

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Impact of National Drug Pricing Policy 2018 on Access to Medicines in Lahore Division, Pakistan: A Pre-Post Survey Study Using WHO/HAI Methodology
AUTHORS	Saeed, Amna; Saeed, Hamid; Saleem, Zikria; Yang, Caijun; Jiang, Minghuan; Zhao, Mingyue; Ji, Wenjing; Aziz, Muhammad Majid; Khan, Faiz; Gillani, Ali Hassan; Atif, Naveel; Fang, Yu; Babar, Zaheer Ud Din

VERSION 1 – REVIEW

REVIEWER	Toine Pieters Utrecht University, Institute of Pharmaceutical Sciences
REVIEW RETURNED	13-Jan-2020

GENERAL COMMENTS	<p>I appreciate the efforts of the researchers to study the impact of a government intervention on drug prices and affordability/accessibility. Given the relative poor accessibility of essential drugs in countries like Pakistan this kind of study is of utmost importance. Between the lines I can read that the authors are surprised to see that the price intervention in essence only makes a slight difference in terms of accessibility and affordability. The authors even state that the prices of both LPGs and OBs/EMs have increased remarkably in the post intervention year, 2019. I would like to know more about the mechanisms behind this obvious government intervention failure. What exactly are the reasons of the failure and what are the lessons to be learned. At least it shows the complexity of the issue at hand, but that does not seem to justify the enormous statistical work that the authors have invested in this study. So what kind of parameters in this study can be used to design an intervention that may have a higher success rate? Furthermore, I would like to advise the authors to hire a native English speaker to edit the paper in an appropriate way.</p>
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REVIEWER	Dr. Sandor Kerpel-Fronius, MD, DSc, FFPM Semmelweis University, Department of Pharmacology and Pharmacotherapy Budapest Hungary
REVIEW RETURNED	10-Mar-2020

GENERAL COMMENTS	<p>The provision of affordable drugs to patients is a major problem everywhere irrespective of the political organization of the countries. However, the methods for organizing affordable drug supply is different in the countries. It is, therefore, very important to compare and learn from the approaches developed by the</p>
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	<p>different communities. In the present paper, the authors compared the effects of the recently reworked National Drug Pricing Policy in Pakistan, which is a Low Middle Income Country (LMIC). The prospective study was planned to collect data from various public and private organizations one year before and one year after changing drug pricing policy. The well established WHO/HAI methodology was meticulously followed by the authors making international comparisons of the findings possible.</p> <p>In the new system, the prices were adjusted to the consumer price index. It was concluded that this increased the affordability of essential medicines in Pakistan. However, the overall mean percent of drug availability remained poor. In addition, the measures resulted in heterogeneous effects on the availability of the lowest priced generics and originator brands in the public and private sectors. It is an advantage that the availability of generics increased but it is alarming that parallel the originator brands decreased dramatically in the public sector providing charge-free medications. In addition, the price of several originator brand drugs was increased illegally decreasing the affordability of medicines for CVD and diabetes. The authors, unfortunately, did not provide any suggestions on how to correct some of the shortcomings of the new system.</p> <p>The paper is well documented; the interested readers might find many interesting data on the prices of individual drugs as well as concerning their availability and affordability.</p>
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REVIEWER	Michael Thiede IUBH University of Applied Sciences, Berlin, Germany
REVIEW RETURNED	19-Mar-2020

GENERAL COMMENTS	<p>The paper is lacking some relevant policy-related information. The analysis therefore appears incomplete. Further, there are some language and style issues.</p> <p>The paper analyses and discusses the findings of a survey at the pharmacy level in Lahore Division, Pakistan, that was conducted on the basis of the WHO/HAI methodology with the objective to assess access to medicines before and after the introduction of Pakistan's National Drug Pricing Policy (NDPP). The 2019 survey is a follow-up to an earlier survey that was described in detail in a PLoS ONE article by the same authors (Saeed et al., 2019). The comparison of the results of the two surveys allows certain conclusions with regard to the effectiveness of the NDPP.</p> <p>The methodological approach (WHO/HAI) has been applied in numerous contexts and does not require further explanation. The idea to use the approach within the analysis of a government's policy to regulate pharmaceutical pricing is appealing. However, the presentation of the overall policy and its instruments remains superficial. It would have been enlightening to learn more about the intended effects as well as the policy tools and pathways. To the international reader it is important to understand what the Pakistani policy is about, what was the initial situation, what</p>
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	<p>are the political measures designed to address the situation. Otherwise the knowledge gain is minimal.</p> <p>In the context of policy analysis, further questions arise, such as: At what point in time after introduction of a nationwide policy would it be realistic to expect the desired results?</p> <p>These types of questions could have been addressed in the discussion or at least identified in the context of a presentation of limitations.</p> <p>Some language edits might further improve the paper - e.g. use of definite/indefinite articles, occasional ambiguous statements, various typos.</p> <p>In general, this is an interesting paper that complements earlier work on access to medicines in Pakistan and in the region. It would be suitable for publication after adding some important aspects of policy analysis and polishing up the style.</p> <p>Saeed A, Saeed H, Saleem Z, et al. Evaluation of prices, availability and affordability of essential medicines in Lahore Division, Pakistan: A cross-sectional survey using WHO/HAI methodology. PloS One 2019;14:e0216122.</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: Toine Pieters

