Author's response to reviews

Title: Analysis of prices paid by low-income countries - how price sensitive is government demand for medicines?

Authors:

Divya Srivastava (divyasrivastava.article@gmail.com)
Alistair McGuire (a.j.mcguire@lse.ac.uk)

Version: 3 Date: 17 June 2014

Author's response to reviews: see over
Dear Editor:

Thank you very much for the reviewers’ useful comments and feedback regarding the manuscript. We have modified the manuscript accordingly, and detailed corrections are listed below point by point:

The manuscript has been resubmitted to BMC Public Health. We look forward to your response.

Sincerely,

Divya Srivastava

We thank the reviewers for their comments and feedback. Please find attached our responses as set out below.

**Reviewer 1 comments**

1. As I am not intimately familiar with this literature, and therefore do not know if there is prior evidence or support for using generic prices as a proxy for marginal cost. Any references about this would be useful to the reader.

**Authors’ reply**

Following: References added.
Following text has been added.

Theory assumes that once generic firms enter the market, the price of the medicine falls and approaches to marginal cost, as number of generic firms increases.

2. (ii) As the authors acknowledge (p 13), generic price can’t be a great approximation to MC, as it causes them to drop 49 of the 139 observations. The authors do sensitivity analysis, but only by varying the generic price by 5 and 10 percent. This is fine, but it may also be interesting and perhaps useful to calibrate the marginal costs that would give elasticities that seem out of line with the literature.

Authors’ reply

The MC continue to stay in line with the literature when varied by up to 33%. When they are increased by 50%, some estimates starts to seem out of line with the literature.

Following text revised.

First, generic prices, which were used as proxies for marginal cost, were varied to see if the results would significantly change the results: they were increased and decreased ranging from 5% to 33%.

(iii) The authors should show some information about the countries/prices/molecules for the 49 observations that were dropped. Are these all the same molecule? Highest price molecules? From any particular therapeutic category? The reader could benefit from understanding whether something
Authors’ reply

The observations that were dropped did not show clear patterns.

The following text has been added:

All of the dropped observations used the MSH reference price where there was no generic in the national market. There was no clear pattern among the therapeutic categories as almost all therapeutic categories were affected. Only five therapeutic categories did not have observations that were dropped: anxiolytics, diuretics, antiparasitic, contraceptive and anti-inflammatory medication. Only a few countries were disproportionately affected. Uganda had 2 observations in the data set and both were outliers. Jordan and Peru, had similar numbers of computed elasticities that were both in the normal range and considered outliers. Seven countries: China (Shandong province), Kazakhstan, Kuwait, Malaysia, Morocco, Nigeria, and Tunisia had some outliers but the majority their observations had computed elasticities in the reported normal range.

(2) The authors provide little information about regulatory or market differences in the 16 countries in their data. To the extent that it is possible, it would be nice to know – for example – what fraction of the market is covered by government procurement, whether the country has national or compulsory health insurance, or even what the gini coefficient is for the country.

Authors’ reply

Procurement data is lacking in these settings as was GINI information for all countries concerned and WHO reports carry some information on health insurance but this is not widely available for the relevant data years. We have included reliable information on THE % GDP against GDP for all the countries.

Following text and graph has been added:
By way of background the countries in the sample had GDP per capita that ranged from 982 $ current international dollars in Nigeria to 20280 in Kuwait. Countries also varied in how much they spent on health as a share of GDP from 2.2% in Pakistan to 11.6% in Lebanon.

![Figure 1 - Total health expenditure % GDP and GDP per capita, 2003](https://example.com/figure1.png)


(3) The authors should discuss why the appropriate element of interest here is of price elasticity and not income elasticity.

Authors’ reply

Following text has been added.

*The focus of the study is on government behaviour and buying power. The interest is to study and understand government behaviour regarding drug procurement, with price being the main response variable.*

(4) The authors should do a more thorough job of explaining how their paper differs from (and contributes to the literature) given the existence of a recent publication by Danzon, Mulcahy & Towse (2013, Health Economics). Obviously, the authors here are estimating price elasticities, whereas the DMT paper is not, but both papers are fundamentally interested in the relationship between income
and pharmaceutical prices.

Authors’ reply

This paper looks focuses on both upstream and downstream prices but for a smaller set of drugs to treat HIV/AIDS, TB and malaria in a select number of middle and low-income countries. The focus of their paper is on understanding the role of procurement of non-government organisations and any potential impact on potential prices of branded and generics in the market.

The following text has been added.

Recent work on a select number of middle and low-income countries analysed the determinants of ex-manufacturer prices for originator and generic drugs as well as retail prices for drugs to treat HIV/AIDS, TB and malaria.\textsuperscript{12} The study concludes that an income elasticity which ranges from 0 to 0.10 suggests that drugs are unaffordable because within-country income contributes to relatively high prices. Tendered procurement using data from large non-government organisations imposes quality standards and reduces the prices of originator and generic drugs compared with their respective retail pharmacy prices.

Minor revisions:

(1) The abstract says the data is from 2006, while the body of the paper says the data is from 2003.

Authors’ reply

Thank you for noting the mistake. The abstract date has been corrected.

(2) It would be nice to see Table 3 in a scatterplot-type form that shows a more comprehensive picture of income and price.

Authors’ reply
Reviewer 2’s comments:

1. The authors indicate that they use the price of the relevant generic drug in the market as the proxy for the marginal cost of the drugs. They also accept as true that these branded drugs were off-patent (p.1, third paragraph) If this is the case, I’m more inclined to believe that the price elasticities calculated in this study are price elasticities for the branded drugs when there’s a generic available in the market instead of that particular medicine itself. The condition of the market is different when there’s a generic available in the market and government has substitutions for the branded drugs in the market. Thus, demand responsiveness should also be different when there’s only one supplier in the market compare to multiple suppliers. It’s not surprising that the study found that low-income countries are more responsive to changes in the price of medicines since there’re generic substitutions and change in price of the branded drugs could drive government to purchase generic drugs instead of branded drugs.
2. If the elasticities calculated from this study are price elasticities for the branded drugs when there’s a generic available in the market, then the conclusion that were drawn from this study about the market access restrictions to new products faces by low-income countries are much weaker.

