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Price Reversal Pattern of ARV Drugs: A Transaction-Cost Approach Digression

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A price reversal pattern of ARV drugs was noted across lower and middle income countries in that the lower-income countries have higher prices relative to higher-income countries based on a 2008-2009 Summary Report by World Health Organization. The transaction costs affecting AVR drug pricing can be broadly classified into two kinds: One between the final users and the opinion/knowledge experts, and the other between the opinion/knowledge experts and the manufacturers. Economist's version of price discrimination needs to be modified by including transaction costs. Transaction costs also point to institution creditability factors that will affect NGO procurement.

***Keywords**: transaction costs, price discrimination, patents, price differentials, health NGOs*

***JEL Classification:** D3, D4*

1. Introduction

Acquired Immune Deficiency Syndrome (AIDS) is a pandemic disease prevailing in many parts of the world. The cause of AIDS is HIV(Human Immune Deficiency virus), which occurs when the transmission of body fluids such as blood, semen, vaginal fluid and breast milk are passed from a HIV positive patient to a healthy human. Patients with AIDS go through a gradual weakening of their immune system as the number of CD4+T cells declines in the plasma in their bodies. AIDS patients therefore catch various types of disease easily, leading to a failing of the immune system, and eventually, death. HIV/AIDS drugs are called antiretroviral (ARV) drugs. The many and different kinds of these drugs vary in dosages according to severity of the disease. The World Health Organization (WHO) conducted a comprehensive survey of antiretroviral drugs in low income countries, low middle income and high middle income countries since 2004, enabling a comparison of ARV drug prices across countries with varying incomes per capita. For exposition purposes,

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we rename the three categories of countries as low, medium and high in this paper, noting that in reality, the high income countries such as USA are excluded from this study. The list of countries in each category is provided in Appendix I.

This paper documents a price reversal pattern of ARV drug prices across these countries, suggesting several significant factors for considerations for global health management generally. A price reversal pattern is one where low income countries pay higher prices for the same drug than higher income countries. Textbook economic theory has argued that price variation across different income countries may be necessary for pharmaceutical companies to capture return on R&D (Hausman and Mackie-Mason, 1988; Danzon and Towse, 2003; Giaccotto, Santerre and Vernon, 2005; Cowan, 2007). Empirical work done on estimating the price-income relationship seems to show a significant positive relationship, but some exceptions were noted. Indeed, a recent study explicitly pointed out the possibility of a price reversal pattern (Morel et.al., 2011). Lichtenberg (2010) revealed that Mexico and Brazil drug price index to be higher than the USA price index, although a regression of price index over per capita GDP in 2006 in his paper showed an overall positive relationship. It is worth noting, however, that there was a more scattered error at the tail end among lower income countries than high income countries. Excellent summary of the results was also provided in a later piece in 2011. Danzon et.al. (2011) reported a price/income elasticity of 0.4, with lower income countries group being even lower at 0.15, p.1534. Danzon and Towse (2013) reported cross-national income elasticity of price being 0.27 across the full income range of countries, but much smaller at o.o-o.1 between countries in middle and low-income countries (MLICs).

We use a WHO 2009 report summary of ARV drugs to motivate thoughts on seeking rationales for the price reversal pattern. Although the WHO 2009 summary report is a snapshot of some moving underlying fundamentals, some positive and normative implications in the health care industry can nevertheless be inferred. The positive aspects of the inquiry focus on ARV drug pricing: Who is responsible for this price reversal? Is it mainly the greed of pharmaceutical companies, dressed in the sheepskin of dynamic economic efficiency of R&D and the protection of patent rights? Or, are there other institutional and socio-political reasons playing their roles as well? Transaction costs in the pharmaceutical industry have been sparingly studied in the literature. The term "transaction costs" has very broad meanings. Classic definitions of it can be found in Coase, 1937, with early formulation of the problem in Cheung (1969, 1987), Williamson (1975, 1981, 1996). A more specific use of the term will be used for analyzing the price reversal problem in this study. We shall further explain this in Section 4 and 5. Surprisingly, these is no mentioning of these factors in the studies of pricing referred to in the previous paragraph. An exception can be found in Frank (2001), who alluded to transaction costs being relevant for analyzing pharmarceutical drug prices, in particular with reference to "unequal bargaining power across different classes of purchasers" and various arbitrage and rebate practices in the USA; but such issues have not been further explored for countries outside North America. Addressing the pricing problem from a framework of transaction costs of marketing, including institutional and socio-political considerations in an international context could be useful.

Aside from inquiring into the price reversal issue from the angle of positive economics, the normative implications of the price reversal pattern can be quite pronounced. Although AVR drug prices have declined globally since 2009, it is still alarming to hear the proposition that "if firms can charge only one price, this price will be what higher-income consumers can pay, and the product will be unaffordable to many lower-income consumers" (Danzon et.al., 2011). Indeed, one can easily conjecture lower-income consumers in lower income countries to be generally ignorant about HIV/AIDS diseases, particularly its possibility of transmission via sexual activities. An excellent description of this problem has been provided in a YouTube video produced by Journeyman Pictures in 2008 entitled "Patents and Patients-India", (https://www.youtube.com/watch?v=dyvojf0YnrI). A study on the socio-economic background of aids patients have also been conducted in Joge et.al. (2012). The price reversal pattern opens up a question "Who *should* be responsible?" as there would be what economists will call an "externality problem" if low-income HIV/AIDS patients do not receive proper care. Recognition of transaction costs factors in marketing as well as on the buyer aide of the industry may be of paramount importance for both drugs manufacturers and policy makers.

The organization of the paper will be as follows: Section 2 describes the WHO data set and its Global Price Reporting Mechanism (GPRM). Section 3 highlights the price reveral pattern across three categories of income country groups. Section 4 discusses the transaction cost factors that may result in this price reversal pattern in the WHO data set. Section 5 explores some normative angles of transaction costs by focusing on the buyers' relationship with the end users.

2. WHO Data Set and its Global Price Reporting Mechanism (GPRM)

The World Health Organization (WHO) is well known for collecting and disseminating data on the incidence and prevalence of communicable and non-communicable diseases. One of the most virulent diseases of our times is HIV/AIDS. In response to a potential worldwide pandemic outbreak of HIV/AIDS in low income countries around the turn of the century, UNAIDS held a meeting on the need for international data collection of ARV drug prices based on observed transactions in 2001 (Sagaon-Teyssier, 2012). WHO brought awareness of the problem by noting the efforts of several NGOs prescribing unlicensed ARVs produced by Cipla and others outside North America (WHO, 2003). In order to provide a more detailed picture of the prices of ARV therapies in these countries, the WHO further established the Global Price Reporting Mechanism (GPRM) in 2004.

The GPRM provides data on the international transaction prices of Antiretroviral (ARV) therapies and HIV diagnostics across countries. This data is provided to the WHO by manufacturers and by procurement organizations such as the Global Fund, PEPFAR and UNITAID, among others. By collecting data from both ends of the spectrum, and by cleaning and validating the data by removing duplicates, the Global Price Reporting Mechanism (GPRM) provides information on prices of Antiretroviral (ARV) therapies and HIV diagnostics across low-income countries, lower middle-income countries and upper middle-income countries. The country classification has been done by the World Bank Atlas classification system.

The GPRM dataset includes information on the median prices of formulations in US$ per patient per year of a defined daily dose for children or adults. The prices are the international EX-WORKS transaction prices (INCOTERMs partially reported) and do not reflect the end-user prices in different countries. The end-user prices can be higher due to taxes, tariffs, transportation costs and markups or lower due to subsidies. The data include volume of transactions, prices, international commercial terms (INCO), country of destination, and procurement date, among others. Additionally, data can also be sorted by commodity, country, income group, region and period of time. The data are available from 2004 onwards for various formulation categories too. The current GPRM database covers nearly 75% of ARV therapies used in low- and middle-income countries but has some limitations in recording information from upper middle-income countries (WHO, 2014).

