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Reiko Laski April 2, 2019

Access to Pharmaceuticals in Developing Countries: Finding the Optimal Suboptimal Solution

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An abstract of
a thesis submitted to the Faculty of Emory College of Arts and Sciences
of Emory University in partial fulfillment
of the requirements of the degree of
Bachelor of Arts with Honors

Department of Economics

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Abstract

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By Reiko Laski

Patent protection for pharmaceutical companies has sparked controversy over the past few decades between the economics of incentivizing research and development and the ethics of denying individuals access to life-saving medicines on the basis of their ability to pay. This paper studies the effect of competition on prices of antiretroviral drugs under specific circumstances when generic production of patented pharmaceutical products is permitted and analyzes changes in the accessibility of these products within a country in response to increased affordability. Using data on NGO procurement of antiretroviral drugs, I estimate the effect of additional competitors on the prices of generic drugs and compare these prices to those offered by patent-holding manufacturers under differential pricing schemes. I furthermore use survey data from Ethiopia to analyze regional and demographic disparity in pharmaceutical access over time.

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Acknowledgements

Sincerest thanks to Dr. O'Connell for his unwavering support and unparalleled dedication and for making this paper possible. Many thanks as well to the rest of my committee, Dr. Howard and Dr. Powers, for their guidance and encouragement.

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1 Introduction

A growing concern for the enforcement of international intellectual property protection has spread throughout the developed countries of the world in recent decades. In the case of the pharmaceutical industry, patents for newly discovered drugs have led to ethical controversy regarding affordability for consumers in low- and middle-income countries. Pharmaceutical production is characterized by high fixed costs and low marginal costs, since the research and development (R&D) investments required to produce drugs are substantial (Varian 2000). In the absence of intellectual property protection, firms lack incentive to innovate, which leads to below-socially optimal levels of R&D spending. Patents give pharmaceutical companies market power for twenty years and allow them to set prices above the marginal cost of production to recoup fixed costs, which incentivizes investment. At the same time, however, the high prices of pharmaceuticals cause many consumers in low- and middle-income countries to be "priced-out" of the market. In the case of pharmaceuticals such as HIV/AIDS antiretroviral treatments, antimalarial drugs, and tuberculosis antibiotics, consumers in these countries constitute a substantial share of the market demand, yet are unable to afford these life-saving drugs.

Literature in both economics and law discusses the implications of international intellectual property protection, particularly the WTO's Trade-Related Intellectual Property Rights (TRIPS) agreement of 1994. The main purpose of TRIPS was to enforce property rights, though exceptions exist for cases of "national emergency or other circumstances of extreme urgency" (TRIPS, Article 31b). In these situations, compulsory or voluntary licensing agreements allow a company to use the intellectual property of a patent-holder to, for example, produce generic antiretroviral drugs (ARVs) used in HIV/AIDS treatment regimens to be sold in low-income countries. To address the humanitarian issues associated with costly pharmaceuticals, economists and legal scholars have proposed many solutions to increase the affordability of life-saving drugs in developing countries. Among the most common is differential pricing of pharmaceuticals based on per capita income. Intercoun-

try differential pricing can theoretically lead to "second-best" efficiency levels in the market for pharmaceuticals for which there exists demand in both high- and low-income countries, because consumers in the high-income markets can subsidize the fixed costs while those in low-income markets pay a price lying somewhere in the range between marginal and average cost. The theoretical justification for differential pricing further asserts that both consumers and pharmaceutical companies benefit from this pricing strategy, since consumers who would have been priced out of the market under a uniform pricing regime have greater access to medicines and pay at least the marginal cost of the drug. In practice, differential pricing schemes are determined by individual pharmaceutical companies who decide which countries are eligible for reduced prices for particular ARVs. Eligibility criteria vary widely by manufacturer but generally depend on income and geographic location. Even with differential pricing, however, developing countries are generally characterized by large degrees of income inequality, which in turn leads to highly convex demand and high prices relative to the purchasing power of most consumers. Therefore, the result of intercountry differential pricing in practice is that brand-name pharmaceuticals in low- and middle-income countries are still widely unaffordable. Further policy suggestions to increase affordability of pharmaceuticals in developing countries involve allowing the production of generic drugs and competition among companies to drive down prices while finding alternative means of financing R&D.

For nearly three decades the debate about access to life-saving medicine in developing countries has focused on the tension between two camps: those that argue that patents provide a necessary protection for pharmaceutical companies who pour millions of dollars into researching and developing drugs and those who argue that low-income countries should be able to import and rely on generic versions of necessary medicines, as the presence of generic drugs in the market necessarily increases competition and drives down price. Since the passage of TRIPS, support for differential pricing of drugs has increased, which would theoretically provide pharmaceutical access to those who could not afford the high prices charged under uniform pricing schemes. While this solution could work in theory, practical

concerns such as parallel trade, price benchmarking, and failure to account for income inequality have left low-income consumers particularly in middle-income countries with little to no access to necessary medications. Additionally, despite increased international patent protection, voluntary licensing agreements and difficulty renewing patents in countries where generic drug production constitutes a large industry has caused the market for these generic substitutes to become more robust since 2005. Since neither solution is currently being employed to its fullest extent in low-income countries, pharmaceuticals are still unaffordable for many consumers as differential pricing schemes are imperfectly implemented and competition among generic drug producers is limited to companies in particular countries under the existing patent regime.

Literature on the pharmaceutical market is likewise split between advocating for these two solutions to increase the affordability of drugs in low- and middle-income countries. Analyses on prices of originator drugs (Scherer and Watal 2002; Danzon, Mulcahy, and Towse 2015) show that, in practice, differential pricing schemes for patented pharmaceuticals based on a country's per capita income alone are insufficient in decreasing prices to an affordable level, particularly when arbitrage opportunities prevent prices from falling to the level predicted theoretically. Furthermore, the degree of income inequality present in low- and middle-income countries further impedes the affordability of patented drugs under differential pricing. On the other hand, empirical research on the effect of generic substitutes on market prices for ARVs (Vasan et al. 2006; Waning et al. 2009; Moon et al. 2011) demonstrates how increased competition in countries where generic drugs are permitted can increase affordability in low-income countries and proposes price-independent means of financing R&D. Under existing intellectual property protection agreements, generic competition only reduces prices in least-developed countries and in nations in which HIV prevalence constitutes a "national emergency," and the limited number of generic producers may each still have enough market power to set prices above equilibrium. The existing literature does not address how the entry of generic substitutes into the market for a particular ARV dosage

form interacts with competitors, both originator and other generic suppliers, or how quickly and to what extent this market saturation occurs.

