Reviewer's report

Title: Antiretroviral drug expenditure, pricing and judicial demand: an analysis of federal procurement data in Brazil from 2004-2011

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Reviewer: Joseph Perriens

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This manuscript is interesting because it documents the temporal relationships between litigation for access to medicines, their initial procurement, even at very high price, and how it influenced their subsequent in national treatment guidelines and negotiated procurement at a lower (but still high) price for several medicines. This information has to date not been systematically collected and published, even though the relationship between judicial action and treatment access was anecdotally known and has been described in several papers, which were appropriately referenced.

The message of the paper would be stronger if the paper focuses on this aspect only.

MAJOR COMPULSORY REVISIONS

ABSTRACT

The authors should state clearly that their data is limited to ARV procurement data from the private sector. This needs to be stated in the Abstract, in the first line of the “Methods” section, and in the first line of the results section (“from private sector sources” instead of “from purchased sources”).

The abstract states that “newer medications were on average four times more expensive than older medications” – but the manuscript does not provide data that would allow a fair comparison of price levels between older and newer drug – specific suggestion on how the pricing section should be revised is given under the header “Results” below.

The manuscript also does not contain data to support the statement “ARVs were purchased at the lowest prices through auction, intermediate prices through single suppliers, and highest prices through emergency procurement resulting from judicial action”.

The second sentence in the conclusion “Medications …/… have been largely eliminated due to domestic production” is unclear and can be misunderstood. The authors likely meant to say they ceased to be supplied by the private sector because the public sector started producing them. However, this does not eliminate their cost. This sentence needs to be revised.

Finally, while the authors are at liberty to state “efforts should be pursued to reduce prices”, the use of “and other public health flexibilities” in the last sentence of the abstract is vague and might not be understood by a general
readership. Why not state something like “and, when possible and needed, enabling the use of cheaper generic drugs through the use of compulsory licensing”?

BACKGROUND

Last paragraph: “The objective of our study” must be clarified: this study deals with procurement from and expenditure related to procurement from the private sector only.

METHODS

First line: “ARV drug procurement from the private sector”, instead of … “ARV drug procurement”

I found it very difficult to understand why the authors expressed the volume procured as DDD per 1000 person under treatment, until I realized that this is in fact an assessment of extent to which procurement from the private sector satisfies the demand for ARVs in the country. One would expect the number of DDD/1000 patient years under treatment to be between 2000 and 3000 – as in Brazil triple drug fixed dose combinations of antiretroviral drugs are not available. If the authors wish to continue presenting this data, they explain that this is what they are aiming to do, and why they used this assessment method. From the explanation provided by the authors on page … I infer that the reason was that data on the volumes and value of public sector procurement was not available to them.

No description is given of the procurement procedures – and this makes it difficult to understand the content of the results section on page 10 and 11 where the different price levels following judicial order, tender, and auction are discussed. Specifically, the difference between “tender” and “auction” not clear. As all drugs discussed as single source drugs, I think that if they are procured in “emergency mode” after judicial decision at “international” prices, i.e. those practiced by the originator company in high income countries, but when entered in routine use, following negotiation of a more reasonable price with the originator. But then I don’t understand why the price would drop in an auction as the price would be determined in a bilateral negotiation. Without more details on this, I cannot understand figure 5, and fear that figure 6 might be comparing different drugs, and is therefore not useful.

RESULTS

Section on “Pricing”. The prices in Figure 2 are prices of individual drugs expressed as $ per tablet. This section needs to be revised, and the prices should be expressed as price per DDD, because older ARVs often require more tablets per DDD than newer ARVs, which would invalidate the conclusion.

Are the prices of “older ART” drugs the average price between 2004 and 2009 ?? And are the prices of “newer ART” drugs the average price between 2007 and 2011 ?? If so, the statement made is that, with time, ARVs became more expensive. Also, atazanavir is not exactly an older ARV drug, and saquinavir, the leading PI in 2004, is not included. And the price evolution of the leading PI, lopinavir/ritonavir, cannot responsibly be excluded.
I would also much prefer to see this data in a table (as annex to the paper if needed), or in a line graph with price per DDD on the vertical axis and year of procurement on the horizontal axis.

Page 11: Line 2 and 3: “tendering” – presumably this refers to orderly procurement following price negotiation. Correction is likely needed.

