

PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

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| TITLE (PROVISIONAL) | Characterizing the costs of the Global Polio Laboratory Network: A survey-based analysis |
| AUTHORS | Duintjer Tebbens, Radboud; Diop, Ousmane; Pallansch, Mark; Oberste, M Steven; Thompson, KM |

VERSION 1 – REVIEW

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| REVIEWER | Luís Velez Lapão Global Health and Tropical Medicine, Instituto de, Higiene e Medicina Tropical, Universidade Nova de, Lisboa, Portugal |
| REVIEW RETURNED | 13-Jun-2018 |

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| GENERAL COMMENTS | <p>This is a very interesting paper. It is focused on the characterization of polio laboratory costs. AFP cases. What is the meaning of AFP (pag 3)? It is explained in pag. 4. Methods The study is based on surveying costs from several laboratories. Additional methods like Time Driven ABC (TD-ABC) could be beneficial to reach more rigor. This TD-ABC has been applied to healthcare. The authors should address also that often there are costs associated with low level of work organization and waste. This should be address on the discussion. Results The results are interesting and respond to the requirements; however, the writing should improve because the text is often confusing (e.g. ES sample processing costs). A clear figure could help as well. Discussion Where there significant differences between laboratories? Can one identify good practices? Could one compare with other lab networks? An idea could be use Data Envelop Analysis. It would be interesting to see some comments on the surveillance costs vs. and eventual outbreak of polio, to better justify the investment. Here TD-BC could also be valuable. The functioning of the laboratory network would also benefit from a services model analysis. Maintenance and training costs are also relevant to the analysis, which should be addressed. Please improved the tables, they require more readability. Moreover, cheese graphics should be avoided.</p> |
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| REVIEWER | Arindam Nandi Center for Disease Dynamics, Economics & Policy, Washington DC, USA |
| REVIEW RETURNED | 07-Aug-2018 |

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| GENERAL COMMENTS | I enjoyed reading this paper titled "Characterizing the costs of the Global Polio Laboratory Network: A survey-based analysis". It's a unique and highly interesting study. I commend the authors for undertaking it. The analysis appears to be well done and the manuscript is nicely written. |
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| | <p>Major comments</p> <ol style="list-style-type: none"> 1. On page 4, please you add a little more background on the GPLN for the uninformed reader? When was it established and how many samples are examined every year etc.? Also, a Table of country names and number of labs in each, or a color-coded world map of the labs will help very much. Do the labs work solely within the host country, or are samples transported across borders if needed? 2. If it's not too much work, please adjust all estimates to 2017 or 2018 \$. Often estimates are reported in the media (or interpreted by readers) as from the same year as the publication of the paper. 3. Page 6, lines 156-158: Please can you explain the rationale for these \$20 and \$400 thresholds? On what basis were these chosen? It is important to know the full details as this affects 59 and 25 labs, as mentioned in line 163. That's close to half the sample. 4. Page 8: Before delving into a regression analysis to predict the missing costs of non-responding labs, it will be first helpful to know whether the non-response was systematic. It will help if you could show the differences in the characteristics of the non-responding labs from the average of other labs in the country or region. A simple summary stats table of the variables obtained from GPLN management system should work, with t-test of differences for each variable across responding and non-responding labs. 5. The Other Findings subsection requires rewriting. There is a lot of information crammed in it, without proper organization. Please consider dividing into more subsections. Also, the Results section of the paper should succinctly present the findings, and not try to explain them or compare with previous estimates. 6. General comments: Please divide text into more paragraphs throughout the paper. For example, pages 10 are 12 are one entire paragraph each. Much of the text is very hard to follow. There is a lot of great data in the paper – but you need better presentation. Please consider moving some results to the appendix (along with their discussion, e.g. the whole Other Findings subsection). The paper is very heavy in its current form. 7. The Discussion section needs a little more balance. The focus is heavily on sustained external funding. Considering that the study is funded by CDC, a key GPEI partner, with authors who are closely involved in GPEI, this may seem to be a little self-serving. I am not an expert on international polio policy, but I would expect that it may be natural to advocate that nations increase their GPEI funding and eventually become self-reliant. If you don't recommend it or if the nations are not ready (again, I am not an expert), please add some discussion. <p>Minor comments</p> <ol style="list-style-type: none"> 1. Abstract line 35 and elsewhere: It will be better to reword "polio-supported staff". Polio-supported sounds a little strange. 2. Abstract line 39-43: Is there any specific reason you are advocating in favor of continued international funding and not for the countries to increase their government expenditure? I think that the policy advocacy is not fully balanced. 3. Page 3, line 77: Please write the full form of AFP. It is used here for the first time. 4. Page 4, line 95: Changing to "The GPLN currently consists of 146 laboratories across 92 countries" is recommended. |
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| | <p>5. Page 5, line 112: Please define ES. First use in the main text.</p> <p>6. Page 5, line 122: Is the survey instrument only for reviewers and not meant for general readers? If not, please include the link as a standard citation. It will be good for all readers to see the instrument, unless there is any embargo.</p> <p>7. Methods section: Please divide the text into more paragraphs for ease of reading Especially on pages 6 and 7.</p> <p>8. Page 7, lines 178-195: The algorithm as written in text is hard to follow. Please consider using equations or some form of algebraic notations for clarity.</p> <p>9. Page 10, line 272: Please define "concentration-only".</p> |
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| REVIEWER | Fabian Alvarez Sanofi Pasteur, France |
| REVIEW RETURNED | 09-Aug-2018 |