This paper uses data on procurement transactions by NGOs from 2004 to 2018 to analyze the structure of the market for ARVs. Since there is a necessary lag time following the certification of a new ARV while generic suppliers reverse engineer the drug and wait for their own WHO certifications, I examine the effects of the availability of generic substitutes on prices for new ARV dosage forms during the years following their initial entrance into the market and estimate the impact of additional competitors. Economic theory and the existing literature suggest that competition among generic drug producers will decrease prices; in this paper, I estimate the extent of competition required to sufficiently achieve affordable, competitively-priced pharmaceuticals. By analyzing the relationship between unit price and the number of competitors in the market, I determine that an additional generic supplier can reduce prices by 20.1–38.4%, with this effect being larger for newly developed products than for older drugs. Moreover, products purchased from patent-holding companies are still estimated to cost 79.4% more than generic substitutes in countries that qualify for reduced prices and up to 272% more in nonqualifying countries. While these results support the idea that differential pricing is a flawed means of achieving widespread access to pharmaceuticals, they also suggest that a reasonably small number of competitors can decrease prices sufficiently, providing evidence that unregulated competition among generic producers which could threaten R&D incentives for brand-name manufacturers is unnecessary.

This paper also examines how the landscape of pharmaceutical accessibility has developed over the past two decades following TRIPS. Using demographic and health survey data to examine changes in access to pharmaceuticals used in the HIV treatment regimens at various points in time in Ethiopia, a low-income country, I address the hypothesis that the inaccessibility of pharmaceuticals and suboptimal levels of use result from unaffordable prices alone. Though much of the existing literature in economics inherently assumes that affordability is equivalent to accessibility, research in health policy (Assefa et al. 2017; Cawley

et al. 2017) challenges this claim, particularly after taking into account intracountry heterogeneity. While the results show that access to pharmaceutical products increases throughout the duration of the survey period, I also find that accessibility varies substantially by region and type of place of residence within a country, which indicates that price is not the only barrier to access in low-income countries. Taken together, this work could identify which factors are most important to take into consideration when formulating both health policy and international trade agreements.

The structure of this paper is as follows: Section 2 reviews relevant literature regarding pharmaceutical pricing and accessibility; in Sections 3 and 4, I describe the data and methodology used in this analysis; Section 5 presents the results; Section 6 concludes by discussing implications for policy and future research.

2 Literature Review

2.1 Strategies to Reduce ARV Prices in Developing Countries

The accessibility of pharmaceuticals in low- and middle-income countries has incited controversy particularly since the enactment of TRIPS in 1994. By decreasing the availability of generic drugs in many developing countries, patent protection enforced by TRIPS has led to increased pharmaceutical prices, as well as increased investment in R&D. Kremer (2002) reviews the main points of debate, highlighting the positive impact of pharmaceuticals on health outcomes and life expectancy in developing countries despite the still-limited extent of their usage. He further emphasizes some of the factors that affect the availability of pharmaceuticals within a country, including market size and characteristics, and notes that market failure, particularly the pricing of pharmaceuticals above marginal cost and failure to account for positive externalities associated with treatment of infectious diseases, leads to suboptimal use. On the other hand, he acknowledges that socially optimal pricing reduces the incentive for pharmaceutical companies to invest in R&D. To estimate empirically the effects of price regulation for pharmaceuticals on investment, Golec and Vernon (2006)

examine drug prices and R&D spending in the United States compared with countries in the European Union and find that investment levels are highly sensitive to pricing regimes. Golec, Hegde, and Vernon (2010) add to the literature on factors affecting R&D spending in the pharmaceutical industry by noting that even the threat of price regulations proposed by the Clinton administration's 1993 Health Security Act may have decreased investment by over one billion dollars. The dynamic problem of optimally setting pharmaceutical prices to allow for not only widespread usage and affordability but also adequate research investment has inspired a host of proposals for potential solutions, based on both theoretical and empirical reasoning.

Extensive literature outlines a framework for differential pricing of patented pharmaceuticals to increase their affordability in developing countries. Hammer (2002) applies a theoretical model of differential pricing to the AIDS epidemic and discusses how this pricing strategy is in compliance with intellectual property laws and the TRIPS agreement. He further argues that this "intuitively obvious" pricing solution solves the humanitarian issues associated with patented drugs since pharmaceutical companies can set prices relative to the income levels of different countries, thus charging lower prices in lower income countries rather than a single uniform price across all nations. Danzon and Towse (2003) similarly advocate for differential pricing of pharmaceuticals based on Ramsey pricing principles, which propose setting prices inversely proportional to price elasticities of demand, and claim that this strategy would in theory increase market efficiency more than alternative solutions such as compulsory licensing. While these papers provide theoretical support for differential pricing as a means of increasing accessibility, Scherer and Watal (2002) analyze empirical data from sales of ARVs in eighteen low- and middle-income countries and regions to estimate the extent to which Ramsey pricing works in reducing prices in practice. Their analysis suggests that prices indeed decrease for countries with lower per capita incomes, consistent with the Ramsey pricing model, though only to a limited extent. The researchers introduce practical concerns such as parallel trade and price benchmarking that may induce suboptimal pricing

schemes and claim that adequately controlling for these factors could lead to Ramsey prices and efficient levels of pharmaceutical use.

A further branch of literature involves other practical considerations associated with intercountry pharmaceutical pricing, suggesting that even optimal pricing schemes may still be insufficient in delivering affordable drugs to developing countries. Lucchini et al. (2003) study the primary determinants of ARV prices in Brazil and various African nations, including the class of ARV drug being sold, existence of generic competition within the country as permitted by TRIPS, and HIV prevalence. In several of these countries, they noted that public initiatives designed to increase access to brand-name drugs led to lower prices, but the main factor associated with widespread access to affordable medicines was local production and importation of generic drugs. Vasan et al. (2006) analyze transactions data for ARVs that include generic and brand-name drugs in an observational study and find consistently low ARV prices in low-income countries but highly varied prices in middle-income countries, leading again to the conclusion that the most effective factor in reducing drug prices is generic competition. Their paper presents early evidence that even under differential pricing strategies, regions with limited competition for generic drugs and high levels of inequality still face unaffordable prices. Waning et al. (2009) use similar transactions data to analyze the effectiveness of other global strategies such as large purchase volumes, third-party negotiation, and differential pricing in reducing ARV costs. In particular, the researchers determined that when generic drugs were made available, they were substantially less expensive than differentially priced, brand-name ARVs, and emphasized that differential pricing schemes are insufficient in providing HIV treatment universally. These papers provide counterevidence to the earlier claims that differential pricing would be adequate in reducing pharmaceutical prices to an affordable level. By demonstrating how generic drug production can further decrease prices, the literature suggests that the degree of affordability produced by differential pricing alone cannot satisfy the humanitarian concerns associated with patented pharmaceuticals and that strategies to finance R&D for pharmaceutical companies that are independent

from drug prices would lead to increased social welfare.