Page 11: Expenditures and price per unit based on method of tender
Without additional methodological detail, this section adds no value, and should be deleted.

DISCUSSION
The discussion needs to focus on the core messages of the paper. The summary of results in not needed. The content of page 13, first paragraph is out of place. The second paragraph makes claims on the basis of data that is not presented in the results section. It may very well be that Brazil save money on procurement of tenofovir compared to the originator price, but its cost has certainly not disappeared (and in higher in Brazil than in international procurement).

Page 14: Results of judicial action. Last line. The results section does provide no data to document that litigation for access to ARVs has detrimental results. It might be that such litigation has led to adverse effects in other treatment programs, but in the case of the ARV programme the data (in figure 1) show that, in spite of litigation and the introduction of novel treatment approaches, the cost of the treatment programme has not escalated to unaffordable levels (figure 1). This is an important conclusion and it should be stated. The last sentence on page 15 is, inferring that litigation compromises program sustainability, is not supported by the facts. Moreover, in the absence of any data or reference to stagnant or worsening clinical outcomes, the contention that it does not improve clinical outcomes is not supported by facts.

Page 16: The view that Global Fund, PEPFAR and Clinton Health Access Initiative can achieve “supernormal” discounts in “certain circumstances” is not warranted, as, in spite of decreasing prices for ARVs in low and middle income countries, the global ARV market remains vibrant and the producers resilient – not leaving the market, which is a strong indicator of the market’s viability. The reference used for this statement is also very old: a much better reference would be the WHO Global Price Reporting Mechanism (at http://apps.who.int/hiv/amds/price/hdd/) or its summary report “Transaction prices for antiretroviral medicines from 2009 to 2012” http://www.who.int/hiv/pub/amds/gprm2012/en/index.html),

MINOR ESSENTIAL REVISIONS
Page 4, Line 3: the savings from the compulsory licensing of efavirenz need to be dated and referenced.

Page 4: text from “As a result, ... “up to and including “...from single source suppliers” could be deleted as this is also stated in the discussion.

Page 5: Line 6: The database cannot be “considered comprehensive”, because it does not include public sector procurement. Also, there is no need to make the
statement made in this sentence. I propose to delete it.

Page 5 line 9: “purchases of ARVs from the private sector” instead of “purchases of ARVs”.

Page 5 second paragraph, line 3: “ARV procurement from the private sector” instead of “ ARV procurement”.

RESULTS

Page 7 Line 6: “drug procurement from the private sector” instead of “drug procurement”.

Page 7 Line 7: “for ARVs purchased from the private sector” instead of “for purchased ARVs”

Page 8 and 9: Section on “Procurement in DDDs....” Prices are given as “XXXX DDDs”. This is confusing. Revise to “XXXX $/DDD/1000patients-day”

Page 7 Line 10 and 18: “drug procurement from the private sector” instead of “drug procurement”

Page 7 Line 14: “procured from the private sector” instead of “procured”

Page 8 Line 1: “purchased from the private sector” instead of “purchased”

Page 8 Line 8: “As can be expected”. Delete – just state the facts.

Page 8: Line 9: “federal expenditures on private sector ARV procurement” instead of “federal expenditures”

DISCUSSION

Second paragraph, line 1: “private sources” instead of “purchased sources”.

Second paragraph line 3: “procurement from the private sector” instead of “procurement”

DISCRETIONARY REVISION

Page 3, Background, Line 4: Prior to 1997, did Brazil have no pharmaceutical patents??

Page 5, Methods: If SIASG data are publicly available, a reference to the database should be provided, or it should be clarified how other researchers can access the data.

Page 6 Simplify language – while correct the average reader would not be familiar with “ATC codes to the 4th level”, but would understand “class of ARV”.

Page 6, last line: can the source of the exchange rate be referenced? The source would be a web-site.

Page 9 and 10 Section on “expanding access to treatment, the relationship .....”

This is the heart of this manuscript, and should therefore excel in clarity. However, in each of the paragraphs on the different drugs the sequence is upside down: first when the drug was included in the national treatment guidelines, and then the legal action that influence that decision. I suggest to reverse this order.

DISCUSSION
Remove the section “Summary of main results” – there is no need for it.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Not suitable for publication unless extensively edited

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests