Journal of Asian Scientific Research, 2014, 4(9): 473-489

Journal of Asian Scientific Research

journal homepage: http://www.aessweb.com/journals/5003

EFFECT OF GOVERNMENT MEDIATED ACCESS PRICING ON PRICES OF TARGETED DRUGS IN THE PHILIPPINES

Jesus N. Sarol, Jr.

National Teacher Training Center for the Health Professions, University of the Philipines Manila, Padre Faura St., Ermita, Rainier Contract Research Services Inc, San Juan City, Philippines

ABSTRACT

Introduction

The Philippines implemented the Cheaper Medicines Act of 2008 to improve access to quality drugs. Thereafter, the government placed 5 drugs under maximum drug retail pricing (MDRP) and influenced pharmaceutical companies to reduce by half prices of 16 branded drugs, referred to as drugs under government-mediated access prices (GMAP). The effect of GMAP on prices of drugs carrying similar molecules has not been well-studied. This study compared the price of selected drug molecules directly affected by the MDRP/GMAP policies in 2009 and 2011.

Methods

The study used data obtained from independent surveys conducted by IMS Health Philippines in 2009 and 2011 using a stratified sample of 600 drug stores each. Prices of the following categories of stock keeping units (SKUs) for 11 drug molecules placed under MDRP/GMAP listing were obtained: 1) innovator brand; 2) competitor brand; and 3) cheapest generic counterpart available. Price data was obtained using a mystery shopper approach. Differences in mean and median drug prices between 2009 and 2011 for each drug were calculated.

Results

Being MDRP/GMAP reference drugs, there were expected compulsory reductions in mean prices of 10 of 11 innovator brands. Reduction of mean prices of competitor drugs occurred on a relatively smaller scale. Mean prices in 2011 of competitor drugs tended to settle near the GMAP reference levels. Mean prices of the cheapest generic drugs all went down significantly.

Conclusion

Government-mediated pricing could be an effective means of reducing prices of targeted drugs in similar fashion as reference pricing.

Keywords: Drug industry, Drug costs, Delivery of health care, Government regulation, Generic drugs, Philippines

Contribution/ Originality

Unlike that of price capping and reference pricing, the effects of government negotiation as a price regulation approach on the pharmaceutical industry, access to drugs and health status of populations have not been well-studied. Government-mediated access pricing is a form of price negotiation that was recently implemented in the Philippines to stimulate effective competition in the drug industry and consequently improve access of the population to quality drugs. This study presents the putative effects of government-mediated access pricing on prices of targeted drugs in the Philippines. No widely published literature on this specific subject tackled on a national level seems to exist.

1. INTRODUCTION

Access to cheap quality drugs has persisted as a big problem in developing countries, especially among the poor [1] Medicine prices in the Philippines are considered too high compared to international reference prices [2], making essential drugs less accessible to its poor population. Expenditure on drugs accounts for a substantial proportion of income of poor households [3]. Even with social health insurance coverage, out-of pocket expenses, mostly on purchased drugs, can amount to 10% of annual average income in a significant proportion (>=13%) of hospitalized patients in the Philippines [4].

In 2008, Republic Act 9502, known as "The Universally Accessible and Quality Medicines Act of 2008" [5] and more popularly as the "Cheaper Medicines Act of 2008" , was signed into law. This law was intended to promote and ensure access to affordable quality drugs and medicines to all Filipinos by encouraging full effective competition in their supply and demand, and in its failure, empowering the government to regulate their prices. After its enactment, the government issued Executive Order No 821 that set the maximum retail prices of 5 drug molecules with the intent to follow through with more molecules [6]. All drug products that carried these drug molecules were required to be sold at the maximum price set by the Philippine Department of Health (DOH). These were called drugs under maximum drug retail pricing (MDRP). A number of drug companies reacted by volunteering to reduce prices by half a list of 16 drugs [7]. These voluntarily price-reduced drugs were collectively referred to as drugs under government-mediated access pricing (GMAP). Drug stores were required to post the reduced prices of these MDRP/GMAP drugs in their premises for the information of their customers. Counterparts of the GMAP drugs carrying the same molecules that are distributed by other companies did not have to follow suit the same pricing.

The public perception, however, apparently showed that the law has had minimal impact on improving access to drugs of the population [8]. The full impact of this law on the different stakeholders so far has yet to be assessed. This study is part of a larger evaluation on the impact of the law on all Philippine stakeholders currently being conducted.

The effect of price regulation, most frequently through price capping (also called maximum pricing) and reference pricing, on drug prices has been the subject of several published reviews. An early published state-of-the-art review on the effects of reference pricing on drug price and other outcomes such as drug choice, insurer savings, expenditures and dynamic efficiency was

done by López-Casasnovas and Puig-Junoy [9]. These authors noted that the price of products covered by reference pricing decreased in all countries that introduced it. Danzon and Ketcham [10] restricted their study to therapeutic reference pricing systems in Germany, Netherlands and New Zealand and uncovered that reference pricing had differential effects on drug prices in the three countries due to their structural differences [10]. The first systematic review was conducted by Aaserud, et al. [11]. It looked into the effects of reference pricing on several outcomes (drug price, drug use, expenditures and health outcomes). However, it included only two European studies on drug price [11]. Puig-Junoy [12] conducted another systematic review on the impact of price regulation, either through price capping or reference pricing, on prices of generic drugs in Europe [12]. The most recent was Galizzi, et al. [13] which concentrated on the effects of reference pricing in Organisation for Economic Cooperation and Development (OECD) countries [13]. This study subsumed the two European studies in the Aaserud, et al. [11] review. The reviews of Puig-Junoy [12] and Galizzi, et al. [13] included bigger sets of studies with drug price as outcome. Both reported similar findings that price regulation, enforced through either price capping or reference pricing, generally brought drug prices down, with greater reduction for innovator and brand-named drugs than for less known generic versions [12, 13].