The data set is rich, with improvement in data collecting methods initiated in UNITAID for Global Data Exchange in 2009, and still continuing to present (Sagaon-Teyssier, 2012). For the purpose of this paper, however, only the summary report of 2009 will be used. This is for several reasons: First, our study of the price refusal pattern does not require the fine details of disaggregating into country by country comparision, as there are bound to be normal price-income observations as well as price reversal observations. Detecting a price reversal pattern based on some averaging aggregates can show the *existence* of the phenomenon if the *frequency based on some consistent statistical counting* is high. Second, even if the price reversal pattern is seen as diminishing over time, which could very well happen if all players in the international market of ARV drugs are set in locomotion over time, it will not negate the fact that at one transitional point in time, the price reversal pattern is found significant. For purposes of probing into the anamolies described in Lichtenberg's paper (2010), it may be sufficient. Third, our academic inquiry here is driven primarily by "second-hand" propositions in the literature in that our intention is not to use this study to discredit many scholarly works in the literature field, but rather, to use it to suggest explanations, and to provide a line of inquiry that can be consistent with a price reversal observation.

The interaction of academic theories with policies is another motivation for a peek at the data for 2008-2009. Sometimes data reflect not only policies, but how ideas can change policies. In 2004, an MIT video conference on "Alternative Models of Differential Pricing For Medicines" illustrated firsthand the thinking of academicians, industry persons, and representatives of NGOs at that time. (http://video.mit.edu/watch/alternative-models-of-differential-pricing-for-medicines-9896/) We found the following proposition to be particularly intriguing: That drug manufacturers should sell "products to wholesalers at uniform prices worldwide, then negotiate confidential rebates with final purchasers…This way, the lower prices offered to lower income countries won't spill over to higher income countries."—proposition offerred by Professor Danzon. The proposal was rather ingenious as a way to combat parallel trade, i.e. transferring drugs from low priced countries to high priced countries, a precondition for practising third-degree price discrimination across countries. It has not been further evaluated in terms of how the real world has been treating the proposition.

The WHO 2009 summary report conveniently gives a point check as to whether the proposition was accepted five years later, perhaps as a gauge of how "unpopular" economic ideas may or may not find their speed for practical implementation. If the proposition was widely adopted, we would not expect to find a price-income pattern, not to mention a price-reversal pattern, as uniform price would imply drug prices across

countries were the same. That not being the case, there must be other aspects of transaction costs that would be of relevance. Or, that the world has simply chosen to ignore a good economic argument.

3. Price Reveral Pattern Across Three Categories of Income Country Groups

In this section, we describe the price reversal pattern observed from the WHO 2009 summary report. Danzon, Mulcahy and Towse (2013) investigated the GPRM data set in great details, but emphasizing the price reversal pattern was not the paper's objective which this section will highlight. The statistical method of counting we used may be "primitive" compared with sophisticated econometric studies, but serves to highlight if the price reversal pattern is the focus. Table 1 shows the evidence of a reversed price/income relationship. A reversed price/income relationship is a phenomenon in which the price of a drug in lower income countries is higher than the same drug's price in higher income countries.

Table 1. *Evidence of Reversed Price/Income relationships from WHO for antiretroviral medicines, 2008-2009*

Classification & Frequency of reversal (%)	**Drug Name & Dosage**	**Price differentials (%)**	**Lower/Middle Income country comparison**	**Middle/High Income Country comparison**
First line Antiretroviral medicines for Adult 29.42%	Stavudine 40 mg	18.18%	✓	
	Lamivudine+ Stavudine 150+30mg	12.39%		✓
	Lamivudine + Nevirapine + Stavudine 150+200+40 mg	0.97%	✓	
	Zidovudine 300 mg	9.25%		✓
	Lamivudine + Nevirapine + zidovudine 150+200+300 mg	4.848%		✓
	Efavirenz 200 mg	4.51%		✓
	Efavirenz 600 mg	6.73%		✓
	Stavudine 30 mg	44.897%	✓	
	Lamivudine 150 mg	8.22%	✓	
	Lamivudine + Navirapine + Stavudine 150+200+30 mg	30.56%	✓	
	Zidovudine 300 mg	9.14%		✓
	Lamivudine + Zidovudine 150+ 300 mg	31.47%	✓	
	Lamivudine + Nevirapine + zidovudine 150+200+300 mg	23.57%	✓	
	Efavirenz 200 mg	57.53%		✓
	Efavirenz 600 mg	35.71%	✓	
	Tenofovir 300 mg	3.92%		✓
Second line Antiretroviral medicines for Adult 33.33%	Didanosine 100 mg	16.85%	✓	
	Didanosine 200 mg	1.67%	✓	
		7.86%		✓
	Lopinavir + Ritonavir 133 + 33 mg	10.76%		✓
	Saquinavir 200 mg	1.21%	✓	
		20.11%		✓
	Fos-amprenavir 700 mg	85.84%		✓
	Abacavir 300mg	11.48%		✓
	Didanosine 100 mg	13.14%	✓	
	Didanosine 250 mg	21.89%	✓	
	Didanosine 400 mg	2.25%	✓	
	Indinavir 400 mg	9.25%	✓	
	Abacavir 20 mg/ml	14.81%		✓
	Didanosine 25 mg	22.95%	✓	
	Lamivudine 10 mg/ml	43.30%	✓	
	Zidovudine 10 mg/ml	68.97%		✓

Antiretroviral medicines for Paediatric treatment (infant weighing 5 kg) 18.367%	Lamivudine+ satvudine 30+6 mg	8%	✓	
	Didanosine 25 mg	77.55%	✓	
	Didanosine 50 mg	27.45%	✓	
	Efavirenz 50 mg	12.70%	✓	
	Nevirapine 10 mg/ml	82.35%		✓
Antiretroviral medicines for Paediatric treatment (infant weighing 10 kg) 27.397%	Didanosine 2 5 mg	23.62%	✓	
		32.52%		✓
	Didanosine 50 mg	26.89	✓	
		30.57%		✓
	Didanosine 100 mg	16.45%	✓	
	Abacavir 20 mg/ml	11.01%		✓
	Didanosine 125 mg	8.90%	✓	
	Efavirenz 50 mg	23.19%		✓
	Efavirenz 200 mg	9.23%		✓
	Nevirapine 10 mg/ml	68.63%		✓
	Stavudine 20 mg	15.38%	✓	
	Zidovudine 10 mg/ml	82.13%		✓
	Lamivudine + Stavudine 150+30 mg	14.29%		✓
	Lamivudine + Nevirapine + Stavudine 150+200+30 mg	17.39%		✓
	Lamivudine + Stavudine 30+ 6 mg	4%	✓	
	Lamivudine + Nevirapine + Stavudine 30 + 50 + 6 mg	12.61%	✓	
	Didanosine 25 mg	34.07%	✓	
	Didanosine 50 mg	29.14%	✓	
	Didanosine 100 mg	7.01%	✓	
	Efavirenz 200 mg	86.34%		✓

The first column of the Table 1 lists the drug classification, and their frequencies of reversal. There are four classifications: (1) First line drugs for adults, (2) Second line drugs for adults, (3) Drugs for pediatrics weighing 5 kg, and (4) Infants weighing 10 kg. First line drug refers to individual drug or the combination of drugs which is recommended as an initial treatment for curing HIV, e.g. Stavudine, lamivudine+stavudine. Second line drug will be applied when the first line drugs fail to alleviate the condition of the patients, due to resistance as HIV transform their characteristics. Examples of second line drugs are Didenosine, lopinavir+ritonavir. The column also shows the frequency of reversal, which are respectively, 29.41% for the 1st classification, 33.33% for the 2nd classification, 18.37% for the 3rd classification, and 27.40% for the 4th classification. We will show how these percentages are calculated later in this section. Suffice to point out here at the outset that these percentages are high indeed, considering the normal expectation that higher income countries pay higher prices.