Furthermore, an additional field of literature suggests that differential pricing, though superior to uniform pricing, is insufficient because intercountry pricing does not account for the large degree of income inequality prevalent in many developing countries. Flynn, Hollis, and Palmedo (2009) develop a theoretical framework to show how convexity of demand for antiretroviral treatment for individuals with HIV would change for countries with different levels of income inequality. They show that countries with high Gini coefficients are expected to have highly convex demand curves and that profit-maximizing monopolists should set high prices relative to the country's per capita income and sell to few consumers. Conversely, countries with low coefficients have flatter, less convex demand curves, and monopolists can maximize profit by selling at lower prices to larger shares of consumers. Their research shows that a heavily skewed income distribution will affect a country's price elasticity of demand and thereby the price set by a patent-holding pharmaceutical company; the result of Ramsey pricing for countries with high levels of inequality is a price level still unaffordable for most consumers. They propose instead open licensing and greater competition in pharmaceutical production in developing countries as solutions to increase the accessibility of life-saving drugs. Moon et al. (2011) similarly advocate for increased competition, supporting their claims with empirical evidence to show that differential pricing leads to high prices particularly in middle-income markets. Danzon, Mulcahy, and Towse (2015) further support the idea that income inequality in low- and middle-income countries leads to drugs being least accessible in these markets by including per capita income and Gini coefficients in their analysis. They also find that competition posed by the availability of generic drugs does not substantially lower prices, though they suggest uncertainty of quality as an explanation for this outcome. These studies contribute to the literature on intercountry pharmaceutical pricing by revealing the significant effect of income inequality within a country on accessibility and further refuting the hypothesis that differential pricing alone could bring about both socially optimal pharmaceutical usage and R&D spending.

The first part of this paper overlaps closely with the research performed by Waning et al. (2009) and Danzon, Mulcahy, and Towse (2015). Both these studies include analysis using data on procurement transactions from the World Health Organization (WHO) or the Global Fund to Fight AIDS, Tuberculosis, and Malaria. These transactions reflect the prices of pharmaceuticals procured by third-party NGOs, which typically results in lower per unit prices than those in the retail channel. Using the procurement transactions data, Waning et al. estimate the effects of global strategies, notably differential pricing, on reducing ARV prices in developing countries. Their paper uses regression analysis, clustering observations by country and year to account for correlation and fixed effects, to estimate the percentage change in price per tablet separately for each of the ARV dosage forms in their sample caused by various pricing strategies. This analysis shows that 83% of ARV dosage forms for which both generic and differentially priced brand-name drugs were available were purchased at significantly lower prices from generic manufacturers compared with brand-name companies. They find that even under differential pricing regimes, the markup of brand-name pharmaceuticals over generics ranges from 23% to 498%. Danzon et al. use data for prices of brand-name and generic therapeutic drugs charged by manufacturers to retail pharmacies across thirty-seven countries to estimate the effect of a country's average per capita income and inequality level on drug prices, as well as procurement transactions data from the WHO to estimate these effects specifically for drugs used to treat HIV/AIDS, malaria, and tuberculosis in low- and middle-income countries. Using regression analysis, the researchers estimate the effect of factors such as procurement volume, per capita income, and income distribution on prices in both the retail channel and the procurement channel. Among their results, they find that income elasticity of price with respect to per capita income is lowest in low- and middle-income countries, thus making pharmaceuticals relatively more unaffordable in these nations. Furthermore, their results suggest that the effects of income distribution on prices are eliminated in the procurement channel, since competition among generic suppliers drives prices to converge with marginal production costs.

This paper intends to fill a gap in the literature on the degree to which competition affects the market for generic ARVs by analyzing the effect of each additional competitor on unit prices, as well as to address the extent to which heterogeneity within a country affects access to pharmaceutical products.

2.2 Efficacy of HIV Treatment Programs

Recent literature in health policy addresses the availability of HIV treatment in low-income countries. Konings et al. (2012) consider the rate of HIV prevalence in Ethiopia, as well as intracountry variation by demography, and analyze some of the ramifications of the 2010 WHO treatment guidelines, which include beginning treatment earlier for HIV-positive individuals. They argue that a major factor inhibiting widespread treatment in Ethiopia, in addition to concerns of cost, is the scarcity of resources in hospitals and health centers. More recently, Assefa et al. (2017) evaluated the performance of treatment programs in Ethiopia and found that while the rate of ARV coverage has increased substantially since 2005, there is significant disparity in coverage by region, age, and gender; like Konings et al., they suggest that additional resources and mechanisms are necessary to reduce these gaps in ARV accessibility. In the second part of this paper, I analyze changes in access to treatment over time, focusing particularly on the asymmetric effects for urban and rural locations. Significant differences in access suggest that, even with the decline of ARV prices, universal coverage among HIV-positive individuals will require revision of health policy to address regional and demographic disparity.

3 Data

3.1 ARV Procurement Transactions

In the first part of this analysis, I use data on procurement transactions involving purchases of ARVs by NGOs from the Global Fund Price and Quality Reports and from the WHO Global Price Reporting Mechanism (GPRM) from 2004 to 2018. These databases

Table 3.1: Summary statistics, ARV Procurement Transactions: 2004-2018

Variable	Obs	Mean	Std. Dev.	Min	Max
Log(Unit Price)	77660	-2.206	1.154	-6.666	4.113
Number of Generic Producers	77660	3.207	1.591	0	7
HHI	77660	.469	.24	.164	1
HIV Prevalence	74984	5.514	6.789	.1	28.4
Antiretroviral therapy coverage	74984	26.936	18.053	0	87
Eligible for reduced prices from originator	57558	.816	.387	0	1

Note: Table reports summary statistics for procurement transactions dataset after the removal of outliers and duplicates. Number of generic producers is computed for each ARV and year and includes only those with at least 5% market share. HIV prevalence is the percentage of individuals ages 15–49 living with HIV. Antiretroviral therapy coverage is the percentage of HIV-positive individuals receiving treatment.

provide details on each transaction, including manufacturer, price, ARV type and dosage, and the country receiving the shipment. I merged the datasets obtained from the Global Fund and from the WHO following the strategy outlined in Waning et al. (2009), which proposes removing "suspect" transactions where unit prices fall outside the range of an accepted interval. To account for differences in drugs purchased from originator and generic manufacturers, this transformation was performed separately for the two categories of drugs, identifying and removing a total of 35 "suspect" transactions. After discarding these outliers and 34,900 duplicate observations from the dataset, I created additional variables to report the number of generic companies selling an ARV both globally and within a particular country at the time of the transaction with market share greater than 5%. I further included in the transactions dataset estimates of HIV prevalence among individuals ages 15 to 49 and rates of ARV coverage among HIV-positive individuals by country and year (both reported as percentages) from UNAIDS and the WHO Global Health Observatory data repository, as well as indicator variables to represent differential pricing eligibility from the patent-holding manufacturer by country and year as reported by Médecins Sans Frontières in *Untangling the Web of Antiretroviral Price Reductions*, editions 6-18.