Price capping uses a maximum value under which prices of all similar drugs must be sold while reference pricing involves setting of maximum reimbursements for a group of drugs used for treatment of a specific medical condition [12]. In the latter, patients are reimbursed for drug purchases for treatment of their medical conditions only up to the stipulated reference prices for those drugs. Government-mediated pricing, such as the one employed in the Philippines, is a rather different mechanism for price regulation [14]. One could classify this into price negotiation schemes. Upon government persuasion, a drug distributor voluntarily reduces the price of a drug of their choice (reference drug). The government accepts this offer and makes this widely known to the general public. Every drug outlet is mandated to comply and sells the reference drug at not more than the publicized price. Competitor brands that carry the same molecules as that of reference drugs are not required by government to follow suit. Clearly, this mechanism is not considered price control. Therefore, this would be more acceptable to the drug distributors. Although government price negotiation in the drug industry is quite commonly employed in European countries [15], the effect of this price regulation approach on drug prices has not been covered in studies cited by the reviews above. This study investigated this question. Specifically, this study compared the prices of selected drugs directly affected by the government-mediated access pricing in 2009 and 2011. The changes were also examined as to whether these trends varied according to location and type of drug store.

2. METHODS

In 2009 and 2011, the Philippine Department of Health (DOH) commissioned IMS Health Philippines (IMS) to conduct surveys on drug price and availability in retail drug stores in the Philippines. This was done as part of the monitoring of the implementation of the Cheaper Medicines Act of 2008. This study used secondary data obtained from these IMS surveys.

Drug prices and availability in the 2009 survey were considered the baseline levels while those for the 2011 survey reflected possible changes in these indicators after implementation of the law. Permission to use data from IMS was covered in a memorandum of agreement between IMS Health and Rainiers Contract Research Services Inc to which the author is affiliated. The National Ethics Committee of the Philippine Council for Health Research and Development (PCHRD) granted ethical clearance for the project. The sampling and data collection procedures employed by IMS are described below.

2.1 Sampling Procedures in the 2009 and 2011 Surveys

IMS Health Philippines maintains a proprietary Drug Store Distribution Database, an exhaustive database of drug stores that covers the whole country. Drug stores were categorized according to retail type (chain or independent), location (Metro Manila, Luzon, Visayas and Mindanao) and volume of sales. From this database, a stratified sample of 600 drug stores was independently obtained each for 2009 and 2011. Stratification was based on location and retail type. The total sample size was allocated according to the size of population in each category created by the cross classification of the stratification variables. Data collectors were then assigned to obtain data on prices of selected drugs in the sample drug stores.

Similar numbers of drug stores by location and retail were obtained by the IMS Health Philippines in 2009 and 2011 (Table 1). Independent drug stores far outnumbered chain ones, 510 to 90. The highest percentage were located in Luzon with 45.5% of independent drug stores and 37.8% of chain ones. The rest of the independent drug stores were quite evenly distributed in the other areas. Among chain drug stores, Metro Manila had twice the number of drug stores as that in Visayas and in Mindanao.

Table-1. Distribution of drug stores according to location and retail type, by year

Location	2009		2011	
	Chain	Independent	Chain	Independent
Metro Manila	28	89	28	89
Luzon	34	232	34	232
Visayas	14	95	14	95
Mindanao	14	94	14	94
Total	90	510	90	510

2.2 Selection of Drugs in the Study

For the 2009 survey, priority molecules were identified by IMS Health using a scoring system that considered the current sales value of molecules, the DOH morbidity and mortality data, Philippine Medical Data Index Prescription Counts (PMDIPC) and Philippine National Drug Formulary (PNDF) Classification. The 100 most saleable molecules were chosen as an initial step. Higher scores were each then given to higher ranking molecules according to sales, morbidity and mortality of diseases associated with the use of the drug molecules and prescription counts. Different scores were also assigned according to whether or not drugs were included in the PNDF

list of essential drugs. The total score was then obtained which became the basis for selection of 33 priority molecules from the list of 100.

Selection of priority molecules in the 2011 survey used a different criteria. Priority molecules included only those that were carried by drugs in the MDRP/GMAP list.

Several drug brands differing in form and strength (stock keeping units or SKUs) could carry a specific priority molecule. Three SKUs for each priority molecule were selected as follows. The first SKU was the brand product with highest volume of sales, i.e. the most saleable brand. Then the SKU with the highest price among all pharmaceutical companies carrying this molecule was taken in. In case the most saleable SKU was also the highest priced, then the next highest priced SKU was chosen. The third SKU was the cheapest generic brand counterpart available in the sampled drug store.

Since change in drug price was the required data in this study, only those drug molecules that were present in both 2009 and 2011 surveys were included. Eleven (11) drug molecules met this requirement. Table 2 presents for each drug molecule the innovator brand, brands under regulated pricing (MDRP or GMAP), most saleable drug and highest priced competitor brand. We noted that for each molecule in this study, the innovator brand was included either as the most saleable drug or the highest priced competitor. This allowed the comparison of an innovator drug with a competitor brand for each molecule. Using this classification of drugs, this would facilitate the comparison of this study to those studies reviewed by Puig-Junoy (2010) [12] on effects of price regulation in European countries. In those studies, innovator brands were also compared with other branded-generic drugs. It is noted that 10 of the 11 innovator drugs were under MDRP or GMAP, i.e. they were the reference drugs. Only one molecule (metronidazole 500 mg tablet) had a GMAP drug that was not the most saleable nor was the highest price. The generic brand counterparts varied across drug stores depending on which was the cheapest among the generic brands available in a particular outlet. For this reason, the cheapest generic brand is not presented in Table 2.

Table-2. List of innovator brand, brands under regulated pricing, most saleable brand and highest priced competitor for each drug molecule

Drug Molecule	Innovator brand	Brand(s) placed under regulated	Most saleable brand	Highest priced competitor
Amlodipine 5 mg tablet	Norvasc	All (MDRP)	Norvasc	Asomex
Losartan 50 mg tablet	Cozaar	Cozaar	Lifezar	Cozaar
Losartan + Hydrochlorothiazide 50 mg + 12.5 mg tablet	Hyzaar	Hyzaar	Combizar	Hyzaar
Telmisartan 40 mg tablet	Micardis	Micardis	Micardis	Pritor
Atorvastatin 10 mg tablet	Lipitor	All (MDRP)	Lipitor	Atopitar

Continue

Clopidrogel 75 mg tablet	Plavix	Plavix	Plavix	Clopivaz
Gliclazide 80 mg tablet	Diamicron	Diamicron	Diamicron	Clizid
Azithromycin 500 mg tablet	Zithromax	All (MDRP)	Zithromax	Azyth
Ciprofloxacin 500 mg tablet	Ciprobay	Ciprobay	Ciprobay	Zalvos
Metronidazole 500 mg tablet	Flagyl	Winthrop[1]	Flagyl	Patryl
Metronidazole 125 mg/5 ml suspension	Flagyl	Flagyl	Flagyl	Patryl

[1] Metronidazole 500 mg tablet produced by Winthrop was included in the GMAP list, neither Flagyl nor Patryl metronidazole 500 mg tablet was.