The percentages are calculated from a method of counting shown in the other columns in the same table 1. Column II gives the drug names and dosages in each classification. The drug names are recommended ARV drugs by WHO for proper treatment in each classification, ranking in ascending order of strength in terms of types and dosages. Because the WHO summary report includes both 2008 and 2009 survey, listing of 2008 counting precedes 2009 counting in the table 1.

Column III calculates the magnitude of the price differential, measured by difference in the Median Transaction Price (MTP) in percentage term between two income country categories. The GDP per capita of the three groups are: Low income country- Countries with gross national income(GNI) per capita of US$ 935 or less, middle income country- Countries with a GNI per capita between US$ 936 and US$ 3,705, high income country-Countries with a GNI per capita between US$ 3,706 and US$ 11,455. Since we have 3 income country categories in the WHO summary report, a price reversal pattern is said to be observed either between the low and middle countries, or between the middle and high income countries. If reversal pattern occured in the first comparison, we put a check in the Column IV. If reversal pattern occurred in the second comparison, we put a check in Column V. We did not count comparisons between low and high income countries, as that would duplicate counting.

We can show the calculation of Column III more precisely using the following stepwise procedure:

1. Reversed price pattern of MTP across country categories is identified.
2. Calculate difference in MTP of lower to middle income country or middle to higher income country (when detecting a reversed price pattern) is calculated.
3. Taking the mean of two MTP as the base value in the denominator, the percentage of the difference is calculated together with calculation in (2).

For example, stavudine 40 mg has MTP in lower income country is 36, and in middle income country is 30. This will give a differential of 6. With a mean of 33, the magnitude of price differential for this drug is 18.18%.

In order to calculate the price reversal frequency reported in Column I of the table 1, we made pairwise comparison for each drug in each classification using the Median Transaction Price (MTP) for low income to middle income countries, and then for middle income to high income countries. Thus, there is a total number of MTP pairwise comparisons. It is the denominator used for the calculation of frequency. The total number of this pairwise counting is made for all the drugs described in the 2009 Summay report, counting both 2008 & 2009, as we considered that to be the domain of a statistical sampling experiment. Thus, the domain pairwise comparison is the sum of all pairwise comparion in the 2009 Summary report, i.e. number of 2008 pair being 29, and the number of 2009 pair being 17. Thus, the domain (the denominator) is 51.

Next, we counted the number of reversed pattern in 2008, which is 7, and add that to the number of reversed pattern in 2009, which is 8. This gives us a total reversed pattern of 15. Thus, for classification 1, the frequency of reversed pattern (%) = (Total reversed pattern/Total MTP sets) x 100

$$= 15/51 \text{ X } 100$$
$$= 29.41\%$$

The same calculation is made for the other three classifications.

Table 1 further reveals that the highest frequency of price revesal being in Classification 2, the second is in Classification 1, with minor difference between these two classifications. Both classifications price reversal frequency seem higher than the children classifications of 3 and 4. This is less disquieting than a result showing a price reversal pattern to be more frequent among children, because it would imply that the most innocent group is being penalized more. In any case, we consider the frequency of occurance of a price reversal pattern to be nontrivial for all four classifications.

We want to next examine the magnitude of the price differentials. We recognize that the MTP prices are averages with standard deviations. If the price differential is small, it would have just been a statistical noise. The intuition is that a larger price differential reduces the possibility that the price reversal pattern is a statistical noise. Furthermore, concentrating on those drugs that have very high magnitude of price differential might allow us to focus on the drug type and to examine the patent strength and the competitive forces of that drug. In Table 2, we select the top 20 drugs from Table 1 that have the largest price differentials, ranging from a top 86.34% to a low 23.62%. The classification of the drug according to the 4 types are labelled corresponding as F, S. P4, and P10 in Column II of that table.

Table 2. *Top 20 drugs with the largest price differentials from WHO 2009 report*

No	Classification	Drug Name & Dosage	Price differentials (%)	Lower/Middle Income country comparison	Middle/High Income Country comparison	Patent ratio
1	P 10	Efavirenz 200 mg	86.34%		✓	0.2
2	S	Fos- amprenavir 700 mg	85.54%		✓	1
3	P 5	Nevirapine 10 mg/ml	82.35%	✓		0.125
4	P 10	Zidovudine 10 mg/ml	82.13%		✓	0.1
5	P 5	Didanosine 25 mg	77.55%	✓		0.125
6	P 5	Zidovudine 10 mg/ml	68.97%		✓	0.1
7	P 10	Nevirapine 10 mg/ml	68.63%		✓	0.125
8	F	Efavirenz 200mg	57.53%		✓	0.2
9	F	Stavudine 30 mg	44.497%	✓		0.05
10	P 5	Lamivudine 10 mg/ml	43.30%	✓		0.074
11	F	Efavirenz 600 mg	35.71%	✓		0.2
12	P 10	Didanosine 25 mg (2009)	34.07%	✓		0.125

13	P 10	Didanosine 25 mg (2008)	32.52%		✓	0.125
14	F	Lamivudine + Zidovudine 150+300 mg	31.47%	✓		0.083
15	P 10	Didanosine 50 mg	30.57%		✓	0.125
16	F	Lamivudine+Navirapine+Stavudine 150+200+30mg	30.56%	✓		0
17	P 10	Didanosine 50 mg (2009)	29.14%	✓		0.125
18	P 5	Didanosine 50 mg	27.45%	✓		0.125
19	P 10	Didanosine 50 mg (2008)	26.89%	✓		0.125
20	P 10	Didanosine 25 mg	23.62%		✓	0.125

Notes: F - First line antiretroviral medicines for Adult
S-Second line antiretroviral medicines for Adult
P 5 - Antiretroviral medicines for Pediatric treatment (infant weighing 5 kg)
P10 - Antiretroviral medicines for Pediatric treatment (infant weighing 10 kg)

An additional column for an estimation of a patent ratio for each drug is also included in Table 2. We want to see whether the price reversal pattern is related to manufactures' strength in its patent right protection. The mirrow image of patent right strength is the degree of competition. A lower patent strength as measured by a patent ratio means a higher degree of competition. It will be interesting to examine whether the price reversal pattern is related to the patent strength of a drug. We propose the patent strength to be estimated by a patent ratio, which is composed by identifying the number of originator drugs and generic drugs for each drug type. A patent is an exclusivity right provided by the governing agency of the country to the inventor in order to protect his innovation from duplication. It also provides the innovator with the financial benefits for the limited time in return to the contribution made towards the development and innovations. We want to know the patent strength of the 20 drugs which has the highest price differentials.

More precisely, the patent ratio of a drug is calculated as follows: Patent ratio = Number of originators/ Total number of companies for that drug, where the total number of company is the sum of the originators and generics of that drug type. Thus, if a drug is dominated by one strong patent, with no generics, the patent ratio will be 1. The lower is this ratio, the weaker is the patent strength of the drug, and the more intense is the competitive force of the drug.

For instance, the patent ratio calculation of Efavirenz. Efavirenz consist of two originator which are Bristol Myers Squib in USA and M.S.D in Europe and 8 generic companies. Therefore the total companies of Efavirenz comes out to be 10, and its patent ratio = 2/10 = 0.2. The list of originator drugs and generic drugs are listed in Appendix II. A rough inspection of the ratios so calculated does not reveal a strong patent strength among the top 20 drugs that has the largest price reversal differential. So the rationale may have to be found on other factors, to which we now turn.