The unit prices in dollars of the 77,660 transactions, shown in Table 3.1, follow a log-normal distribution. The number of generic producers reported includes only manufacturers

Table 3.2: Summary statistics, Ethiopia DHS

Variable	Year	Obs	Mean	Std. Dev.	Min	Max
Heard of AIDS	2005	13603	.86	.347	0	1
	2011	30585	.974	.16	0	1
	2016	28371	.938	.24	0	1
Heard of PMTCT	2005	13603	.293	.455	0	1
	2011	30585	.511	.5	0	1
	2016	28371	.938	.24	0	1

Note: Table reports summary statistics for DHS data in Ethiopia for the years 2005, 2011, and 2016. *Heard of AIDS* and *Heard of PMTCT* represent the proportion of respondents who answered "yes" when asked if they had heard of AIDS and prevention of mother-to-child transmission respectively.

whose global sales constitute at least 5% of market share for a particular ARV in a given year, whereas the calculation of the Herfindahl-Hirschman index (HHI) includes all originator and generic manufacturers.

3.2 Demographic and Health Surveys

The second part of this analysis uses data from the USAID's Demographic and Health Surveys Program in Ethiopia from the years 2005, 2011, and 2016. Each of the samples contains data from between thirteen thousand and seventeen thousand households, and responses were collected for men and women between the ages of 15 and 49. In addition to demographic characteristics, such as age, education, income, and region, the dataset includes individuals' responses to several HIV-related questions. To estimate whether access to HIV/AIDS treatments has increased since 2005, this analysis uses knowledge of the existence of drug regimens to prevent mother-to-child transmission of HIV during pregnancy, delivery, and breastfeeding (PMTCT) as a proxy for ARV accessibility, which was not directly available in the data. As summarized in Table 3.2, overall knowledge of the existence of PMTCT has increased substantially, from 29.3% in 2005 to 93.8% in 2016.

4 Methodology

4.1 Effect of Competition on ARV Prices

First, I estimated the effects of generic competition on prices of NGO-procured ARVs. The existing literature suggests that ARV prices vary significantly based on the characteristics of the drug being sold and the country in which the transaction occurs. Patent restrictions limit transactions of generic ARVs except by WHO-prequalified suppliers to select countries, while originator manufacturers each have their own eligibility requirements for receiving reduced prices. Moreover, the evolving HIV/AIDS treatment regimens recommended by the WHO and the introduction of new dosage forms leads to changing demand for ARV types and the degree to which competition by generic drug producers can depress prices. When new drugs enter the market even where there exists an opportunity to produce and sell a generic version, there is a lag between when the drug is introduced and when generic substitutes become available since manufacturers of generics need to reverse engineer the drug and have it certified. During this lag time, the first manufacturer to produce the drug has complete market power.

Using data on procurement transactions, I estimated the following model using OLS to measure the effects of competition among generic suppliers on the price of ARVs:

$$\begin{aligned}\log UnitPrice_i = {} & \beta_0 + \beta_1\, TotalGeneric_i + \beta_2\, TotalGeneric_i^2 + \beta_3\, \log HHI_i \\ & + \beta_4\, Originator_i + \beta_5\, Eligible_i + \beta_6\, Originator_i \times Eligible_i \\ & + \beta_7\, ShippingMethod_i + \beta_8\, OralLiquid_i \\ & + \beta_9\, HIVprevalence_i + \beta_{10}\, ARVcoverage_i + u_i,\end{aligned}$$

where *TotalGeneric* is the number of generic producers of the particular ARV that appear in the dataset in the same year as the transaction, *Originator* indicates whether the transaction is from a producer of originator drugs rather than generics, *Eligible* signifies whether the country receiving the shipment was eligible for reduced prices from the originator that

year, $ShippingMethod$ captures whether the cost of shipping was included in the unit price, and $OralLiquid$ indicates whether the drug was a pill or liquid dosage. The specific independent variables of interest in this regression analysis are the number of generic competitors producing and selling the particular type of drug in the market at the time of the transaction and the degree of market concentration. To account for correlated errors, standard errors were clustered by country, year, and therapeutic class and the model includes factors such as countries' HIV prevalences, antiretroviral therapy coverages, and eligibilities for differentially priced products. This analysis demonstrates the means by which competition reduces ARV prices by estimating the effect that increasing the number of producers has on the market.

4.2 Effect of Price on ARV Accessibility

In the next part of this paper, I analyze how affordability actually affects access to pharmaceutical products in practice. Using cross-sectional survey data from Ethiopia, I analyzed changes in access to treatment to determine if there are asymmetric effects for different demographic groups. In particular, I focused on responses to the question of whether individuals had heard of drugs to prevent mother-to-child transmission of HIV. This variable should be highly correlated with access to ARVs since having heard of PMTCT likely reflects having been offered treatment in the past or knowing where to get treatment if the need should arise. Using the survey data, I estimated an initial model to determine the factors that affect an individual's likelihood of having heard of PMTCT,

$$\begin{aligned} heardOfPMTCT_i = \beta_0 + \beta_1\, Urban_i + \beta_2\, Age_i + \beta_3\, Education_i + \beta_4\, Male_i \\ + \beta_5\, Tested_i + \beta_6\, Income_i + \beta_7\, Year2011_i + \beta_8\, Year2016_i + u_i, \end{aligned}$$

then continue the analysis by including interaction terms between $Urban$ and the two year indicators to determine if knowledge of PMTCT treatment regimens changes symmetrically in urban and rural localities. This analysis shows that even if affordability increases access in the country overall, there are other factors aside from price that contribute to pharma-

ceutical accessibility, such as location and knowledge of healthcare conditions. Increases in affordability can help to justify the introduction of generic competition into the market for pharmaceuticals, but additional intracountry efforts need to be made in order to ensure their widespread availability.

5 Results

5.1 Determinants of ARV Prices

Economic theory suggests that greater competition could lead to decreases in unit prices for ARVs. Table 5.1 reports coefficients estimated by OLS for the effect of the number of generic competitors on the log unit price of ARVs, with standard errors clustered by country, year, and drug class. The first column of the table presents estimates of the parameters of the model using the full sample of ARV procurement transactions and predicts that each generic producer reduces ARV unit prices by 21.1%, on average. Moreover, note that ARVs purchased from originator manufacturers are estimated to cost as much as 272% more than generic drugs; even in countries qualifying for reduced prices, these drugs cost around 79.4% more than generics. Since pharmaceutical prices offered by originator manufacturers are expected to react differently to generic competition than the prices of other generic producers, I estimated the parameters of the same model using only the subsample of transactions involving generic drugs. Column (2) of the table reports these estimates. The effect of the number of generic producers on prices remains approximately the same as before, though the effect of market concentration, captured by log HHI, behaves counterintuitively. While theory would suggest that highly concentrated markets exhibit higher prices, the results in column (2) indicate an inverse effect.