2.3. Data Collection

Information on drug prices was obtained using a mystery shopper approach. A member of the survey team was assigned to visit a sample drug store and posed as a buyer of the drugs in the list.

2.4. Data Analysis

The mean and median of the drug prices in 2009 and 2011 were derived where the denominator is the number of drug stores that sold a specific drug in the list. Differences in the mean prices between 2009 and 2011 were tested for statistical significance using Student's t-test. The Mann-Whitney U test was used for the comparison of medians.

The changes in drug prices from 2009 to 2011 were also examined across locations (island groups - Luzon, Visayas, Mindanao and Metro Manila) and by retail type of drug store (chain or independent). The significance of the interaction effects of location and type of drug store with year on drug prices was evaluated by performing an analysis of variance (ANOVA) that included the respective interaction terms [16]. From the ANOVA, the variance of the interaction effects σ_{ab}^2 was estimated by the equation,

$$\hat{\sigma}_{ab}^2 = \frac{MS(AB) - MS(Error)}{\bar{n}_h}$$

where MS(AB)and MS(Error) are the respective mean squares of the interaction and error sources of variation and $\bar{n}_h$ is the harmonic mean of the sample sizes per cell. This was truncated to 0 if MS(AB) ≤ MS(Error). To adjust for the differences in mean prices, the ratio $\hat{\sigma}_{ab}/\bar{x}$ was used to gauge the estimated size of the interaction effects.

Location-specific and type-specific assessments of trends are presented in more detail in the text only when these interactions were statistically significant and sizeable for the innovator and competitor drugs. We used the criteria $\alpha<0.05$ for testing interaction effects in the ANOVA and $\hat{\sigma}_{ab}/\bar{x} \geq 10.0\%$ to identify the important interactions. Moreover, the interaction effects of location and store type with year on prices of cheapest generic drugs are also not shown in this report. The generic drugs were not brand-specific, that is, the cheapest generic brand was not the same across drug stores. This precluded meaningful interpretations of interaction effects similar to those for innovator and competitor drugs.

Data analyses were generated using STATA Ver 10.1 [17].

3. RESULTS

The changes in the mean and median drug prices from 2009 to 2011 are shown in Table 3 to 5. Ten of the 11 innovator drugs had highly statistically significant reductions ($p<0.001$) in mean prices between 32.8% and 50.1% (Table 3). The sizeable reductions in prices among these innovator brands were expected because these drugs were in the GMAP list. The 2011 mean prices of these drug were very close to their regulated prices. Compliance of drug stores to MDRP and GMAP was high, with a minimum of 68.5% for Flagyl 125 mg/5 ml suspension to a high of 97.3% for Lipitor 10 mg tablet. The pricing for the only innovator drug excluded from the MDRP/GMAP list, Flagyl 500 mg tablet, evidently did not follow the government-mediated price. This drug was sold at the mean price of P23 in both 2009 and 2011, almost twice of the GMAP price of P11.75. In 2011, there were only 1.1% of drug stores selling it at the reduced price.

Table-3. Mean and median drug prices (in pesos) of specific innovator drugs in 2009 and 2011 and percent of drug stores selling drug below MDRP/GMAP price in 2011

Drug	Price under MDRP/ GMAP	Number of drug stores sold		Percent ≤ MDRP/ GMAP		Mean			Median		
		2009	2011	2009	2011	2009	2011	Percent change	2009	2011	Percent change
Norvasc 5 mg tablet	22.85	452	408	1.0	71.8	43.1±5.4	23.3±1.7	-46.0***	44.5	22.9	-48.7***
Cozaar 50 mg tablet	21.50	261	247	0.0	76.5	42.9±2.8	22.2±2.4	-48.2***	43.0	21.5	-50.0***
Hyzaar 50 mg/12 mg tablet	23.75	220	204	0.0	87.8	46.9±2.2	23.9±3.0	-49.2***	47.5	23.8	-50.0***
Micardis 40 mg tablet	25.75	383	398	0.0	85.2	50.4±2.4	25.7±1.7	-49.1***	50.0	25.0	-50.0***
Lipitor 10 mg tablet	34.45	255	255	57.5	97.3	62.4±2.7	34.1±2.1	-45.4***	62.5	34.4	-45.0***
Plavix 75 mg tablet	61.75	312	277	0.3	91.3	119.6±6.9	60.6±4.8	-49.4***	119.9	61.8	-48.5***
Diamicron 80 mg tablet	9.75	427	428	1.4	90.0	14.6±1.0	9.8±1.1	-32.8***	14.8	9.8	-33.9***
Zithromax 500 mg tablet	151.43	279	292	0.0	82.2	297.2±16.3	151.5±7.1	-49.0***	298.8	151.3	-49.4***
Ciprobay 500 mg tablet	41.91	323	307	0.3	80.5	77.9±6.6	42.0±2.8	-46.1***	79.2	41.9	-47.1***
Flagyl 500 mg tablet	11.75	366	368	0.0	1.1	23.0±1.4	23.0±1.8	0.0	22.8	23.0	0.7
Flagyl 125 mg/5ml suspension	65.50	359	219	0.0	68.5	133.8±4.6	66.8±4.1	-50.1***	132.2	65.5	-50.5***

* p<0.05, ** p<0.01, *** p < 0.001 (Student's t-test for means and Mann-Whitney U test for medians)

