However, it relies on broad categories of drugs, does not differentiate between branded and generic drugs, and contains no information on locally produced products. Comtrade data may be a useful source for future studies of TRIPS-Plus intellectual property laws, but it lacks the precision of data on individual products.

BIBLIOGRAPHY

Abud, María José, Bronwyn Hall, and Christian Helmers. 2015. "An Empirical Analysis of Primary and Secondary Pharmaceutical Patents in Chile." *PLoS One*. https://doi.org/10.1371/journal.pone.0124257.

Anderson, Gerard, Peter Hussey, Bianca Frogner, and Hugh Waters. 2005. "Health Spending In The United States And The Rest Of The Industrialized World." *Health Affairs* 24 (4). doi:https://doi.org/10.1377/hlthaff.24.4.903.

Australian Government Productivity Commission. 2016. *Intellectual Property Arrangements.* Inquiry Report no. 78, Canberra: Australian Government. Accessed October 2020. https://www.pc.gov.au/inquiries/completed/intellectual-property/report/intellectual-property.pdf.

Biadgleng, Ermias Tekeste, and Jean-Christophe Maur. 2011. *The Influence of Preferential Trade Agreements on the Implementation of Intellectual Property Rights in Developing Countries.* Issue Paper no. 33, Geneva: UN/International Centre for Trade and Sustainable Development.

Bollyky, Thomas. 2016. "A Dose of the TPP's Medicine: Why P Trade Deals Haven't Exported U.S. Drug Prices." *Foreign Affairs*, March 23. https://www.foreignaffairs.com/articles/2016-03-23/dose-tpps-medicine.

Bouchard, Ron, Richard Hawkins, Robert Clark, Reider Hagtvedt, and Jamil Sawani. 2010. "Empirical Analysis of Drug Approval-Drug Patenting Linkage for High Value Pharmaceuticals." *Northwestern Journal of Technology and Intellectual Property* 8 (2): 174-227.

Deere, Carolyn. 2008. *The Implementation Game: The TRIPS Agreement and teh Global Politics of Intellectual Property Reform in Developing Countries.* Oxford: Oxford University Press.

Flynn, Michael McCarthy. 2018. *Hard to Swallow: Facilitating tax avoidance by Big Pharma in Ireland.* Oxfam Ireland. Accessed 2020. https://www.oxfamireland.org/sites/default/files/pharma-report.pdf.

Helbe, Matthias, and Toshiaki Aizawa . 2017. "International Trade and Determinants of Price Differentials of Insulin Medicine." *Health Policy and Planning* 32 (1): 1-10. doi:10.1093/heapol/czw085.

Hu, Yuanqiong, Dimitri Eynikel, Pascale Boulet, and Gaelle Krikorian. 2020. "Supplementary Protection Certificates and Their Impact On Access to Medicines in Europe: Case Studies of Sofosbuvir, Trastuzumab and Imatinib." *Journal of Pharmaceutical Policy and Practice* 13 (1). doi: https://doi.org/10.1186/s40545-019-0198-6.

IFPMA. 2011. *Data Exclusivity: Encouraging Development of New Medicines.* White Paper, International Federation of Pharmaceutical Manufacturers and Associations. Accessed November 2020. https://www.ifpma.org/resource-centre/data-exclusivity-encouraging-development-of-new-medicines/.

I-MAK. 2018. *Overpatented, Overpriced: How Excessive Pharmaceutical Patenting is Extending Monopolies and Driving up Drug Prices.* White paper., I-MAK. https://www.i-mak.org/wp-content/uploads/2018/08/I-MAK-Overpatented-Overpriced-Report.pdf.

Kapczynski, Amy, Chan Park, and Bhaven Sampat. 2012. "Polymorphs and Prodrugs and Salts (Oh My!): An Empirical Analysis of "Secondary" Pharmaceutical Patents." *PLoS One.* https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0049470.

Kyle, Margaret, and Yi Qian. 2014. *Intellectual Property Rights and Access to Innovation: Evidence from TRIPS.* Working Paper 20799, National Bureau of Economic Research. https://www.nber.org/system/files/working_papers/w20799/w20799.pdf.

Lekhan, V N, V M Rudiy, M V Shevchenko, Kaluski D Nitzan, and E Richardson. 2015. "Ukraine: Regluations." *Health Systems in Transition* (European Observatory on Health Systems and Policies (a partnership hosted by WHO)) 17 (2). https://www.who.int/health-laws/countries/ukr-en.pdf.

Médecins Sans Frontières. 2016. *Untangling the Web of Antiretroviral Price Reductions, 18th Edition.* White Paper, MSF Access Campaign. https://msfaccess.org/untangling-web-antiretroviral-price-reductions-18th-edition.

Moeller IP Authors. 2008. *General Overview About the Current Extension of Text Data Protection in Latin Amercia.* Intellectual Property Owners Organization. https://ipo.org/wp-content/uploads/2013/03/TestDataProtection_Municoy.pdf.

Morin, J.F., and J. Surbeck. 2020. "Mapping the New Frontier of International IP Law: Introducing a TRIPs-plus Dataset." *World Trade Review* 19 (1): 109-122.

Mullard, Asher. 2018. "2017 FDA Drug Approvals." *Nature Reviews Drug Discover.* https://www.nature.com/articles/nrd.2018.4.pdf?origin=ppub.

Palmedo, Michael. 2021. "United States: Unilateral Norm Setting Using Special 301." In *Intellectual Property Law and Access to Medicine: TRIPS Agreement, Health, and Pharmaceuticals*, edited by Amaka Vanni and Srividhya Ragavan. Routledge.

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The views expressed in this Working Paper are strictly those of the author(s) and do not represent the position of Boston University, or the Global Development Policy Center.

Pavenik, Nina. 2002. "Do pharmaceutical prices respond to potential patient out-of-pocket expenses?" *Rand Journal of Economics* 33 (3): 469-87.

Pharmaceutical Research and Manufacturers of America. 2020. *Special 301 Submission.* Submission to U.S. Trade Representative for the 2020 Special 301 Review, Washington, DC: PhRMA. https://phrma.org/Policy-Paper/PhRMA-Special-301-Submission-2020.

Shaikh, Owais H. 2016. *Access to Medicine Versus Test Data Exclusivity.* Berlin: Springer-Verlah GmbH.

Thrasher, Rachel, Veronika Wirtz, Warren Kaplan, Kevin Gallagher, and Hattie Werk. 2019. *Rethinking Trade Treaties and Access to Medicines.* Boston University Global Development Policy Center Working Group on Trade, Investment Treaties, and Access to Medicines. https://www.bu.edu/gdp/files/2019/11/Trade-Report-2019-GDP-Center-3.pdf.

Trachtenberg, Danielle, Warren Kaplan, Veronika Wirtz, and Kevin Gallagher. 2020. "The Effects of Trade Agreements on Imports of Biologics: Evidence from Chile." *Journal of Globalization and Development* 10 (2). doi: https://doi.org/10.1515/jgd-2019-0030.

UNCTAD-ICTSD. 2005. *Resource Book on TRIPS and Development.* Edited by Pedro Roffe and Ricardo Melendez-Ortiz. Cambridge: Cambridge University Press. https://doi.org/10.1017/CBO9780511511363.

Urata, Shujiro, and Misa Okabe. 2014. "Trade Creation and Diversion Effects of Regional Trade Agreements: A Product-level Analysis." *The World Economy* 37 (2): 267-289.

USTR. 2009. *Special 301 Report.* Washington, DC: United States Trade Representative. https://ustr.gov/sites/default/files/2008%20Special%20301%20Report.pdf.