4. Transaction Cost Factors that May Result in the Price Reversal Pattern of WHO's Data Set

Transaction costs are costs of implementing exchanges beyond the intrinsic values and production costs of goods and services. They include various efforts in seeking information (and at a more sophisticated level intelligence gathering) on product and buyer characteristics, reference pricing, bargaining and negotiation of terms, monitoring and enforcement of contractual terms, etc.; indeed, any costs beyond economists' formulation of marginal benefits (willingness to pay) and marginal costs (willingness to sell) can be considered transaction costs. Marginalism is the standard economic methodology used in neoclassical economics. Coase (1937) alerted economists that many interesting problems in economics can be assumed away if the analysis is confined to a framework with zero transaction costs. Aside from Frank (2001), application of transaction costs for problems in pharmaceutical industry has been mostly on contracting for production, i.e. the manufacturing process, e.g. Nogiera and Bataglia (2012). At the outset, there is an undeclared ignorance and indeed a hidden guilt in the economic profession that there is neither a presumption nor any empirical evidence that a uniform pricing method has lower transaction costs than price discrimination generally for any products sold anywhere. The same can be said about the transaction costs of different forms of price discrimination. Pigou (1920) defined three forms of price discrimination as 1st, 2nd, and 3rd. The first charges buyers each unit according to maximum they are willing to pay. The second gives different prices based on blocks of purchase, usually a larger block with a bigger discount. The third segregates buyers into types and charge each type a different price.

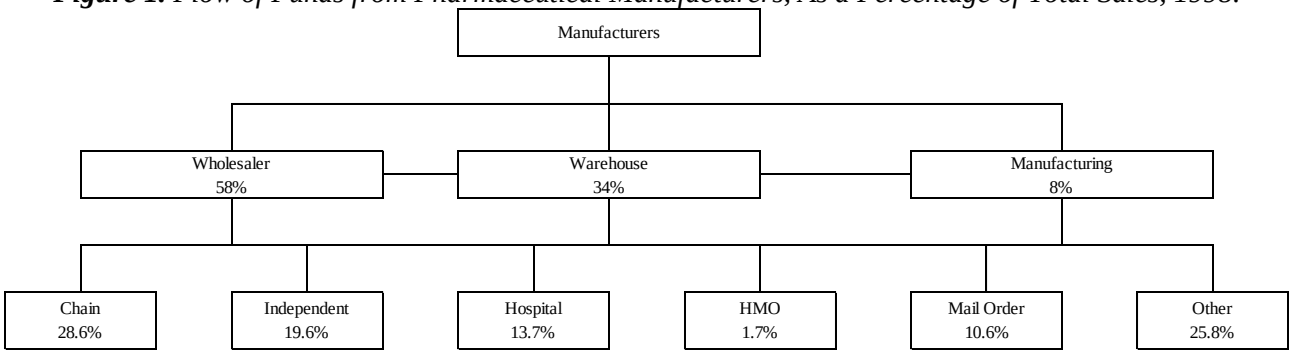
In a static world where consumer preference and technology are given, all transaction cost problems can be theorized as some forms of asymmetric information problem, i.e. one party knows more about some

parameters of exchange than the other party. Transaction costs (also known as agency costs) problems are sometimes referred to as Principal-agent problems. Early formulation of this concept can be found in (Cheung, 1969), and (Ross, 1973). Most transaction costs problems can be classified into pre-contractual problems known as adverse selection, or post-contractual problems known as moral hazard. An additional factor of asset specificities was later added also to capture opportunistic bargaining, (Klein, Crawford and Alchian, 1978; Williamson, 1975, 1981, 1983). For the demand for drugs, the distribution of information is such that most people have to rely on some sort of opinion experts to tell the person what to take. This assumption might appear odd to free market economists, but it is not different in concept from the demand for a mechanic to fix your car, or learning from a teacher/consultant for useful skills and knowledge. For the medical health industry, the expert opinions are vested in physicians, hospitals, and various health management organizations. Patients largely reply on their care takers, and pharmaceutical companies must sell through these expert opinion providers including over-the-counter pharmacists.

Transaction costs problems can arise between end users and opinion experts, as well as between manufacturers and opinion experts. For the price reversal pattern in the WHO 2009 data set described in the last section, we want to address here first the one between manufacturers and opinion experts of health care, keeping in mind that there might be transaction costs issues between end users and opinion experts also that emerge dynamically to be addressed in the next section. Frank (2001) describes the distribution of pharmaceutical drugs in USA in a schematic diagram that is reproduced in Figure 1. Although we do not have the equivalent numbers of Figure 1 for the countries in the WHO data set, we expect a general structure developing in that direction, as economic gain existed in one country is in principle duplicable in another country. Commenting on the situation in United States, the author noted,

> "Perhaps most striking is that about 92 percent of sales [in US] flow through either full-line wholesalers or warehouses owned by chain drug stores, buying groups, or other distributors. This means that very few sales are made directly from manufacturers to drug retailers or end users (such as hospitals). *Thus, price negotiations between manufacturers and end users must involve other parties*." (italics added, p.123)

Figure 1. *Flow of Funds from Pharmaceutical Manufacturers, As a Percentage of Total Sales, 1998.*



Source: Frank, 2001, pp.115-128.
Author's estimates based on data from national health Accounts, IMS, and National Wholesale Druggists Association (NWDA).
Notes**:** HMO is health maintenance organization. "Other" includes nursing homes, clinics, and other health care organizations.

According to the author, price concessions in US include chargeback, rebates and discounts. The author did not classify them in terms of the three types of price discrimination. It can be inferred, however, that the former two resemble 2nd degree price discrimination as the practice rewards volume and frequent purchase, while discounts to different expert/outlet categories could be considered as 3rd degree. No inference has been made with 1st degree price discrimination, i.e. charging each buyer the maximum willingness to pay; perhaps in agreement with Pigou that perfect price discrimination is untenable.

Yet, an important middleman to enable the distribution process between manufacturers and experts/outlets is the pharmaceutical sales representatives (PSRs). This is so whether a pharmaceutical company licenses local companies to market their products or chooses to do it themselves by its own marketing outlets. Either way, the drug manufacturers have to reply on PSRs, assisted by company policies of advertising and promotion, referencing various local institutional constraints according to needs. All PSRs should have good understanding of pharmacology—the science of medications and their effects on human body, as they

should have the intellectual capacity to understand the science behind the products they sell. They should know the chemistry of a drug, the method of action, side effects and potential interactions with other drugs. PSRs also specialize in certain expert opinion groups, class of drugs, and geographical territories with specific cultural specificities, as they must be skillful in building relationships and earning the trust of their clients. Understandably, a good PSR would also monitor physicians' prescription patterns or gauging reactions to new treatments. For all "asymmetric information" effort expected, PSRs usually are paid by commissions. The selection of PSR can be itself a transaction cost problem too. A drug manufacturer must pay careful attentions to the selection of PSRs, as they represent the brand name of the manufacturer.

PSRs process client information and enable communication with manufacturers and expert opinion leaders (rather than estimating price elasticity). Even in N. America, physicians will not easily accept a new treatment method: "[The physicians] often cling to those certainties even in the face of strong evidence to the contrary." (MacDonald and Linde-Zwirble, 2014). In countries outside N. America, these rigidity is expected to be stronger. It may be a matter of good business instinct too, for a PSR to know well the constraints of each of his/her clients for particular types of outlets under his/her account. In view of country specificities that might not be known easily to manufacturers headquarters, we expect PSRs in low income countries representing a similar if not more important role than those in N. America.

As a side note, and at least for general practice, it is not uncommon for physcians in countries outside N. America to own their pharmacies, with drug expense included as a component of medical consultation (especially in rural areas). Thus, the willingness to pay can be gauged at a very decentralized local level, particularly for customers who are brand conscious and who view high price as an assurance of quality. In a world of zero transaction costs and with full patent protection, no patients who want treatment will be denied of it. That is the concept of 1st degree price discrimination. With positive transaction costs, it is not uncommon to see manufacturers setting high prices, while allowing price concessions to be made for individual clients on a case by case basis. To some people, including perhaps A. C. Pigou, this might not be considered exactly as 1st degree price discrimination, which he considered for the case of identical demand. But he added, "Apart from this method, discrimination of the first degree might still conceivably be established by detailed separate bargaining with every separate customer. But that method would involve enormous cost and trouble. Furthermore, since it implies separate bargains with individuals, it opens the way, not only to error, but also to the perversion of agents through bribery." (Pigou, 1920, p.281).