Among the competitor brands, the percent reduction in mean and median prices were of relatively smaller magnitudes compared to those of the innovator drugs (Table 4). Only two drugs, Pritor 40 mg tablet and Atopitar 10 mg tablet, had reduction of greater than 40% in mean price ($p<0.001$). Eight drugs had percent mean reduction ranging from 1.9% to 27.5%. This range was lower than that for the percent mean price reduction for the 10 innovator drugs in the GMAP list. One drug, Patryl 500 mg tablet, even had a significant increase in mean price by 53.2% ($t=4.68$, $p<0.001$). It is quite noticeable that the mean 2011 prices of several drugs, namely Lifezar 50 mg tablet, Combizar 50 mg/12 mg tablet, Pritor 40 mg tablet, Atopitar 10 mg tablet, Clizid 80 mg tablet, Azyth 500 mg tablet and Patryl 125 mg/5 ml suspension, settled near the regulated price under MDRP and GMAP. The percent of drug stores that sold these drugs under the MDRP or GMAP price were from 77.3% to 97.1%. This pattern resulted in the smaller percent reduction in

prices of competitor drugs compared to innovator drugs since the former were usually sold at lower prices in 2009. Pricing for Zalvos 500 mg tablet did not follow this trend. The mean and median prices of Zalvos in 2011 were P55.8 and P60.0, respectively, more than 33% higher than the GMAP price of P41.9. Surprisingly, Asomex 5 mg tablet, a drug under MDRP, was sold in 2011 at the mean and median prices around P26. This was above the regulated price of P22.85. Compliance to MDRP among drug stores for Asomex 5 mg tablet was low at only 6.9%.

Table-4. Mean and median drug prices (in pesos) of specific competitor drugs in 2009 and 2011 and percent of drug stores selling drugs below MDRP/GMAP price in 2011

Drug	Price under MDRP/ GMAP	Number of drug stores sold		Percent ≤ MDRP/ GMAP		Mean			Median		
		2009	2011	2009	2011	2009	2011	Percent change	2009	2011	Percent change
Asomex 5 mg tablet	22.85	117	73	4.3	6.9	26.6±2.2	26.1±2.1	-1.9	26.0	26.0	0.0
Lifezar 50 mg tablet	21.50	417	427	2.9	77.3	24.3±2.2	22.0±1.4	-9.7***	24.0	21.5	-10.4***
Combizar 50 mg/12 mg tablet	23.75	357	420	16.0	92.4	25.1±1.5	22.1±2.1	-12.0***	25.0	21.5	-14.0***
Pritor 40 mg tablet	25.75	338	356	0.6	88.5	50.4±3.0	25.5±2.2	-49.3***	50.6	25.0	-50.6***
Atopitar 10 mg tablet	34.45	17	25	11.8	80.0	50.0±13.7	29.3±7.6	-41.3***	51.5	29.0	-43.6***
Clopivaz 75 mg tablet	61.75	148	164	98.7	100.0	45.0±3.8	34.5±5.6	-23.2***	44.5	36.3	-18.5***
Clizid 80 mg tablet	9.75	158	29	86.7	96.6	9.6±1.0	9.1±1.4	-5.4*	9.6	9.0	-6.3***
Azyth 500 mg tablet	151.43	213	237	2.4	97.1	180.5±14.6	141.5±8.2	-21.6***	184.3	144.0	-21.9***
Zalvos 500 mg tablet	41.91	36	33	5.6	33.3	64.0±12.1	55.8±19.8	-12.8*	61.6	60.0	-2.6
Patryl 500 mg tablet	11.75	53	26	83.0	57.7	10.2±3.2	15.7±7.1	53.2***	9.0	12.0	34.1***
Patryl 125 mg/5ml suspension	65.50	35	23	99.0	97.0	92.4±17.5	67.1±12.3	-27.5**	85.0	63.9	-24.8***

* p<0.05, ** p<0.01, *** p < 0.001 (Student's t-test for means and Mann-Whitney U test for medians)

Five drug molecules, amlodipine 5 mg tablet, gliclazide 80 mg tablet, ciprofloxacin tablet 500 mg tablet, metronidazole 500 tablet and 125 mg/5 ml suspension, already had cheaper generic versions sold in more than 15% (n≥92) of drug stores in the study in 2009 (Table 5). In more than 2 of 3 drug stores that sold them, the cheapest generic prices in 2009 were already below the MDRP/GMAP prices. Still, mean prices for cheapest generic drugs had marked percent reductions, ranging from 13.4% to 57.0%. All of these reductions were highly statistically significant (minimum t=3.23, p<0.0013), except for azithromycin 500 mg tablet and telmisartan 40 mg tablet. The non-statistical significance of the reduction in the latter two drugs could be attributed to the fact that generic versions for these were rarely available in 2009. Only 2 drug outlets then sold generic brands of these drugs. Cheap generic versions of telmisartan remained rare in drug stores in 2011 due to its existing patent in the Philippines.

Table-5. Mean and median drug prices (in pesos) of cheapest generic drugs in 2009 and 2011 and percent of drug stores selling drugs below MDRP/GMAP price in 2011

Drug	Price under MDRP/ GMAP	Number of drug stores sold		Percent ≤ MDRP/ GMAP		Mean			Median		
		2009	2011	2009	2011	2009	2011	Percent change	2009	2011	Percent change
Amlodipine 5 mg tablet	22.85	92	351	97.8	100.0	12.8±4.4	7.8±2.9	-38.9***	11.0	7.0	-36.4***
Losartan 50 mg tablet	21.50	27	267	92.6	100.0	16.5±3.4	11.8±3.1	-28.8***	15.0	12.0	-20.0***
Losartan + Hydrochlorothiazide 50 mg/12 mg tablet	23.75	9	124	77.8	96.8	18.5±6.7	13.3±3.8	-28.1***	22.0	13.0	-40.9*
Telmisartan 40 mg tablet	25.75	2	2	100.0	100.0	25.1±0.0	13.6±17.5	-45.6	25.1	13.6	-45.6
Atorvastatin 10 mg tablet	34.45	2	50	50.0	98.0	44.4±19.3	19.1±9.5	-57.0***	44.4	18.9	-57.5*
Clopidrogel 75 mg tablet	61.75	22	145	31.8	100.0	57.7±10.7	25.7±5.3	-55.4***	63.5	26.5	-58.3***
Gliclazide 80 mg tablet	9.75	93	140	100.0	100.0	6.1±1.3	5.2±1.3	-13.4***	6.0	5.0	-16.7***
Azithromycin 500 mg tablet	151.43	2	83	50.0	98.8	130.8±64.7	109.8±18.9	-16.1	130.8	113.0	-13.6
Ciprofloxacin 500 mg tablet	41.91	167	307	98.2	100.0	20.6±11.2	12.3±7.1	-40.4***	19.0	10.0	-47.4***
Metronidazole 500 mg tablet	11.75	97	300	99.0	97.0	6.9±3.2	5.5±3.7	-19.5**	5.0	5.0	0.0***
Metronidazole 125 mg/5ml suspension	65.50	92	203	67.4	97.0	55.5±21.8	40.3±15.4	-27.4***	49.9	35.0	-29.8***