Further restricting the sample, I estimated the model using only transactions for which ARVs were purchased from generic producers while an originator manufacturer was also actively producing and selling the same drug. This subsample excluded transactions where the product sold was available only from generic producers, whether because the originator man-

Table 5.1: Estimation of the effect of competition on log of ARV unit prices

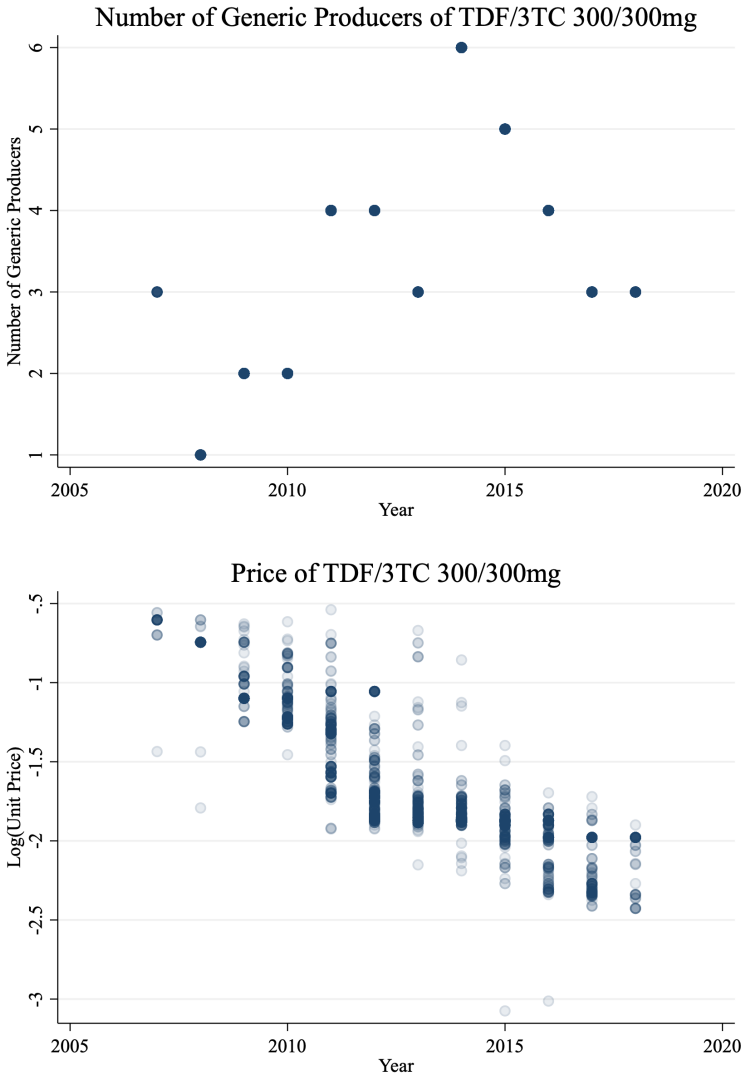
	(1)	(2)	(3)
Number of Generic Producers	-0.21088***	-0.20111***	-0.38454***
	(0.03724)	(0.03978)	(0.04661)
Number of Generic Producers Squared	0.01899***	0.01380***	0.03249***
	(0.00374)	(0.00409)	(0.00552)
Log(HHI)	-0.04882	-0.13692**	-0.11119
	(0.07022)	(0.06778)	(0.08098)
Originator	2.72310***		
	(0.07656)		
Eligible for reduced prices from originator	-0.03424	-0.06152***	-0.06286***
	(0.02355)	(0.02304)	(0.02345)
Eligible × Originator	-1.92879***		
	(0.10312)		
Shipping Costs Included	0.07475***	0.08109***	0.10158***
	(0.00997)	(0.01033)	(0.01155)
Oral Liquid	-2.20365***	-2.32407***	-2.43557***
	(0.03124)	(0.02447)	(0.02872)
HIV Prevalence	0.00353	0.00766*	0.00891*
	(0.00368)	(0.00391)	(0.00488)
Antiretroviral therapy coverage	-0.00226***	-0.00208***	-0.00511***
	(0.00078)	(0.00079)	(0.00098)
N	76530	72291	52320
R^2	0.4312	0.4149	0.4603
Mean of outcome	-2.1982	-2.2512	-2.3289
St. dev. of outcome	1.1517	1.1151	1.2019

Note: Table reports coefficients estimated via OLS. Column (1) uses the full sample of transactions, Column (2) estimates coefficients using all sales by producers of generic drugs, and Column (3) uses a subsample of generic drug sales for which an originator company also manufactured and sold the drug that year. Standard errors are clustered by country, year, and therapeutic class. Significance levels are indicated by * $p < .1$, ** $p < .05$, *** $p < .01$.

ufacturer's patent expired or because individual components of the drug were patented by different manufacturers and the combination could only be produced by a generic company. Restricting the analysis to the subsample consisting only of drugs for which the generic version is a perfect substitute for an originator drug allows for more precise estimates of how competition affects the market for patented pharmaceuticals in permissible countries. The coefficient estimates reported in column (3) suggest that competition in these cases can reduce prices by 38.5%, on average, with each subsequent producer.

5.2 Relationship between Price and Competition

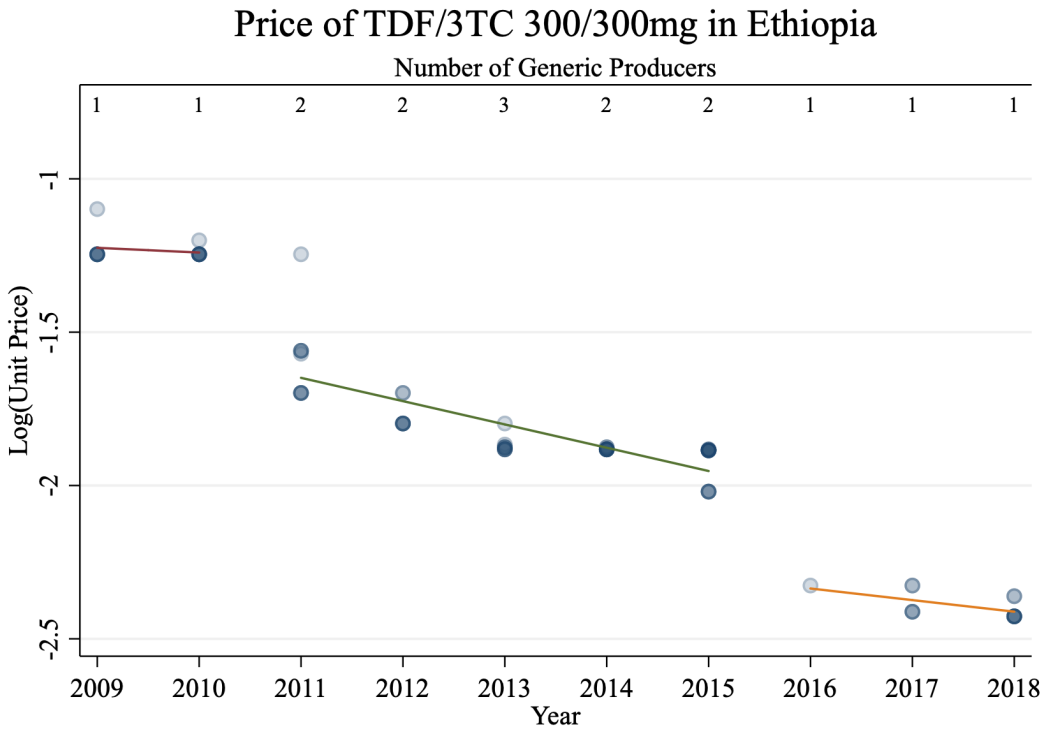
In the next part of this analysis I focused on different ARV treatments separately to determine how competition in a particular market drives price reduction. Consider the tenofovir disoproxil fumarate/lamivudine (TDF/3TC) 300/300mg tablet featured in Figure 5.1. This product is exclusively produced by generic manufacturers. A 2009 report from the