Authors’ reply

Comments for: 1 & 2

We agree with the reviewer that the size of the market share of the branded drug as well as the number of substitutes have been shown in previous research to have an impact on wholesale prices and retail prices in the pharmaceutical market.

In the data that were used, the majority of observations did not have a generic equivalent in the market. In these cases, the MSH reference price, which is considered the gold standard of pharmaceutical pricing data was used. The MSH reference price was used for 57 observations. The generic price was used as a proxy for 33 observations.

<table>
<thead>
<tr>
<th></th>
<th>MSH reference price to compute price elasticity</th>
<th>Generic reference price to compute price elasticity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Max</td>
<td>-1.0</td>
<td>-1.0</td>
</tr>
<tr>
<td>Min</td>
<td>-2.0</td>
<td>-1.9</td>
</tr>
<tr>
<td>Ratio</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>Mean</td>
<td>-1.3</td>
<td>-1.4</td>
</tr>
<tr>
<td>CV</td>
<td>-0.2</td>
<td>-0.2</td>
</tr>
<tr>
<td>STD</td>
<td>0.3</td>
<td>0.2</td>
</tr>
</tbody>
</table>
A counter argument would be we are not looking at a situation where companies have market power and to investigate this, we divided the sample where there were and were not generic substitutes as according to the above hypothesis that the expected price mark-up should be lower and price elasticity higher but we find no evidence.

The following text has been added:

In this study, two-thirds of the observations used the MSH reference price where there was no generic in the market and one-third of the observations used a generic price that was available in the market to calculate a price elasticity. There was, however, no systematic differences (e.g. by therapeutic category or by country) in the computed price elasticities between the set of data that use the MSH price compared with the generic price. The cross-sectional nature of this study cannot capture the lagged or residual price of effect when there are generic equivalents in the market. One reason might be that generics in these country settings are not real substitutes and do not act as a constraint as observed in high-income countries. In middle and low-income these settings, there is evidence to suggest that generics are perceived as low quality (Danzon et al., 2013). This suggests that other factors could drive price differences between originators and their equivalents, such as regulatory skill and procurement ability.

3. In p.13, the authors indicate that some of the observations were dropped in the cases when the branded price was below the generic price and when the branded price and generic price were relatively similar. I believe that this is also an explanation of how the company reacts when there’s generic available in the market and prices of the branded drugs and generic drugs are pretty similar or even lower.

Authors’ reply

The following text has been added:

All of the dropped observations used the MSH reference price where there was no generic in the national market. There was no clear pattern among the therapeutic categories as almost all therapeutic categories were affected. Only five therapeutic categories did not have
observations that were dropped: anxiolytics, diuretics, antiparasitic, contraceptive and anti-inflammatory medication. Only a few countries were disproportionately affected. Uganda had 2 observations in the data set and both were outliers. Jordan and Peru, had similar numbers of computed elasticities that were both in the normal range and considered outliers. Seven countries: China (Shandong province), Kazakhstan, Kuwait, Malaysia, Morocco, Nigeria, and Tunisia had some outliers but the majority their observations had computed elasticities in the reported normal range.

4a. Minor essential revisions includes the use of term “molecule level”. I’m not sure does the author mean the analysis was done at the “generic name” level. Please clarify.

Authors’ reply

The analysis was done using prices per pill and then aggregated up to pack size. The term "molecule level" refers to the chemical active ingredients that are used to manufacture the drug. These are standardised definitions based on the Anatomical Therapeutic Chemical (ATC) Classification System controlled by the WHO Collaborating Centre for Drug Statistics Methodology (WHOCC). Regulatory agencies that grant market authorisation such as the Food and Drug Administration in the United States, the Medicines and Healthcare products Regulatory Agency in the United Kingdom, European Medicines Agency (EMA) use this system to classify medicines that apply for market authorisation.

The following text has been added.

The study uses government procurement (upstream) price data at the molecule level or price per pill that was aggregated up to pack size, drawing on a large cross-sectional sample of low-income countries.

4b. In p.14, the correlation between income and price was reported. However, the only the magnitude of the correlation was reported but not the significance level.
Authors’ reply

Following p-values have been added.

<table>
<thead>
<tr>
<th>Correlations</th>
<th>GDP per capita</th>
<th>GNI per capita</th>
<th>Govt HE per capita</th>
<th>THE % GDP</th>
<th>THE per capita</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pill price</strong></td>
<td>0.0075 (p-value 0.83)</td>
<td>-0.0044 (p-value 0.97)</td>
<td>0.0079 (p-value 0.35)</td>
<td>-0.0221 (p-value 0.62)</td>
<td>0.0495 (p-value 0.18)</td>
</tr>
<tr>
<td></td>
<td>-0.0007 (p-value 0.59)</td>
<td>0.0111 (p-value 0.55)</td>
<td>0.0656 (p-value 0.72)</td>
<td>0.1196 (p-value 0.10)</td>
<td>0.2152 (p-value 0.05)</td>
</tr>
<tr>
<td><strong>Pack price</strong></td>
<td>0.0075 (p-value 0.83)</td>
<td>-0.0044 (p-value 0.97)</td>
<td>0.0079 (p-value 0.35)</td>
<td>-0.0221 (p-value 0.62)</td>
<td>0.0495 (p-value 0.18)</td>
</tr>
</tbody>
</table>