Institution and Country: Utrecht University, Institute of Pharmaceutical Sciences

Please state any competing interests or state 'None declared': None

Please leave your comments for the authors below

I appreciate the efforts of the researchers to study the impact of a government intervention on drug prices and affordability/accessibility. Given the relative poor accessibility of essential drugs in countries like Pakistan this kind of study is of utmost importance.

Response: Thank you for your positive comments and valuable suggestions to improve our paper.

Between the lines I can read that the authors are surprised to see that the price intervention in essence only makes a slight difference in terms of accessibility and affordability. The authors even state that the prices of both LPGs and OBs/EMs have increased remarkably in the post intervention year, 2019. I would like to know more about the mechanisms behind this obvious government intervention failure. What exactly are the reasons of the failure and what are the lessons to be learned. At least it shows the complexity of the issue at hand, but that does not seem to justify the enormous statistical work that the authors have invested in this study. So what kind of parameters in this study can be used to design an intervention that may have a higher success rate?

Response:

Thank you for asking this. Yes, our results have shown the ineffectiveness of the policy, we have elaborated the reasons in discussion sections as “These data suggested that these intentional malpractices by the drug sellers might be driven by poor price control regulation by price enforcement authorities. Therefore, the current drug pricing policy NDPP 2018, is not the sole reason of price hike,

probably main stakeholders in drug supply chain are also contributing towards medicine inflated prices.” We have also highlighted the reasons more specifically as follows “The increases in prices of both OBs and LPGs may fairly be attributable to the NDPP 2018 that allows an annual increase in the prices of scheduled drugs up to 70% of CPI compared to 50% of CPI as per NDPP 2015 [9, 10]. These changes in price calculations seems to accentuate the substantial impact on overall prices of medicines, thus, making them more expensive. The increase in LPGs prices were more significant as compared to OBs suggesting that with already expensive OBs, the price increase in LPGs would impoverish the overall access to medicines, imputable to the changes in formula for LPGs (new entrants) price calculation. According to NDPP 2018, the MRP of new entrant first generic should be fixed at 20% less than that of OB compared with 30% less than MRP of OB as per NDPP 2015. Another possible variable is the prior availability of generics in the market for price calculation, where, according to NDPP2018, the MRP of a new entrant (LPGs) was fixed equal to the highest MRP of the available generics in the market, while as per NDPP2015 practice, MRP was fixed by taking the average of other generics in the market. Therefore, these changes in price calculating mechanisms might have led to higher prices of many new LPGs in the market. Hence, contrary to NDPP 2018’s price steerage objectives, the increase in medicine prices was more distinct for NEML medicines as compared to non-NEML medicines.” (See page 12, Line 336 to 354). “Although the formation of a national scale pricing policy is laudable but it seems to be a collection of drug price calculation formulas only. It could also include the mechanism for price monitoring, an aspect which seems to be one of the major reasons behind failure to achieve the goals of NDPP 2018. Inclusion of WHO/HAI based surveys on regular basis could also be an option, in this case.” (See page 13, line 385).

We have added a possible intervention to improve the policy in discussion section as “Inclusion of WHO/HAI based surveys on regular basis could also be an option, in this case. The WHO has developed a mobile application named “WHO Essential Medicines and Health Products Price and Availability Monitoring (WHO EMP MedMon)”, which can be used to collect and analyze price and availability data from health care outlets. This application is based on standard WHO/HAI methodology and it can be used both online and offline, make it both time saving and cost effective [33]. The drug inspectors or a third party can be given this responsibility to monitor and report the prices using WHO EMP MedMon on regular basis, ensuring the compliance by drug manufacturers and sellers to NDPP.” (See page 14, line 388).

(World Health Organization. MedMon - WHO Essential Medicines and Health Products Price and Availability Monitoring Mobile Application. 2016. Available: <https://www.who.int/medicines/areas/policy/monitoring/empmedmon/en/>. [Accessed: 30 March 2020].

Furthermore, I would like to advise the authors to hire a native English speaker to edit the paper in an appropriate way.

Response: Thanks for your advice. We have got the paper edited by a native English speaker and tried our best to leave no mistake.