Note: Count of generic producers in the top graph includes all non-patent holding manufacturers of the TDF/3TC 300/300mg tablet with at least 5% market share in a given year. Each point in the bottom graph represents the unit price of the tablet for a single transaction.

Figure 5.1: Trends in number of generic producers and price for the TDF/3TC 300/300mg tablet

WHO encouraged the use of TDF-based treatments in place of toxic d4T-based regimens, providing a potential explanation for the spike in the number of generic companies selling the TDF/3TC 300/300mg tablet between 2007 and 2014 shown in the top panel of the figure. Despite the decline in the number of suppliers after 2014, a downward trend in the price of the tablet persists over the entire time period from 2007 to 2018. One potential explanation for this anomaly could be that after the peak in the number of suppliers in 2014, those which could not adequately reduce their costs of production to compete with the falling prices of their competitors either lost substantial market share or stopped producing TDF/3TC entirely. Noting that the number of producers observed in recent years remains above two, the persistant downward trend suggests that competition among the remaining manufacturers



Note: Count of generic producers includes all non-patent holding manufacturers of the TDF/3TC 300/300mg tablet with at least 5% market share in Ethiopia in a given year. Each point represents the unit price of the tablet for a single transaction. Slopes of trend lines show average annual reductions in price for years 2009-2010, 2011-2015, and 2016-2018.

Figure 5.2: Trend in price of the TDF/3TC 300/300mg tablet within Ethiopia

Table 5.2: Test for Structural Breaks

	Log(Unit Price)
Year	-0.01539
	(0.03748)
Year 2011-2015 × Year	-0.06058
	(0.03814)
Year 2016-2018 × Year	-0.02241
	(0.04856)
Year 2011-2015	-0.21149***
	(0.07167)
Year 2016-2018	-0.82396***
	(0.30013)
Constant	-1.20952***
	(0.06043)
N	78
R^2	0.9649
Mean of outcome	-1.8105
St. dev. of outcome	0.3735

Note: Significance levels are indicated by
* $p < .1$, ** $p < .05$, *** $p < .01$.

is still sufficient to induce price reduction. This would mean that the sharp increase and immediate decline in the number of competitors in the market may depict the rush to enter a profitable new market, an overshooting of the equilibrium number of suppliers, and firm exit when prices near the level of marginal cost.

To assess the relationship between price and number of producers, I restricted the sample further to transactions consisting of purchases of the TDF/3TC 300/300mg tablet in a single country. Figure 5.2 illustrates the downward trend in the price of the tablet in Ethiopia while also reporting the number of producers with at least 5% market share within Ethiopia each year. The figure suggests three distinct trends in log unit prices depending on year of purchase. By overlaying a count of the number of suppliers, we can see the alignment of the potential structural breaks with changes in the degree of intracountry competition. Table 5.2 shows evidence of distinct intercepts for transactions occuring in the time periods from 2009 to 2010, from 2011 to 2015, and from 2016 to 2018.

Recall that TDF/3TC is manufactured exclusively by generic producers; thus having a