This would be consistent with the vision suggested at the 2004MIT conference mentioned in Section 2, but the price would have to be set towards the high end of willingness to pay in order for this to approximate 1st degree price discrimination.

Any rational profit maximizing drug manufacturer would pay more attention to the bottom line than particular pricing model of economists absent of transaction costs. In setting prices for drugs, it could be the willingness to pay that matters most. Economists would not disagree with that, as revenues under 1st degree price discrimination always exceed the 2nd or the 3rd degree price discrimination. However, the transaction costs of the three types of discrimination may vary depending on a country/regional setting that may not be preset at company headquarter, as tremendous asymmetric information is likely to be associated with local conditions. It may be more realistic to say that a more practical guidance for drug manufacturer's pricing for a country would be a *combination of the three forms of price discrimination net of the transaction costs of each, subject to competition and the regulatory constraints of a country.*

That a drug manufacturer's pricing strategy cannot be solely depended on second or third degree price discrimination across countries have much to do with the transaction costs of preventing parallel trade. A precondition for any price discrimination is the inability of low priced buyers to resell to high priced buyers. If a uniform low price is set to a low income country, an entity in that country can buy large quantity and resell to a higher income country that is paying a higher price. Parallel trade can be prohibited with the cooperation of the regulatory authority in the two countries, but not with zero transaction costs. Particularly for 2nd degree price discrimination, which caters to buyers of volume purchase by charge backs or rebates, the incentive to resell to higher income countries for higher prices could be quite attractive if not explicitly prohibited. The same is true for 3rd degree price discrimination both within a country as well as across countries. Considerable coordination with regulatory authorities between countries had to be involved, and often become part of the negotiation of international trade agreements.

A search of regulatory authority of the countries in the WHO data base is shown in Table 3. This table consists of country name, drug regulatory authority name and the website links of the regulatory agencies. There are few countries in which the regulatory agency is not mentioned; therefore, in such case "NF" or "Not Found" is written. Like previous tables, countries are divided in three categories i.e. low income countries, middle income countries and high income countries. There were also websites identified that cannot be opened,

suggesting fuzziness in interpreting what is the relevant authority in a country. Thus, it seems equally uncertain that a manufacturer may or may not be able to establish an understanding with the authority for some countries, which itself is a transaction cost. The creditability of regulatory authority in low income countries also undermines a within-country price discrimination model, offering low income patients in low income countries super low or even zero price. A manufacturer will find it difficult to know whether quantities used for low income usages are for the country's internal usages or for resale. It would seem that elaborate monitoring scheme has to be set up by the manufacturers. Those are factors that add to transaction costs.

Table 3. *Drug regulatory authorities for low-middle-high income countries*

Country	Web site name	Authority name
Low income countries		
Burundi	http://www.minisante.bi/	Ministry of public Health and fight against AIDS (ministre de la santepublique et de luttecontre le sida)
Liberia	http://www.moh.gov.lr/index.php	Ministry Of Health
Eritrea	NF	
Congo	NF	
Malawi	http://www.malawi.gov.mw/index.php?option=com_content&view=article&id=55&Itemid=85	Government of the Republic of Malawi
Ethiopia	http://www.daca.gov.et/	Drug Administration and Control Authority
Niger	http://www.gouv.ne/index.php?id_page=30	Ministry of Public Health
Guinea	NF	
Madagascar	http://www.sante.gov.mg/index.php	Ministry of Public Health of Madagascar
Zimbabwe	http://www.mcaz.co.zw/	Medicines control authority of Zimbabwe
Mozambiqe	http://www.misau.gov.mz/pt/medicamentos	Mozambique - Ministry of Health
Togo	NF	
Uganda	http://www.nda.or.ug/	National Drug Authority
Afghanistan	NF	
Rwanda	http://www.moh.gov.rw/	Republic of Rwanda Ministry of health
Central African Republic	NF	
Nepal	http://www.dda.gov.np/req_modern_medicine.php	Department of Drug Administration
Sierra Leone	http://www.health.gov.sl/home/regulatory-bodies/pharmacy-board	
Tanzania	http://www.tfda.or.tz/	Tanzania Food and Drugs Authority
Guinea-Bissau	NF	
Burkina Faso	http://www.dgpml.sante.gov.bf/	General Direction of Pharmacy, Medicine and Laboratories
Gambia	http://www.moh.gov.gm/	Ministry of Health & Social Welfare
Bangladesh	http://www.dgda.gov.bd/	Directorate General of Drug Administration
Mali	http://www.sante.gov.ml/index.php?option=com_content&task=view&id=31&Itemid=72	Ministry Of Health And Public Hygiene
Tajikistan	http://health.tj/	State Scientific Centre for Expertise and Certification
Haiti	NF	
Cambodia	http://www.moh.gov.kh/?lang=en	Department of Drugs and Food, Ministry of Health, Cambodia
Benin	http://www.sante.gouv.bj/dpm.php	
Kenya	http://pharmacyboardkenya.org/	Pharmacy and Poisons Board
Comoros	NF	
Solomon Islands	NF	
Chad	http://www.sante-tchad.org/	Minister of Health, Social Action and National Solidarity

Kyrgyz Republic	http://www.pharm.kg/	Department of Drug supply and Medical Equipment
Laos	NF	
Lower middle income country		
Mauritania	http://www.sante.gov.mr/MSAS/Left/Presentation/Administrationcen/DirectionPharmacieLaboratoires.htm	Minister Of Health
Senegal	http://www.sante.gouv.sn/	Ministry of Health, Hygiene and Prevention
Pakistan	http://www.dcomoh.gov.pk/	Drug Control Organization
Zambia	http://www.zamra.co.zm/	Zambia Medicines Regulatory Authority
Sao Tome and Principe	NF	
Lesotho	NF	
Vietnam	http://www.dav.gov.vn/	Drug Administration of Vietnam
Sudan	http://www.nmpb.gov.sd/	National Medicines and Poisons Board
Uzbekistan	NF	
Cameroon	http://www.minsante.cm/intro.htm	Ministry Of Public Health
Nigeria	http://www.nafdac.gov.ng/	National Agency for Food and Drug Administration and Control
India	http://cdsco.nic.in/	Central Drugs Standard Control Organization
Papua New Guinea	http://www.health.gov.pg/	Department of Health
Cote d'Ivoire	http://www.dpmci.org/	Directorate of Pharmacy and Medicines Cote d'Ivoire
Ghana	http://www.fdbghana.gov.gh/	Food and Drugs Board
Yemen	http://www.sbd-ye.org/	Supreme Commission for Drugs and Medical Appliances
Nicaragua	NF	
Moldova	NF	
Bolivia	http://www.sns.gob.bo/	Ministry of Health Surveillance Agency
Mongolia	http://www.moh.mn/	Ministry of Health
Honduras	http://www.dgrs.gob.hn/	Directorate General of Health Regulation
Bhutan	http://www.dra.gov.bt/	Drug Regulatory Authority
Kiribati	NF	
Republic of the Congo	http://www.minisanterdc.cd/new/index.php	THE MINISTRY OF PUBLIC HEALTH
Sri Lanka	http://203.94.76.60/DRA/home.htm	Drug Regulatory Authority
West Bank and Gaza	NF	
Indonesia	http://www.pom.go.id/new/	food and drug regulatory agency
Egypt	http://www.eda.mohp.gov.eg/	Egyptian Drug Authority
Timor-Leste	NF	
Paraguay	http://www.mspbs.gov.py/v3/	Ministry of Health and welfare
Philippines	http://www.fda.gov.ph/	Food and Drug Administration Philippines
Guyana	http://www.health.gov.gy/prg_adm_food_drugs.php	Food & Drug Department
Georgia	http://gdna.georgia.gov/	Georgia Drugs & Narcotics Agency
Vanuatu	NF	
Samoa	NF	
Swaziland	http://www.gov.sz/	Ministry of Health and Social Welfare
Guatemala	http://www.mspas.gob.gt/index.php/en/	Ministry of Health and Welfare
Federated state of Micronesia	NF	