Reviewer: 2

Reviewer Name: Dr. Sandor Kerpel-Fronius, MD, DSc, FFPM

Institution and Country: Semmelweis University, Department of Pharmacology and Pharmacotherapy
Budapest

Hungary

Please state any competing interests or state ‘None declared’: None

Please leave your comments for the authors below

The provision of affordable drugs to patients is a major problem everywhere irrespective of the political organization of the countries. However, the methods for organizing affordable drug supply is

different in the countries. It is, therefore, very important to compare and learn from the approaches developed by the different communities. In the present paper, the authors compared the effects of the recently reworked National Drug Pricing Policy in Pakistan, which is a Low Middle Income Country (LMIC). The prospective study was planned to collect data from various public and private organizations one year before and one year after changing drug pricing policy. The well established WHO/HAI methodology was meticulously followed by the authors making international comparisons of the findings possible.

In the new system, the prices were adjusted to the consumer price index. It was concluded that this increased the affordability of essential medicines in Pakistan. However, the overall mean percent of drug availability remained poor. In addition, the measures resulted in heterogeneous effects on the availability of the lowest priced generics and originator brands in the public and private sectors. It is an advantage that the availability of generics increased but it is alarming that parallel the originator brands decreased dramatically in the public sector providing charge-free medications. In addition, the price of several originator brand drugs was increased illegally decreasing the affordability of medicines for CVD and diabetes. The authors, unfortunately, did not provide any suggestions on how to correct some of the shortcomings of the new system.

The paper is well documented; the interested readers might find many interesting data on the prices of individual drugs as well as concerning their availability and affordability.

Response: Thank you for your positive comments and valuable suggestions to improve our paper. In addition to previously provided suggestion we have now added a new suggestion in the discussion section as “Although the formation of a national scale pricing policy is laudable but it seems to be a collection of drug price calculation formulas only. It could also include the mechanism for price monitoring, an aspect which seems to be one of the major reasons behind failure to achieve the goals of NDPP 2018. Inclusion of WHO/HAI based surveys on regular basis could also be an option, in this case. Inclusion of WHO/HAI based surveys on regular basis could also be an option, in this case. The WHO has developed a mobile application named “WHO Essential Medicines and Health Products Price and Availability Monitoring (WHO EMP MedMon)”, which can be used to collect and analyze price and availability data from health care outlets. This application is based on standard WHO/HAI methodology and it can be used both online and offline, make it both time saving and cost effective [33]. The drug inspectors or a third party can be given this responsibility to monitor and report the prices using WHO EMP MedMon on regular basis, ensuring the compliance by drug manufacturers and sellers to NDPP.” (See page 13, line 385)

Reviewer: 3

Reviewer Name: Michael Thiede

Institution and Country: IUBH University of Applied Sciences, Berlin, Germany

Please state any competing interests or state 'None declared': None declared

Please leave your comments for the authors below

The paper is lacking some relevant policy-related information. The analysis therefore appears incomplete. Further, there are some language and style issues.

The paper analyses and discusses the findings of a survey at the pharmacy level in Lahore Division, Pakistan, that was conducted on the basis of the WHO/HAI methodology with the objective to assess access to medicines before and after the introduction of Pakistan's National Drug Pricing Policy (NDPP). The 2019 survey is a follow-up to an earlier survey that was described in detail in a PLoS ONE article by the same authors (Saeed et al., 2019). The comparison of the results of the two surveys allows certain conclusions with regard to the effectiveness of the NDPP. The methodological approach (WHO/HAI) has been applied in numerous contexts and does not require further explanation. The idea to use the approach within the analysis of a government's policy to regulate pharmaceutical pricing is appealing.

However, the presentation of the overall policy and its instruments remains superficial. It would have been enlightening to learn more about the intended effects as well as the policy tools and pathways. To the international reader it is important to understand what the Pakistani policy is about, what was the initial situation, what are the political measures designed to address the situation. Otherwise the knowledge gain is minimal.

Response: Thank you so much for your comments and valuable suggestion to improve our paper.

The NDPP 2018 in fact lacks the framework for its implementation and follow-up. So, we have highlighted this issue in discussion section as “Although the formation of a national scale pricing policy is laudable but it seems to be a collection of drug price calculation formulas only. It could also include the mechanism for price monitoring, an aspect which seems to be one of the major reasons behind failure to achieve the goals of NDPP 2018.” (See page 13, line 385)

In order to provide more information about Pakistani policy and initial situation we have added these statements in Introduction section, “The medicines are provided free of cost at public sector health facilities, while patient pays out of pocket to get medicines from private sector, in Pakistan [5]. In fact, the poor availability of medicines at public sector compels the patients to buy medicines from private sector that escalates the burden on patient’s pocket, while 24.3% (in 2015) of the population is living below the national poverty line [3, 4, 7, 8]. Besides, medicine prices have increased up to 100%, both legally or illegally, in the past few years [3]. The ministry of National Health Services Regulation and Coordination (NHSRC) of Pakistan has been taking different policy measures to curb these issues through Drug Regulatory Authority of Pakistan (DRAP). The drug prices are fixed by the federal government and NHSRC. The regional drug inspectors (DIs) are responsible for price monitoring in the pharmacies of their area.” (See page 4, line 70).