* p<0.05, ** p<0.01, *** p < 0.001 (Student's t-test for means and Mann-Whitney U test for medians)

The statistical significance of the differences in the change of drug prices from 2009 to 2011 across locations and type of drug stores was assessed through the examination of both the statistical test for interaction in the ANOVA and the estimate of the ratio, $\hat{\sigma}_{ab}/\bar{x}$. Among the innovator drugs, the trends in drug prices were not much different across regions. This can be gleaned from the estimates of $\hat{\sigma}_{ab}/\bar{x}$ as shown in Table 6, which had a maximum of only 3.9% for Norvasc (amlodipine 5 mg tablet). To illustrate, the percent reduction in Norvasc was smallest in Luzon at 43.6% while the largest reduction was not far at 48.0% in Mindanao (table not shown). The variations in price reduction of the other innovator drugs across locations would be smaller than the variation for Norvasc.

Among the competitor drugs, the variations in price reductions across locations were both statistically significant and substantial (i.e. $\hat{\sigma}_{ab}/\bar{x} \geq 10\%$) for Atopitar (atorvastatin), Zalvos (ciprofloxacin) and Patryl tablet (Table 6). The mean price of Atopitar significantly decreased in Visayas (P52.8 in 2009 vs P29.3 in 2011, t=7.04, p<0.0001) and Mindanao (P63.1 in 2009 vs P26.8 in 2011, t=16.85, p<0.0001) but not in Luzon (P42.9 in 2009 vs P30.9 in 2011, t=1.55, p=0.1502) (Table 7). There were only 1 outlet in 2009 and 4 in 2011 that sold Atopitar in Metro Manila precluding a statistical test of the decrease in price. The mean price of Zalvos went up in the Visayas from P58.6 in 2009 to P65.6 in 2011, but this did not reach statistical significance (t=1.78, p=0.0941). The opposite trend was seen in Luzon and Mindanao. In Luzon, the mean price of Zalvos decreased from P67.4 in 2009 to P51.3 in 2011 (t=2.51, p=0.0182) while it similarly declined to P49.0 in 2011 from P61.8 in 2009 (t=3.15, p=0.0084) in Mindanao. In Metro Manila,

the change in price was not statistically significant (P73.5 in 2009 vs P66.7 in 2011, t=0.29, p=0.7855). The mean price of Patryl tablet significantly increased in Metro Manila (P8.5 in 2009 vs P13.7 in 2011, t=2.77, p=0.0170) and Luzon (P10.2 in 2009 vs P18.1 in 2011, t=4.84, p<0.0001) but not in Visayas (P12.0 in 2009 vs P10.4 in 2011, t=-0.87, p=0.3976). Since there were only 2 stores in 2009 and 1 in 2011 in Mindanao that sold this product, statistical testing could not be performed.

Table-6. Assessment of effect of interaction of year with location on drug price using analysis of variance (ANOVA)

Drug molecule	Innovator			Competitor		
	$\hat{\sigma}_{ab}/\bar{x}$ [1]	F-test[2]	p-value[3]	$\hat{\sigma}_{ab}/\bar{x}$ [1]	F-test[2]	p-value[3]
Amlodipine 5 mg tablet	3.92	11.35	<0.0001	1.10	1.39	0.2464
Losartan 50 mg tablet	0.00	0.97	0.4047	0.00	0.64	0.5864
Losartan + Hydrochlorothiazide 50 mg/12 mg tablet	0.00	0.53	0.6601	0.40	1.42	0.2369
Telmisartan 40 mg tablet	0.00	0.84	0.4705	0.69	1.75	0.1545
Atorvastatin 10 mg tablet	0.00	0.78	0.5083	17.46	2.36	0.0884
Clopidrogel 75 mg tablet	0.00	0.30	0.8249	3.37	3.67	0.0126
Gliclazide 80 mg tablet	0.00	0.05	0.9852	1.22	2.83	0.0399
Azithromycin 500 mg tablet	1.11	3.46	0.0163	1.98	5.40	0.0012
Ciprofloxacin 500 mg tablet	0.40	1.17	0.3216	16.11	2.04	0.1171
Metronidazole 500 mg tablet	0.87	2.28	0.0776	40.93	5.38	0.0021
Metronidazole 125 mg/5ml suspension	0.60	1.58	0.1928	5.80	1.45	0.2387

[1] – $\hat{\sigma}_{ab}/\bar{x}$, expressed as 100%, is used as the estimated measure of size of interaction effects. Calculation of this estimate is described in data analysis part of the methods section.

[2] – F-test for the interaction effect in the ANOVA with interaction model.

[3] – p-value corresponding to the interaction effect in the ANOVA.