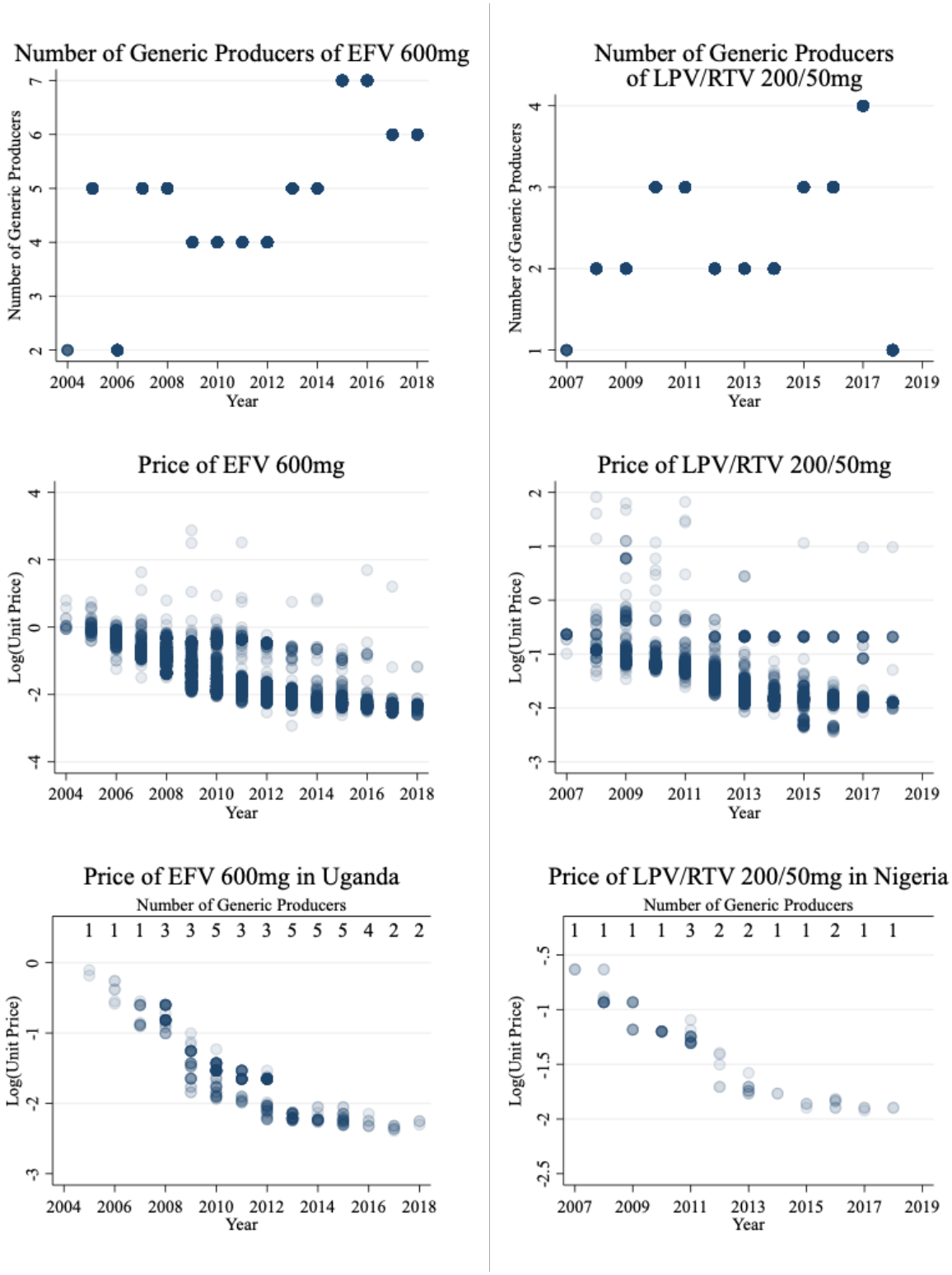


Figure 5.3: Trends in other ARV prices over time

single supplier of this drug in the market effectively constitutes a monopoly, at least at the country-level. This is the case in the period from 2009 to 2010 in Ethiopia, during which the reduction in the price of the tablet was practically and statistically insignificant. From the figure we can see that in 2011, an additional supplier of the TDF/3TC 300/300mg tablet entered the market in Ethiopia, causing its average unit price to decrease by nearly 28.7%. Between 2011 and 2015, the number of producers fluctuated between two and three, causing a decrease in price of approximately 7.6% per year during this period. Another structural break occurs between 2015 and 2016, at which point the number of producers drops back to one. Since the number of suppliers worldwide remains above two, the transition to a single supplier in Ethiopia, when considered in the context of a larger global market, still favors the hypothesis of market competition resulting in the reduction of prices. If global competition continues to force prices to decrease, then NGOs can choose to buy from the supplier offering the lowest price. Note, however, that yearly price reduction appears to slow with only one supplier. Additional examples of the inverse relationship between price and competition for particular ARVs are shown in Figure 5.3.

5.3 ARV Accessibility

Many analyses on ARV affordability make the implicit assumption that cost is the greatest barrier to treatment access. For nearly two decades the government of Ethiopia has implemented health programs to expand access to health facilities, spread awareness of HIV/AIDS and preventive measures, and increase ARV coverage among HIV-positive individuals. While ARV affordability is critical to widespread access, existing evidence suggests that coverage rates vary substantially by region and demographic characteristics. Analyzing knowledge of special ARVs used in the prevention of mother-to-child transmission (PMTCT) to approximate how widely accessible any form of antiretroviral treatment is among different individuals can help to inform policy on how to allocate resources to achieve maximal coverage. Table 5.3 shows the effects of various factors on the probability of having heard of PMTCT in Ethiopia. Standard errors are clustered by region since regional rates of HIV

Table 5.3: Effects on knowledge of PMTCT in Ethiopia

	OLS	Logit
Urban	0.07516*	0.37206**
	(0.03757)	(0.18524)
Age	0.00031	0.00422***
	(0.00030)	(0.00118)
Education	0.02277***	0.12578***
	(0.00195)	(0.00711)
Male	0.03517**	0.15638***
	(0.01221)	(0.06040)
Ever been tested for HIV	0.13942***	0.73675***
	(0.01894)	(0.11023)
Low Income	0.07448***	0.35038***
	(0.02131)	(0.11147)
Middle Income	0.09171***	0.41443***
	(0.02514)	(0.12770)
High Income	0.11807***	0.50475***
	(0.02001)	(0.10916)
Highest Income	0.22653***	1.01437***
	(0.03657)	(0.17338)
Year 2011	0.15198***	0.75873***
	(0.03737)	(0.18223)
Year 2016	0.12572***	0.63582***
	(0.02180)	(0.10744)
Constant	0.06755*	-2.17432***
	(0.03240)	(0.13682)
N	70651	70651
R^2	0.2409	
Mean of outcome	0.5037	0.5037
St. dev. of outcome	0.5000	0.5000

Note: Table reports coefficients estimated via OLS. Standard errors are clustered by region. Significance levels are indicated by * $p < .1$, ** $p < .05$, *** $p < .01$.

prevalence vary widely. Knowledge of PMTCT varies as expected with income and education and substantially increases throughout time. Since the 2005 panel, we see knowledge of PMTCT increase by around 12–15 percentage points. However, heterogeneity in rates of HIV prevalence by regional and demographic characteristics suggest that this estimate oversimplifies the changes in likelihood of having heard of PMTCT across various groups of people.