More specific information about the policy has been provided in the discussion section as “The increases in prices of both OBs and LPGs may fairly be attributable to the NDPP 2018 that allows an annual increase in the prices of scheduled drugs up to 70% of CPI compared to 50% of CPI as per NDPP 2015 [9, 10]. These changes in price calculations seems to accentuate the substantial impact on overall prices of medicines, thus, making them more expensive. The increase in LPGs prices were more significant as compared to OBs suggesting that with already expensive OBs, the price increase in LPGs would impoverish the overall access to medicines, imputable to the changes in formula for LPGs (new entrants) price calculation. According to NDPP 2018, the MRP of new entrant first generic should be fixed at 20% less than that of OB compared with 30% less than MRP of OB as per NDPP 2015. Another possible variable is the prior availability of generics in the market for price calculation, where, according to NDPP2018, the MRP of a new entrant (LPGs) was fixed equal to the highest MRP of the available generics in the market, while as per NDPP2015 practice, MRP was fixed by taking the average of other generics in the market. Therefore, these changes in price calculating mechanisms might have led to higher prices of many new LPGs in the market. Hence, contrary to NDPP 2018’s price steerage objectives, the increase in medicine prices was more distinct for NEML medicines as compared to non-NEML medicines.” (See page 12, Line 336 to 354)

In the context of policy analysis, further questions arise, such as: At what point in time after introduction of a nationwide policy would it be realistic to expect the desired results? These types of questions could have been addressed in the discussion or at least identified in the context of a presentation of limitations. In general, this is an interesting paper that complements earlier work on access to medicines in Pakistan and in the region. It would be suitable for publication after adding some important aspects of policy analysis and polishing up the style.

Response: Thanks for identifying this important issue. We have addressed this as a limitation in the manuscript: “Moreover, the post survey was conducted after about a year from the launch of new drug pricing policy 2018, so the results do not reflect the long term impact of the policy. Further surveys could be conducted in future to gauge the long term effects of the policy as it was done by Fang et al in two such surveys conducted after the health reform in China [17].” (See page 14, Line 425)

Some language edits might further improve the paper - e.g. use of definite/indefinite articles, occasional ambiguous statements, various typos.

Response: Thanks for your advice. We have got the paper edited by a native English speaker and tried our best to leave no mistake.

Saeed A, Saeed H, Saleem Z, et al. Evaluation of prices, availability and affordability of essential medicines in Lahore Division, Pakistan: A cross-sectional survey using WHO/HAI methodology. PloS One 2019;14:e0216122.

VERSION 2 – REVIEW

REVIEWER	Toine Pieters Utrecht University
REVIEW RETURNED	09-Jul-2020

GENERAL COMMENTS	Dear Authors, You have improved the manuscript significantly! However there are still some questions left (See PDF). I would also encourage you to improve the language quality of the English text! The reviewer provided a marked copy with additional comments. Please contact the publisher for full details.
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REVIEWER	Michael Thiede IUBH University of Applied Sciences, Berlin, Germany
REVIEW RETURNED	29-Apr-2020

GENERAL COMMENTS	I believe that you have addressed all comments and suggestions appropriately and look forward to the publication of your interesting article.
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VERSION 2 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: Toine Pieters

Institution and Country: Utrecht University

Please state any competing interests or state 'None declared': None

Please leave your comments for the authors below

Dear Authors,

You have improved the manuscript significantly! However there are still some questions left (See PDF).

I would also encourage you to improve the language quality of the English text!

Response: Many thanks for your constructive comments and suggestions to improve this manuscript.

We have made changes as suggested. Besides, manuscript has been reviewed by an English language expert. Thank You.

Reviewer: 3

Reviewer Name: Michael Thiede

Institution and Country: IUBH University of Applied Sciences, Berlin, Germany

Please state any competing interests or state 'None declared': None declared

Please leave your comments for the authors below

I believe that you have addressed all comments and suggestions appropriately and look forward to the publication of your interesting article.

Response: We are grateful to you for your constrictive comments and suggestions to improve this article. Thank you.

We are thankful to the editor and the reviewers for the constructive criticism to improve the manuscript. All the necessary changes have been made as requested. Thank You.