Morocco	http://srvweb.sante.gov.ma/Medicaments/Pages/default.aspx	Ministry of Health
Ukraine	http://www.pharma-center.kiev.ua/view/en/index	The State Expert Center
Armenia	http://www.pharm.am/index.php?langid=2	Scientific centre of drug and medical technology expertise
El Salvador	http://www.salud.gob.sv/	Ministry of Health
Kosovo	NF	
Tonga	NF	
Cape Verde	http://www.arfa.cv/index.php	Agency for Regulation and Supervision of Pharmaceutical and Food Products
Turkmenistan	NF	
China	http://eng.sfda.gov.cn/	China food and Drug Administration
Upper middle income countries		
Marshall Islands	NF	
Angola	http://www.minsa.gov.ao/	Ministry of Health
Thailand	http://www.fda.moph.go.th/eng/index.stm	Food and Drug Administration Thailand
Jordan	http://www.jfda.jo/	Jordan Food and Drug administration
Fiji	http://www.health.gov.fj/ira.html#.U9LtIK02y_p	Inspectorate & Regulatory Authority
Iraq	NF	
Ecuador	NF	
Namibia	http://www.nmrc.com.na/	Namibia Medicines Regulatory Council
Peru	http://www.digemid.minsa.gob.pe/	general direction of inputs medicines and drugs
Tunisia	http://www.dpm.tn/anglais.html	management of pharmacy and medicine
Algeria	http://www.ands.dz/pharmacie-med/sommaire.htm	Department of Pharmacy and Medicine
Belize	http://health.gov.bz/www/	Ministry of health
Iran	NF	
Albania	http://www.qkkb.gov.al/	National Center for Drug Control
Macedonia	NF	
Jamaica	http://www.pcoj.org/	Pharmacy Council Of Jamaica
Dominican Republic	http://www.drogasyfarmacias.gov.do/index.php	Directorate General of Drugs and Pharmacies
Bosnia and Herzegovina	http://www.alims.gov.ba/	Agency for medicinal products and medical devices of Bosnia and Herzegovina
Azerbaijan	http://www.pharm.az/	Ministry of Health of Azerbaijan Republic
Colombia	https://www.invima.gov.co/	National Institute of Food and Drug Monitoring
Maldives	http://www.mfda.gov.mv/	Maldives Food and Drug Authority
Tuvalu	NF	
Botswana	http://www.moh.gov.bw/	Ministry of Health, Botswana
Cuba	http://www.cecmed.cu/	Centre for State Control of Drugs, Medical Devices
Belarus	http://www.rceth.by/	Center of expertise and testing in health care
South Africa	http://www.mccza.com/	Medicines Control Council
Serbia	http://www.alims.gov.rs/ciril/	Medicines and Medical Devices of Serbia
Costa Rica	http://www.ministeriodesalud.go.cr/	
Bulgaria	http://www.bda.bg/	Bulgarian Drug Agency
St. Vincent and the Grenadians	NF	
Dominica	NF	
St. Lucia	NF	
Montenegro	http://sntcg.com/ulms/	Ministry Of Health Montenegro
Kazakhstan	http://www.dari.kz/?lang=rus	National Center of Expertise of medicines, medical products and medical equipment
Grenada	NF	
Suriname	NF	
Mauritius	http://www.gov.mu/English/Pages/default.aspx	Ministry of Health & Quality of Life

Panama	http://www.minsa.gob.pa/	Ministry of Health, Panama
Malaysia	http://portal.bpfk.gov.my/index.cfm	National Pharmaceutical Control Bureau
Lebanon	http://www.moph.gov.lb/Pages/Home.aspx	Ministry of Public Health
Gabon	NF	
Brazil	http://portal.anvisa.gov.br/wps/portal/anvisa/anvisa/home	National Health Surveillance Agency
Mexico	http://www.cofepris.gob.mx/	Federal Commission for the Protection against Sanitary Risk
Uruguay	http://www.msp.gub.uy/subcategorias_8_1.html	Ministry of Public Health
Romania	http://www.anm.ro/anmdm/en/	National Agency for Medicine and Medical Device
Turkey	http://www.iegm.gov.tr/	Ministry of Health of Turkey General Directorate of Pharmaceuticals and Pharmacy
Palau	NF	
Russian Federation	http://www.roszdravnadzor.ru/	Federal Service on Surveillance in Healthcare and Social Development
Chile	http://www.ispch.cl/	Public Health Institute of Chile
Venezuela	http://www.inhrr.gob.ve/	National Institute of Hygiene
Seychelles	http://www.health.gov.sc/index.php?option=com_content&view=article&id=255&Itemid=260	Ministry Of Health

Source: http://www.who.int/medicines/areas/quality_safety/regulation_legislation/list_mra_websites_nov2012.pdf
http://budding-regulatory-professionals.blogspot.ca/p/globally-identified-websites-of.html
http://www.pharmweb.net/regulatory.html#pg

We emphasize again, the hypothesized objective function of drug manufacturers does not preclude the use of third degree price discrimination, it only suggests its usage to be considered in conjunction with other price discrimination methods inclusive of transaction costs. That RSPs can approximate 1st degree discrimination is a conjecture, probably used more widely outside N. America as in India and China. In India, RSPs are called Marketing Representatives (MR). (see an article of the alleged practice: http://forbesindia.com/article/special/will-pharma-companies-have-to-stop-gifting-doctors/34031/1). In China, the distribution process entails incurring transaction costs at three levels: The foundation level entails manufacturers educating various customer groups, through advertising or group meetings. Manufacturers also have to factor in training costs for physicians, via academic conferences, medical seminars, on-site meetings, etc. The middle level of sales efforts rely greatly on commissions. That involves commission pays to doctors, hospital pharmacies, hospital purchase departments, and managers of drugstores. Lastly, there is a terminal level of sales efforts involving contractual understandings with presidents of hospitals, vice presidents in charge of procurements, hospitals' procurement departments, physicians in general or specialized diseases. All drug sales in China must first be listed on a national Health Insurance directory. At the regional level, there is also a pharmaceutical commercial company drug list that a drug must first go through the approval process before it can be marketed. All these are some type of transaction costs.

In some way, the transaction-cost advantage of using RSPs for price concessions is also its limitation: That it is small scale. A face-to-face one-on-one sales interaction (small scale) can be more informative and persuasive than large scale purchase resulting from advertising or direct negotiation from the headquarter of a manufacturer. However, a small scale transaction can also reduce the possibility reselling of large scale parallel trade with highly organized third party middleman. Thus, a manufacturer may be more comfortable with that type of price concessions than giving large discounts to the representatives of the alleged needy patients, but only find later that the ordered merchandise was re-exported elsewhere where higher prices are charged.

The price reversal pattern thus suggests a cornering of the high-willingness-to-pay buyer segment in low income countries. The following contrived examples can show how a *structure of transaction cost*s will lead to that outcome. Suppose a low income country has one wealthy individual who is willing to pay 1 million for a drug while there are 2 million patients each with willingness to pay of $1, it is not necessarily the case that if firms can charge only one price, this price will be what higher-income consumers can pay, and that the product will be unaffordable to lower-income consumers. It all depends on the structure of transaction costs. Suppose a 1st degree price discrimination of a patented drug entails individual bargaining costs of C1 for each customers while 3rd degree price discrimination entails a headquarter fixed cost decision of C3 in preventing parallel trade. The wealthy individual's willingness to pay is generalized to m, and the number of patients

willing to pay \$1 is generalized to n. If C1 is slightly higher than \$1, while C3 is greater than n, a uniform price of m will be charged only. Access by the "poor" can only be enabled if C1 is less than \$1, and for that, the choice between 1st and 3rd degree price discrimination will depend on whether n(1-C1) is greater or less than C3.