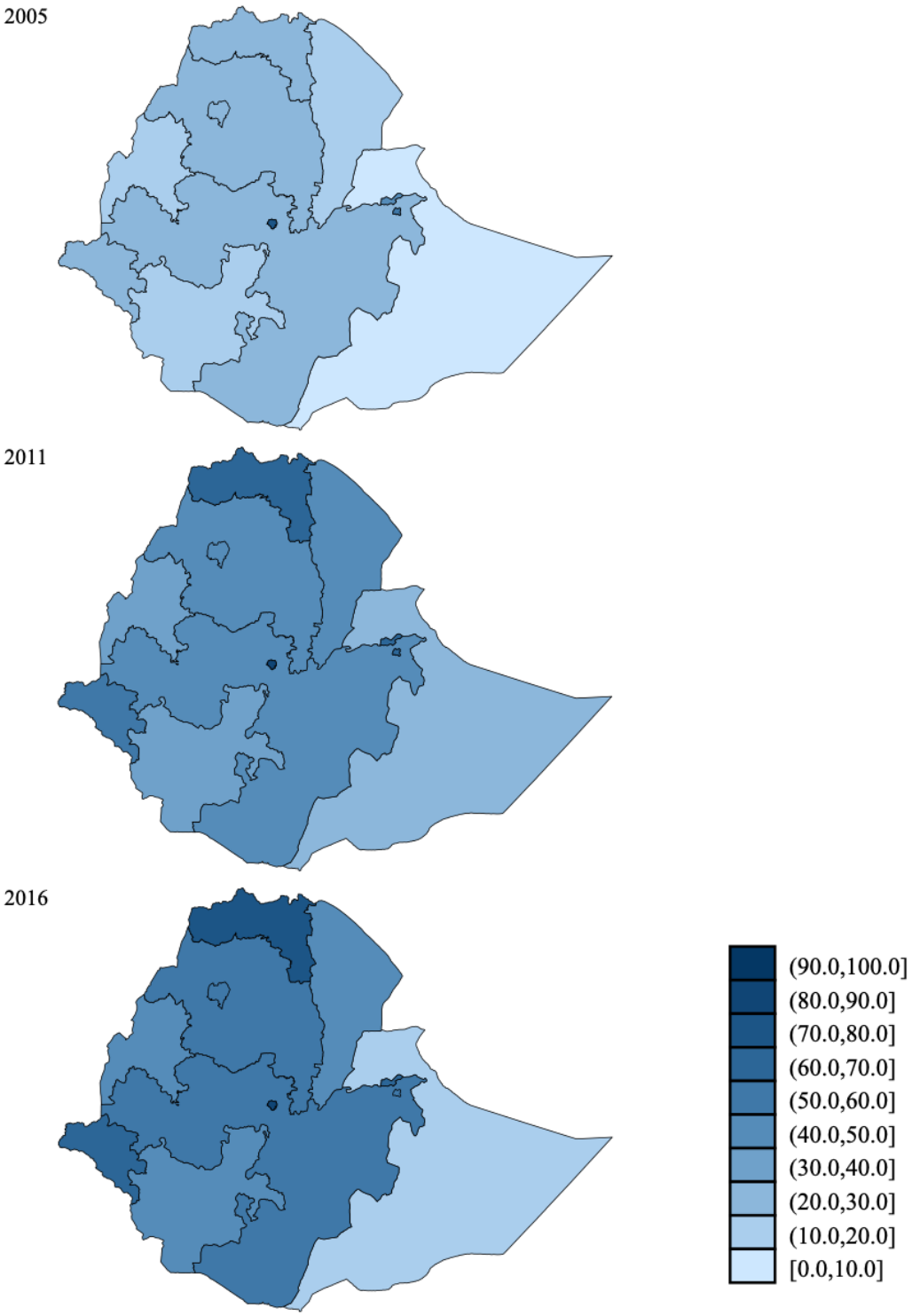


Figure 5.4: Knowledge of drugs to prevent mother-to-child transmission of HIV in Ethiopia (2005; 2011; 2016)

Issues with regional disparity in PMTCT knowledge rates in Ethiopia can be seen in Figure 5.4. In 2005, with the exception of the three small urban regions (Addis Ababa, Dire Dawa, and Harari) in central Ethiopia, the percentage of survey respondents having heard of PMTCT ranged from 4.3% (Somali Region) to 23.6% (Amhara Region). In 2016, rates in these regions ranged from 16.9% (Somali) to 71.9% (Tigray). While the lower rates of knowledge of PMTCT in Somali likely result from its comparatively low overall rate of HIV prevalence, this means that individuals living with HIV may be less aware of the treatment options available. This lack of accessibility has had detrimental effects for the region; UNAIDS estimates show a steady decline in HIV prevalence in the country overall (from 1.3% in 2011 to 1.1% in 2014), while the WHO reports increased prevalence in the Somali Region (from 0.7% in 2011 to 1.1% in 2014) with particularly high prevalence (4.2%) among pregnant women in rural areas. Since differences in knowledge of HIV treatments can have significant effects on health outcomes for HIV-positive individuals, understanding how access to ARVs varies within a country can help determine ways to ensure that increased affordability of treatment actually leads to widespread use.

Table 5.4 adds heterogeneous effects to the probability model estimated earlier. Existing research suggests that both HIV prevalence and ARV coverage differ significantly between urban and rural areas. By including interaction terms between urban and year indicators in the model, we can better understand how access to HIV treatment has changed over time for individuals living in different places of residences within the same country. The estimates shown in the table suggest that the gap in knowledge of PMTCT services between urban and rural localities has decreased overall since 2005. The coefficients estimated by the linear probability model indicate that after controlling for other factors, the 16.5 percentage point difference in knowledge rates caused by location in 2005 almost disappears by 2011 before emerging again in 2016. The results suggest two factors responsible for the reappearance of this gap. In urban areas, knowledge rates go up consistently, increasing by 4.3 percentage points between 2005 and 2011 and by 4.1 points between 2011 and 2016; at the same time,

Table 5.4: Heterogeneous effects on knowledge of PMTCT

	OLS	Logit
Urban	0.16504***	0.74365***
	(0.04220)	(0.18425)
Year 2011	0.20209***	0.98417***
	(0.03251)	(0.14200)
Year 2011 × Urban	-0.15899***	-0.71318***
	(0.02677)	(0.12935)
Year 2016	0.14421***	0.74277***
	(0.02089)	(0.10116)
Year 2016 × Urban	-0.06057**	-0.23047**
	(0.02391)	(0.11726)
Constant	0.03733	-2.32331***
	(0.02607)	(0.14415)
N	70651	70651
R^2	0.2440	
Mean of outcome	0.5037	0.5037
St. dev. of outcome	0.5000	0.5000

Note: Standard errors are clustered by region. All specifications include controls for income, age, gender, education, and whether the individual had been tested for HIV. Significance levels are indicated by * $p < .1$, ** $p < .05$, *** $p < .01$.

rates in rural areas rise dramatically between 2005 and 2011, increasing by 20.2 points, then drop by 5.8 points between 2011 and 2016. A potential explanation for this trend is that since the rate of knowledge of these services among individuals in rural areas began at such a low level in 2005, even modest efforts by health officials to increase access to ARVs and other preventive medications may have had significant effects at first. However, the health centers in these areas likely lacked the resources necessary to meet this increased demand for services, causing accessibility to stagnate in rural areas while still increasing in urban centers where resources are more abundant.

6 Conclusion

Cost reduction strategies are an essential component in achieving universal ARV coverage. Evidence from the procurement transactions databases suggest that generic competition is far more effective than differential pricing at reducing prices to an affordable level in low- and

middle-income countries. Differentially priced products from patent-holding manufacturers are estimated to cost 79% more than generic substitutes. Moreover, competition among generic producers can be expected to reduce prices by 20.1–38.4% with each additional competitor. The number of competitors in a given market with greater than 5% market share never exceeds seven producers and the total number is at most eleven. Nonetheless, we still see significant price reductions despite only moderate levels of competition, which suggests that opening up the market to unregulated competition may jeopardize R&D incentives with marginal added benefit. While there does not exist an obvious optimal solution to the problem of increasing ARV affordability, these results suggest that voluntary licensing agreements that enable the production of generic versions of patented drugs may be the next best alternative. The conclusions that can be drawn from this data are limited because it includes only procurement transactions by NGOs, in addition to endogeneity and other unobservable contextual factors. Future studies might add to these results by considering retail prices for ARVs, which would contribute more to our understanding of how these prices react to competition given the distribution of income within a country.

Moving beyond the idea that affordability is the key to widespread ARV access, this paper considers additional factors that may impede universal coverage within a country. By evaluating the extent of knowledge of prevention of mother-to-child transmission treatment in Ethiopia over time, it becomes clear that there are extreme disparities in access depending on regional and demographic characteristics. Even as ARV prices decline nationally, we see that individuals in urban and rural areas within the same country are affected differently. The results of this study point to a need for further research to compare treatment program implementations in different areas of the country in order to find and address specific mechanisms that limit health centers' abilities to meet demand for treatment.

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