Table-7. Mean (±standard deviation) of prices of Atopitar 10 mg tablet, Zalvos 500 mg tablet and Patryl 125 mg/5 ml suspension in 2009 and 2011, by area

	Atopitar 10 mg tablet					Zalvos 500 mg tablet					Patryl 500 mg tablet				
	2009		2011			2009		2011			2009		2011		
Area	n	Mean ±sd	n	Mean ±sd	% change	N	Mean ±sd	n	Mean ±sd	% change	n	Mean ±sd	N	Mean ±sd	% change

Continue

Metro Manila	1	63.8 ±0.0	4	29.9 ±13.8	53.0	3	73.5 ±13.1	4	66.7 ±38.7	9.3	11	8.5 ±0.2	3	13.7 ±7.2	-62.5*
Luzon	8	42.9 ±15.5	5	30.9 ±9.4	28.0	14	67.4 ±15.2	16	51.3 ±19.4	23.9*	27	10.2 ±2.8	15	18.1 ±7.6	-77.3***
Visayas	6	52.8 ±8.0	12	29.3 ±6.0	44.5***	11	58.6 ±9.7	7	65.6 ±4.5	-11.9	13	12.0 ±4.7	7	10.4 ±1.5	13.2
Mindanao	2	63.1 ±0.1	4	26.8 ±2.9	57.6***	8	61.8 ±3.5	6	49.0 ±10.9	20.7**	2	9.03 ±0.5	1	21.85 ±0.0	-142.0

* p<0.05, ** p<0.01, *** p < 0.001 (Student's t-test for comparing means of 2009 and 2011 prices)

The largest interaction effect (maximum $\hat{\sigma}_{ab}/\bar{x}$) of year and type of drug store was only 4.4% for Norvasc among the innovator drugs. In the chain drug stores, the mean prices were P45.2 and P23.0, respectively, for 2009 and 2011 (data not shown in tables). The corresponding mean prices were P42.6 and P23.3, respectively, among the independent drug stores. Clearly this was a small difference in price trends between the types of stores. Since the ratios of $\hat{\sigma}_{ab}$ to $\bar{x}$ for other innovator drugs were smaller than that for Norvasc, this indicated that the trends in prices of these drugs were also similar for chain and independent drug stores.

Table-8. Assessment of effect of interaction of year with type of drug store on drug price using analysis of variance (ANOVA)

Drug molecule	Innovator			Competitor		
	$\hat{\sigma}_{ab}/\bar{x}$ [1]	F-test[2]	p-value[3]	$\hat{\sigma}_{ab}/\bar{x}$ [1]	F-test[2]	p-value[3]
Amlodipine 5 mg tablet	4.43	20.34	<0.0001	2.12	3.84	0.0515
Losartan 50 mg tablet	0.42	3.89	0.0492	0.00	0.35	0.5537
Losartan + Hydrochlorothiazide 50 mg/12 mg tablet	0.26	2.02	0.1563	0.00	0.03	0.8566
Telmisartan 40 mg tablet	0.29	1.39	0.2384	1.83	10.01	0.0016
Atorvastatin 10 mg tablet	0.00	0.13	0.7155	9.30	1.90	0.1762
Clopidrogel 75 mg tablet	0.99	3.90	0.0489	3.09	5.98	0.0151
Gliclazide 80 mg tablet	2.39	11.80	0.0006	4.60	5.48	0.0203
Azithromycin 500 mg tablet	0.19	1.14	0.2857	1.32	4.55	0.0334
Ciprofloxacin 500 mg tablet	0.00	1.00	0.3181	0.00	0.26	0.6113
Metronidazole 500 mg tablet	0.19	1.10	0.2949	33.22	15.43	0.0002
Metronidazole 125 mg/5ml suspension	0.34	1.77	0.1842	13.24	8.49	0.0052

[1] – $\hat{\sigma}_{ab}/\bar{x}$, expressed as 100%, is used as the estimated measure of size of interaction effects. Calculation of this estimate is described in data analysis part of the methods section.

[2] – F-test for the interaction effect in the ANOVA with interaction model.

[3] – p-value corresponding to the interaction effect in the ANOVA.

Among competitor drugs, the interaction effects of year and type of retail store were statistically significant and of considerable degree only for Patryl tablet ($\hat{\sigma}_{ab}/\bar{x}$=33.2%) and suspension ($\hat{\sigma}_{ab}/\bar{x}$=13.2%) (Table 8). In chain drug stores, there was only minimal change in mean price of Patryl tablets, P9.9 in 2009 to P9.7 in 2011 (t=0.18, p=0.8603), while a relatively large increase was observed among independent outlets, (P10.7 in 2009 vs P18.8 in 2011, t=4.60, p=0.0001) (Table 9). For Patryl suspension, there was reduction in prices in both retail types, but it was considerably greater in independent stores (P107.1 in 2009 vs P64.8 in 2011, t=4.60, p=0.0001) than in chain stores (P87.4 in 2009 vs P68.8 in 2011, t=5.14, p<0.0001).

Table 9. Mean (±standard deviation) of prices of Patryl 500 mg tablet and 125 mg/5 ml suspension in 2009 and 2011, by type of drug store

	Patryl 500 mg tablet					**Patryl 125 mg/5 ml suspension**				
	2009		**2011**			**2009**		**2011**		
Type of Drug Store	n	Mean ± sd	n	Mean ± sd	% change	n	Mean ± sd	n	Mean ± sd	% change
Chain	34	9.9 ± 3.4	9	9.7 ± 0.9	2.0	26	87.4 ± 6.5	13	68.8 ± 6.1	21.3***
Independent	19	10.7 ± 3.0	17	18.8 ± 6.9	-75.7***	9	107.1 ± 29.0	10	64.8 ± 3.1	39.5***

* p<0.05, ** p<0.01, *** p < 0.001 (Student's t-test for comparing means of 2009 and 2011 prices)

4. DISCUSSION

This study serves two purposes. First, it presents the effects of a particular price negotiation scheme which the Philippines calls government-mediated access pricing on price of drugs. This is not a direct price control mechanism so it may be more amenable to the drug companies to consider. In this scheme, the action to reduce prices comes from a drug distributor who volunteers to include their product in the GMAP list. This information about price reduction is widely disseminated through a government mandate to post this information in all drug outlets including drug stores and hospitals. This could actually benefit the volunteer drug company because of the impression in the public derived that their drug price has been reduced. Other drug companies could follow suit with their price reduction, maybe forced by competition, but they are not given the same privilege of freely posting their price reductions for general public information. The new information from this study would be an important addition to the scanty published literature on the effects of government price negotiation on drug prices.