We conclude the discussion in this section on the transaction costs of pricing by noting a recent report in the *Economist* (2014):

> "Until recently in poorer countries pharmaceutical firms mainly sold off-patent branded drugs, which command a premium over local generics, since patients trust their quality. The pricier patented ones they marketed only to the few very rich patients who could pay out of pocket, says Kalipso Chalkidou of NICE International, the British agency's foreign advisory arm. The private Aga Khan University hospital in Nairobi's leafy suburbs, for example, offers cancer care to the Kenyan elite that comes close to what they would receive in the rich world."

5. Normative Angles of Transaction Costs based on Buyers' Relationship with End Users

There is also a normative implication of the price reversal pattern that can be examined from a transaction costs angle. In addition to possibly human rights and social justice issues, the "externality" component of HIV/AIDS diseases may require government intervention although that is not necessarily the only remedy. Elinor Ostrom, in her Nobel prize winning work, has provided inspirational guidance in this possibility. Her emphasis had been on the environmental problems addressing to the tragedy of commons, (Ostrom, 1990). A transaction costs angle can shed lights on the type of institutions that may emerge to handle the problem. Specifically, the transaction costs between final users and expert opinion organizations. The evolvement of the latter can be of crucial importance for the handling the externality problem. To whom the final users, and for that matter, the governments, would or should trust for conducting medical related services in a way that can enhance individuals' and society's benefits?

The credibility of an expert opinion organization is of major issue here. At the most direct level, it is needed for the building of trust in a patient-physician relationship. As pointed out in earlier sections, the distribution of asymmetric information in this principal-agent problem is of a peculiar one—the principal here does not know what he/she really needs. But that is only part of the health care infrastructure. When organizations such as the insurance companies, HMOs, and various new health care management methods are added to the infrastructure, it can complicate the analysis tremendously. Moral hazard and adverse selections can lead to an insurmountable market failure that exceeds that created by distortions of patent created monopolies. To be sure, this belongs to a general class of problem being confronted in all countries including the USA. An institutional development angle to the problem is of great importance beyond the pricing strategies of manufacturers. The discussion of transaction costs in this context is quite normative, as no one can say whether a health reform adopted by a country will be successful with absolute certainty.

For lower income countries, the institutional answers to the HIV/AIDS pandemic problem have been tackled neither exclusively by the governments nor by the private sectors, but often by the nongovernmental organizations (NGOs). As WHO's GPRM has indicated, the price procurement data set itself came from a large number of NGOs, including well-known names such as the Clinton's Foundation, HIV/AIDS Initiative/UNITAID, the Global Fund, the International Dispensary Association, USAID/deliver, Management Sciences for Health, Mission pharma, Supply Chain Management System, the United Nations Children's Fund, and the WHO's Contracting and Procurement Service (WHO, 2009)

Clearly, on price bargaining with manufacturers, NGOs have been playing a significant role, counteracting to the patent exploitation incentives of the manufacturers, in addition to the force of competition from the generic drugs. Through the emergence of these organizations, the drug pricing problem is no longer a monopoly problem (thus making the discussion of different forms of price discriminations in the last section to be rather irrelevant), but in many situation, a bilateral monopoly bargaining problem**.** There is a set of asymmetric information problems (transaction costs problems) that can be addressed to in this direction. However, there is no need to model this explicitly here, suffice to say in this inquiry that the NGOs' negotiations with manufacturers have been quite successful. AVERT.org (Avert.org, 2015) provides an excellent history of these negotiations; and indeed, illuminating on how "tiered pricing" had emerged in the industry:

> "Negotiations with Big Pharmaceutical companies have led to a system of 'tiered' pricing. Tiered pricing means that the price at which the big pharmaceutical companies sell their drugs is calculated using formulas based on average income per head, leading to lower prices in poor countries."

That might be so, as the empirical works on price-GDP/capita across countries indeed have shown a general positive relationship; but that intent alone would not negate the price reversal pattern reported in this paper. So perhaps from this perspective, it was the failure of NGOs to negotiate down the drug prices in lower income countries that had led to the price reversal pattern. It is an easy target for price reforms.

Academically speaking, of greater intellectual interests to us are the emergence of these bargaining bodies. How do they gain their credibility and emerge as the appropriate representatives of the end users in the first place? On the one hand, there are large NGOs that are supported by world famous personalities such as William Clinton and Bill Gates; and indeed, brand names such as the World Bank and WHO are in one form of another, some type of an NGO. But these high profile organizations are the exceptions rather the norm within the institution classification of NGOs.

Literature on the studies of transaction costs of NGOs is not rich; and in our opinion, a barren area that badly needs to be studied. One can perhaps understand the international, cross-border advantages of NGOs easily, and their bargaining power when supported by recognizable brand names; but what about other NGOs? What qualifies the success of one and the failure of another? In what way can transaction costs economics help us to understand the seemingly superior advantages of NGOs, and in what dimensions are these institutional structure of importance?

Guinness (2011) provided a good start in examining the nature of the problem, addressing to four angles of transaction costs problems: institutional environment (the legal system or bureaucracy's governance), information problems on targeted population (frequency of contacts and patients mobility, etc.), opportunism (corruptions), and asset specificities (project staff and site-specific advantages). But the study, while pioneer in spirit, focused on the execution of preventive cares at the grass root level. It did not address to the brand-name emergence of NGOs, and for that matter, the ability of NGOs in bargaining with the patent protected drug manufacturers.

From the perspective of drug manufacturers, doing business with an NGO that can handle preventive cares may not be of high priority. Indeed, a cynical view will assume their sole interest is to increase the demand for the drugs they sell, not the reduction of them via preventive cares. They may be quite selective in choosing (1) NGOs knowledgeable about the institutional environment in the countries that they operate, and (2) NGOs that have sufficient asset specificities and not fly-by-nights. One can imagine that a contractual negotiation would necessarily entail having an NGO's promise of not deliberately engage in parallel trade to dilute a manufacturer's contemplated pricing strategy across different countries. In any case, considerable trust is to be expected.

The inquiry raised in this section is similar to one that has been asked for centuries in the area of sustainable development. Who can be the best representative of environments? The transaction costs angle raised in this section similarly asks: Who can be the best representative of helpless victims of diseases? The philosophical responses to the two questions may be similar too—both involve addressing to the efficiency or deficiency of governments in one extreme and that of the private incentive in the other extreme. Like addressing to the tragedy of the common problem, a transaction costs approach must address to how the economic problem of externalities will be resolved. In Coasian language, how the problem of social costs is to be handled. The digression in this paper hopefully can open up some normative questions as to how health reform in different countries may want to proceed as well.

6. Conclusion

This study highlights a price reversal pattern observed across lower- and middle-income countries in the AVR drug industry. The pattern is not consistent with either third-degree price discrimination or tiered pricing, both being the current dominant views for explaining price differentials across countries for pharmaceutical drugs. It is suggested that transaction costs can play a significant role in affecting drug prices, often country specific. The transaction costs affecting AVR drug pricing can be broadly classified into two kinds: One between the final users and the opinion/knowledge experts, and the other between the opinion/knowledge experts and the manufacturers. Addressing drug pricing problem from these two angles can capture essential aspects of transaction costs on the demand as well as the supply side of AVR drugs, in addition to the relatively well known factors of patents and competition.