It also provides a part of the assessment of the impact of the Philippine legislation. Five years after the implementation of Republic Act 9502, or the "The Universally Accessible and Quality Medicines Act of 2008" [5], an evaluation of its overall impact is wanting. One of the most visible interventions related to this implementation was the issuance of government directives on MDRP and GMAP. At the time of the study, there were 22 drug molecules in the list. This study

included only 11 molecules for which data on pricing were collected in the 2009 and 2011 IMS Health Philippines surveys.

Except for Flagyl (metronidazole) 500 mg tablet, all innovator drugs in the study were under MDRP/GMAP. All drugs volunteered by pharmaceutical companies for GMAP reduced their prices by half. Strict compliance of drug stores to the GMAP policy was apparently observed in informing consumers of these prices. In the Philippines, nearly all drug stores display the list of GMAP drugs in a conspicuously located part of the drug store. Thus, the results showing substantial reduction in mean prices of the innovator drugs were only expected because it was compulsory for these drugs to be sold at reduced prices.

Prices of competitor drugs in this study, though not required by the GMAP directive, also went down. The percent reductions of the competitor drugs were, however, smaller in magnitude since these were already priced lower in 2009 than their innovator counterparts. The greater impact of price regulation on prices of innovator brands compared to branded generics is consistent to those reported in previous reviews [12, 13]. Since the 2009 price levels of competitor drugs were higher than the GMAP prices, these drugs were compelled to reduce their prices presumably to maintain their share of the market. This reduction would be expected since elasticity of consumer demand could be the primary market force on pricing of these drugs [18]. Interestingly, it was observed that the mean prices of several competitor brands seemed to settle near the GMAP levels. This behavior of prices of competitor drugs in this study seemed to follow that reported for European countries wherein generic drug prices converged to the reference prices [12]. A larger study involving more competitor drugs in the same classes would however be needed to confirm this pattern of behavior in the Philippines.

There were some significant interaction effects of location and type of drug store with year on the price of competitor drugs. These interaction effects were reflected as variations in the trends of prices of competitor drugs from 2009 to 2011 according to location and drug store. Notably, it was seen only for drugs that were available in relatively smaller number of stores (<10%) but not for drugs that were commonly sold. For Atopitar 10 mg tablet and Patryl 125 mg/5 ml suspension, the interaction effects could be explained by the fact that the 2009 prices of Atopitar tablet varied by location while Patryl suspension differed by type of store. The 2011 prices of both drugs settled to the GMAP levels in all locations and types of drug stores. For Zalvos 500 mg tablet and Patryl 500 mg tablet, the prices of these drugs did not follow the pattern of settling at the GMAP level. Pricing differences and trends of these drugs according to location persisted in 2009 and 2011. For Patryl 500 mg tablet, price difference between chain and independent drug stores was also occurring.

It could be argued that the effect of GMAP on drug price could have been confounded by the rapidly growing market for cheaper generic drugs. An accompanying paper has documented the large increase in drug availability of cheaper generic drugs in retail stores. [19] Moreover, generic drug use among Filipinos has also been reported to increase [20]. However, this author had also argued that the increase in generic drug availability could have also been brought about by the GMAP policy [19]. This increasing cheaper generics market could be acting as both a confounder and an intervening variable. Overall, given the similarity of this study's results for innovator drugs

and its competitors to those in Europe and OECD [12, 13], it can be surmised that prices of these drugs can be reduced with government-mediated pricing, an effect akin to that of reference pricing.

This study also provided some interesting exceptions to these general findings. For metronidazole 500 mg tablet, the brand submitted for GMAP was Winthrop, which was neither an innovator drug (Flagyl) nor a competitor drug (Patryl) in this study. In short, it was not among the market leaders. The study showed that having a GMAP-listed drug did not automatically result to price reduction for all drugs in its class. The price of Flagyl 500 mg tablet did not change and remained the same in 2009 and 2011. This is corroborated by the result for its competitor, Patryl 500 mg tablet, which even significantly increased its mean price by more than 50% in 2011. This absence of a reducing effect of having a GMAP-listed drug on the prices of Flagyl and Patryl 500 mg tablets could indicate a possible limitation on the effectiveness of government-mediated approach to price regulation. It might not lead to the anticipated lowering of prices for other drugs if the manufacturer/distributor that volunteers for reduced pricing is not an industry leader. The other oddity is the observed non-compliance of drug stores to MDRP for Asomex 5 mg tablet. Given that MDRP/GMAP posters were exhibited in almost all drug stores as required by the DOH, it is surprising that the MDRP-listed drug Asomex was sold at prices above the price cap in 93% of the stores where it was available (see Table 4). The government should ensure strict monitoring of compliance to MDRP/GMAP of the drug stores for the public benefit.

Even with prices in 2009 already lower than the GMAP reference levels, significant reduction in the prices of the cheapest available generic drugs in the outlets was observed. Apparently, this is in contrast to Puig-Junoy [12] where no price reductions in generic drugs were observed when generics are priced lower than the reference price. He referred to this phenomenon as the absence of price competition below the reference price [12]. Unfortunately, the data used in our study have limitations in illuminating this apparent disagreement in findings. In this study, the price data on generic drugs indicated only the presence and price of the lowest generic drug regardless of its brand. Thus it is not clear whether these results meant prices of specific generic brands were also declining due to the competition from the reduced prices of the more popular brands, or that it was merely a manifestation of a rapidly expanding list of new generic brands introduced at lower prices as expected.

5. CONCLUSIONS AND RECOMMENDATIONS

Being MDRP/GMAP reference drugs, there were expected compulsory reductions in mean prices of 10 of 11 innovator brands. Competitor drugs also generally followed the decreasing trend in mean prices but on a smaller magnitude of reduction. Prices for several competitor drugs in 2011 tended to settle near the GMAP references levels. Mean prices of the cheapest generic drugs in drug stores all significantly went down. The implementation of the MDRP/GMAP policies could lead to the reduction of prices of directly affected drugs similar to the effect of reference pricing.

On the short-term, reduction of drug prices undoubtedly benefits the patient population. At present, the number of drugs under MDRP/GMAP listing in the Philippines is very small relative to the total list of essential drugs. The over-all impact of these policies may not be that palpable yet.

The Philippine government should consider the expansion of the list of drugs under MDRP/GMAP, hoping that the findings here would be replicated in other essential drugs. However, these interventions should be carefully monitored as pharmaceutical policies, including price regulation, may not always lead to an over-all benefit to the public and may even cause harm by discouraging introduction of new products to a country.

This paper had only presented the effect of GMAP on the price of directly affected drugs. The limited conditions represented in the study may not be replicated under other situations. For example, what would be the effect of GMAP on prices of drugs with the same molecule if the drug volunteered for price reduction were not a market leader like those in this study? Another interesting topic would be to investigate that effect of GMAP on drugs carrying different molecules but with the same therapeutic indications, such as candesartan and valsartan. In an analogous discussion, the topic of effect of reference pricing on drugs not subject to it has generated interest. However, even for reference pricing, the number of available studies is very few [13]. Further studies on other outcomes of these government interventions have to be examined too. The effect on drug expenditures, drug use, drug quality, health outcomes, procurement practices of hospitals, innovation, et al need to be addressed in future studies to determine the impact of government mediation on other stakeholders in the Philippines.

6. ACKNOWLEDGEMENTS

This study is a part of a larger study on the impact evaluation of the cheaper medicines law on the different stakeholders in the Philippines. Funding for this study is provided by a grant from the Department of Health/Philippine Council for Health Research and Development. The authors would like to thank IMS Health Philippines, particularly Mr. Sof Casuple, for facilitating the delivery of the data on the 2009 and 2011 IMS Health surveys and for providing additional information on the technical details of these surveys and Ms. Regine Philline del Rosario for assistance in obtaining background information on the pharmaceutical industry in the Philippines.

REFERENCES

[1] MDG Gap Task Force Report, "Millenium development goal 8: The global partnership for development – making rhetoric a reality. United Nations," pp. 61-63, 2012.

[2] D. Batangan, C. Echavez, A. Santiago, D. A. Curz, and E. Santos, "The prices people have to pay for medicines in the Philippines," *World Health Organization/Health Action International/Philippine Department of Health*, Available http://www.haiweb.org/medicineprices/surveys/200502PH/sdocs/survey_report.pdf, 2005.

[3] D. Batangan and N. Juban, "Philippines pharmaceutical situation: 2009 WHO health facility survey on medicines," *World Health Organization/Department for International Development/Medicines Transparency Alliance*, Available http://www.medicinestransparency.org/fileadmin/uploads/Documents/countries/Baseline_Component_2_WHO_Surveys/Philippines_baseline_Component_2_WHO_level_II_Household__Survey.pdf, 2009.

[4] M. Tobe, A. Stickley, J. D. R. Rosario, and K. Shibuya, "Out-of-pocket medical expenses for inpatient care among beneficiaries of the national health insurance program in the Philippines," *Health Policy and Planning,* vol. 28, pp. 536-48, 2013.

[5] Republic Act 9502, "Universally accessible and quality medicines act of 2008. The congress of the Philippines," 2008.

[6] Executive Order No 821 S, "Prescribing the maximum drug retail prices for selected drugs and medicines that address diseases that account for the leading causes of morbidity and mortality. The official gazette," *The Philippine Government,* 2009.

[7] K. Marin, "Philippine government intervention to increase access to medicines: A case study on the maximum drug retail price," *Asian Institute of Management – Dr. Stephen Zuellig Center for Asian Business Transformation, Makati City, Philippines,* 2011.

[8] S. Ocampo, "Cheaper medicines law hasn't served the poor. Philippine star," Available http://www.philstar.com/opinion/2012-06-09/815179/cheaper-medicines-law-hasnt-served-poor, 2012.

[9] G. López-Casasnovas and J. Puig-Junoy, "Review of the literature on reference pricing. Health policy," vol. 54, pp. 87-123,, 2000.

[10] P. Danzon and J. Ketcham, "Reference pricing of pharmaceuticals for medicare: Evidence from Germany, The Netherlands, and New Zealand," *Front Health Policy Res,* vol. 7, pp. 1-54, 2004.

[11] M. Aaserud, A. Dahlgren, J. Kösters, A. Oxman, C. Ramsay, and H. Sturm, "Pharmaceutical policies: Effects of reference pricing, other pricing, and purchasing policies.," *Cochrane Database Syst Rev,* p. CD005979, 2006.

[12] J. Puig-Junoy, *Impact of European pharmaceutical price regulation on generic price competition: A review, Pharmacoeconomics,* vol. 28, pp. 649-663, 2010.

[13] M. Galizzi, S. Ghislandi, and M. Miraldo, "Effects of reference pricing in pharmaceutical markets: A review," *Pharmacoeconomics,* vol. 29, pp. 17-33, 2011.

[14] Advisory Council for Price Regulation, "Resolution 2009-001 entitled Implementing the voluntary price reduction for at least 16 molecules or 41 drug preparations (Also Known as Government Mediated Access Prices). Philippine Department of Health," 2009.

[15] P. Kanavos, "Overview of pharmaceutical pricing and reimbursement regulation in Europe. London school of economics health and social care," 2001.

[16] J. Neter, N. Kutner, C. Nachtshem, and W. Wasserman, *Applied statistical linear models*, 4th ed. Chicago: Richard D Irwin, 1996.

[17] StataCorp, *Stata statistical software: Release 10. College station*. TX: Stata Corp LP, 2007.

[18] M. Holt, "International prescription drug cost containment strategies and suggestions for reform in the United States," Available http://www.bc.edu/dam/files/schools/law/lawreviews/journals/bciclr/26_2/07_TXT.htm.

[19] J. J. Sarol, "Effect of government-mediated access pricing on availability of directly affected drugs in retail drug stores in the Philippines from 2009 to 2011," *Acta Medica Philippina,* vol. 48, pp. 9-17, 2014.

[20] O. Picazo, "Review of the cheaper medicines program of the Philippines. Philippine Institute for Development Studies " Available http://www.dbm.gov.ph/wp-content/OPCCB/fpb/b_DOH-CheaperMedicines/i-Cheaper%20Medicines%20Program%20Review.pdf, 2011.