The study of price reversal thus also reflects on the topic of pricing behavior in economics, which is usually analyzed without transaction costs, and heavily based on demand price elasticities. A.C. Pigou in his 1920 classic entitled *The Economics of Welfare* examined three forms of price discrimination but concluded that the monopolists "cannot, except in extraordinary circumstances, introduce either the first- or the second-degree of discrimination, and that the third- degree is of chief practical importance," (p.282). Economic

literature on drug pricing has largely endorsed this viewpoint. The price reversal pattern of AVR drugs across lower- and middle- income countries in 2008-2009 suggested a combination of reasons beyond monopoly pricing of the simplest type, relying on a structure of transaction costs with all three forms of price discrimination co-existing.

At a practical level, the question of who *was*, or *should* be, responsible for the price reversal pattern involves different players and institutional constraints for any country that can be theoretically captured in terms of some notions of transaction costs in the context of that country. Our study suggests a framework for thinking, and provides some preliminary findings to identify features of importance. Thus, instead of asking who is responsible, the appropriate question to examine is how institutional development in different country setting will enable the lowering of the transaction costs in that country. The answer could well be found in the structure of NGOs serving that country, but the answer at this stage is not certain. This normative question actually is of relevance to lower-income countries as well as to advanced countries such as USA, where health care reform is under way. Long before Obamacare, Frank (2001, p.128) made the following prophetic insight for North America:

> "….*incentive formularies* appear to be effective in allowing health plans to obtain *price concessions*. Both the Clinton administration plan and the House Republicans counted on such [transaction] mechanisms to control costs under a Medicare prescription drug benefit. The differences lie not in their perceptions of how to get price concessions but rather in how to create an *institutional structure* that protects against market failure stemming from *adverse selection* (the Clinton administration) or government's inability to restrain itself from intervening in the *price-setting* arrangements (the House Republican)." (emphasis not in the original, added in *italics*)

Our price-reversal-study-led digression of transaction costs in the ARV drug world suggests that the above could be the norm rather than an exception. It could well be equally relevant that such forces are at work in less developed low-income countries as in the USA.

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Appendices

Appendix I. *List of Country Names*

Low-income country (34)	Burundi, Liberia , Eritrea ,Congo , Malawi, Ethiopia , Niger, Guinea , Madagascar, Zimbabwe, Mozambique , Togo, Uganda, Afghanistan, Rwanda, Central African Republic, Nepal, Sierra Leone, Tanzania, Guinea-Bissau, Burkina Faso, Gambia, The , Bangladesh , Mali, Tajikistan, Haiti, Cambodia, Benin, Kenya, Comoros, Solomon Islands, Chad, Kyrgyz Republic, Leo PDR
Lower middle-income country (49)	Mauritania, Senegal, Pakistan, Zambia, Sao Tome and Principe, Lesotho, Vietnam, Sudan, Uzbekistan, Cameroon, Nigeria, India, Papua new guinea, Cote d'Ivoire, Ghana, Yemen , Nicaragua, Moldova, Bolivia, Mongolia, Honduras, Bhutan, Kiribati, Republic of the Congo, Sri Lanka, West Bank and Gaza, Indonesia, Egypt, Timor-Leste, Paraguay, Philippines, Guyana, Georgia, Vanuatu, Samoa, Swaziland, Guatemala, Federated state of Micronesia, Morocco, Ukraine, Armenia, El Salvador, Kosovo, Tonga, Cape Verde, Turkmenistan, China
Upper middle-income country(51)	Marshall Islands, Angola, Thailand, Jordan, Fiji, Iraq, Ecuador, Namibia, Peru, Tunisia, Algeria, Belize, Iran, Albania, Macedonia, Jamaica, Dominican Republic, Bosnia and Herzegovina, Azerbaijan, Colombia, Maldives, Tuvalu, Botswana, Cuba, Belarus, South Africa, Serbia, Costa Rica, Bulgaria, St. Vincent and the Grenadians, Dominica, St. Lucia, Montenegro, Kazakhstan, Grenada, Suriname, Mauritius, Panama, Malaysia, Lebanon, Gabon, Brazil, Mexico, Uruguay, Romania, Turkey, Palau, Russian Federation, Chile, Venezuela, Seychelles

Source:http://data.worldbank.org/indicator/NY.GNP.PCAP.CD?order=wbapi_data_value_2009+wbapi_data_value+wbapi_data_value-first&sort=asc

Appendix II. *Pharmaceutical Originator and Generic Drugs Companies*

Sr. No.	Drug name	Brand Names	Generic Names
1.	Efavirenz	1. Bristol-Myers Squibb 2.Msd	1. Sub-Saharan Africa Aspen Pharma care 2. Mcneil& Argus 3. Cipla 4. Emcure Pharmaceuticals 5. Ranbaxy Laboratories 6. Hetero Drugs Ltd 7. Alkem Laboratories 8. Aurobindo Pharma
2.	Fosamprenavir	1. Glaxosmithkline 2. ViiV	NF
3.	Nevirapine	1.Boehringer Ingelheim	1. Mcneil& Argus 2. Cadila 3. Cipla 4. Ranbaxy 5. Emcure 6. Alkem 7. Hetero Drugs Ltd
4.	Zidovudine	1. Glaxosmithkline 2. ViiV	1. Aurobindo Pharma Ltd Inc 2. Genix pharma Ltd 3. PharmaforceInc 4. AurobindoPharma Ltd 5. Hetero Drugs Ltd 6. Matrix Laboratories Ltd 7. Ranbaxy Laboratories Ltd 8. Roxane Laboratories Inc 9. Lupin Ltd 10. Teva Pharms 11. Luitpold 12. Mylan Pharms Inc 13. Sunshine Lake

			14. Emcure 15. Alkem 16. Cadila 17. Mcneil& Argus 18. Zydus
5.	Didanosine	1.Bristol Myers Squibb	1. Aurobindo Pharma Ltd 2. Barr Laboratories Inc 3. Matrix Laboratories Ltd 4. Mylan Pharms Inc 5. Alkem 6. Spinogen 7. Ranbaxy
6.	Stavudine	1.Britol-Myers Squibb	1. Alkem 2. Actavis 3. Spinogen 4. Wujing Medicine 5. Ranbaxy Laboratories 6. Biotoscana 7. Biogen 8. Flamingo Pharmacueticals 9. Landsteiner 10. Filaxis 11. Meijisi Pharmaceutical 12. Ivax 13. Negpf 14. Stadine 15. Hetero 16. Lkm 17. Aurobindo 18. Cipla 19. Paylos
7.	Lamivudine	1. Glaxosmithkline 2. ViiV	1. Teva Pharms 2. Lupin Ltd 3. AurobindoPharma Ltd 4. Hetero labs limited V 5. Apotex 6. Dosa 7. Mebiphar 8. Beximco 9. Ranbaxy Laboratories 10. Flamingo Pharmacueticals 11. Ivax 12. Square 13. Cadila 14. Paylos 15. Zydus 16. Zifam India 17. Incepta 18. Alkem 19. Emcure 20. Khandelwal 21. Mcneil& Argus 22. Zy.Alidac 23. Synmedic Laboratories 24. Sppl 25. Shantha Biotech
8.	Lamivudine+Zidovudine	1. ViiV	1. Hetero Labs Ltd V 2. Lupin Ltd 3. Teva Pharms 4. Alkem 5. Cipla 6. Cadila

			7. Mcneil& Argus 8. Synmedic Laboratories 9. Zydus 10. Ranbaxy Pharma 11. Emcure
9.	Lamivudine/Stavudine/Nevirapine	No originator	

Source: http://www.drugsupdate.com/brand/showavailablebrands/341
http://apps.who.int/medicinedocs/documents/s18716en/s18716en.pdf
http://www.drugbank.ca/drugs/DB00238?utf8=%E2%9C%93&query=Nevirapine&search_type=drugs&button=
http://www.accessdata.fda.gov/scripts/cder/ob/docs/queryai.cfm