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| GENERAL COMMENTS | <p>The authors objective is to "highlight both the importance of contributions that countries make to the GPLN and the need to sustain external funding to support laboratories worldwide in their surveillance for polioviruses and other diseases". I believe that they successfully attain their objective.</p> <p>The authors are certainly among the most influential researchers on polio modeling (broad definition of modeling), with tens of papers published around the polio eradication. The current manuscript is an update of a similar analysis published in 2003. As usual, the paper is well written, with clear objectives, methods, and outcomes, and tackles a crucial problem, funding of GPLN in the close to- and post-eradication ages.</p> <p>However, I have a concern regarding the "communication mood" of this manuscript for which I feel is closer to a technical report than to a scientific communication with the above mentioned objective.</p> <p>The results are so deeply described that the key messages may be drown by the excess of details on how each estimation/extrapolation has been performed. To illustrate my point I mention a couple of examples (I could mention more but "communication mood" is subjective:</p> <ul style="list-style-type: none"> - the "one concentration laboratory that responded to the survey" does not have any impact on the global picture (as mentioned by the authors), but its contribution is depicted for each topic. I would prefer to forget about and exclude from the whole analysis to simplify the reading and the resulting messages - lines 328-352 provides a lot of numbers but it's difficult for the reader to understand which is the message behind <p>I would then encourage the authors to simplify the Results section and to illustrate (visually) their messages in order to reach a larger audience:</p> <ul style="list-style-type: none"> - simplify/shorten explanations in the Results section - merge Figs 2 and 3 which are pretty similar (2a and 2b could be an option, but merging both would be better) - provide a figure with a diagram representing of the different laboratories capabilities and funding sources - provide a world map accounting for the relative investments on AFP, ES and risks related to polio |
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| | <p>In any case, there is no doubt that this manuscript is an important contribution to the objective of sustaining the funding over the next years in order to succeed the polio eradication</p> <p>Minor comments</p> <ul style="list-style-type: none"> - line 63: can be updated to mid 2018 - line 77: AFP not defined before (in fact defined line 88) - line 88 (or 77): could be helpful for naïve readers to mention that AFP could be engendered by other causes than polio. - line 112: ES not mentioned before (just in the abstract) - line 133: is geographical area correlated at some point with the corresponding population pool? (even if it does not impact absolute costs it might impact the "cost-effectiveness" of the laboratory - lines 176-195: it's not clear which is impact of this lack of separated costs. My understanding is that it was minor, so maybe all these details could be avoided. - lines 304:306: I couldn't understand the reason for "only a fraction... ". Could you please improve your rationale for this? - page 28, Fig. 4 : I would add something in the legend to make explicit that numbers in parenthesis are response rates, e.g (Resp. rate=). Even if explained in legend it's somewhat disturbing to see different % in the pie and in the legend. |
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: Luís Velez Lapão, Institution and Country: Global Health and Tropical Medicine, Instituto de, Higiene e Medicina Tropical, Universidade Nova de, Lisboa, Portugal, Please state any competing interests or state 'None declared': None declared. Please leave your comments for the authors below

Comments: "This is a very interesting paper. It is focused on the characterization of polio laboratory costs. AFP cases. What is the meaning of AFP (pag 3)? It is explained in pag. 4. Methods The study is based on surveying costs from several laboratories. Additional methods like Time Driven ABC (TD-ABC) could be beneficial to reach more rigor. This TD-ABC has been applied to healthcare. The authors should address also that often there are costs associated with low level of work organization and waste. This should be address on the discussion. Results The results are interesting and respond to the requirements; however, the writing should improve because the text is often confusing (e.g. ES sample processing costs). A clear figure could help as well. Discussion Where there significant differences between laboratories? Can one identify good practices? Could one compare with other lab networks? An idea could be use Data Envelop Analysis. It would be interesting to see some comments on the surveillance costs vs. and eventual outbreak of polio, to better justify the investment. Here TD-BC could also be valuable. The functioning of the laboratory network would also benefit from a services model analysis. Maintenance and training costs are also relevant to the analysis, which should be addressed. Please improved the tables, they require more readability. Moreover, cheese graphics should be avoided."

Response: Thank you very much for your comments. We edited the text to add the requested clarifications. Other approaches (e.g., Time-based Activity-Based Costing) are relevant for personnel, but our focus is much broader and every method comes with its limitations. We expanded our discussion to include more limitations and to note the potential use of different approaches and their

potential to provide different results. We changed the “cheese” graphics (by which we assumed the reviewer meant the bar charts) to regular bar charts.

Reviewer: 2

Reviewer Name: Arindam Nandi, Institution and Country: Center for Disease Dynamics, Economics & Policy, Washington DC, USA, Please state any competing interests or state ‘None declared’: None declared, Please leave your comments for the authors below

Comments: “I enjoyed reading this paper titled “Characterizing the costs of the Global Polio Laboratory Network: A survey-based analysis”. It’s a unique and highly interesting study. I commend the authors for undertaking it. The analysis appears to be well done and the manuscript is nicely written. Major comments 1. On page 4, please you add a little more background on the GPLN for the uninformed reader? When was it established and how many samples are examined every year etc.? Also, a Table of country names and number of labs in each, or a color-coded world map of the labs will help very much. Do the labs work solely within the host country, or are samples transported across borders if needed?”

Response: Thank you very much for your comments. We edited the text to provide more context about the GPLN and included a list of the laboratories that responded by WHO region, laboratory type, and country to the appendix.

Comments: “2. If it’s not too much work, please adjust all estimates to 2017 or 2018 \$. Often estimates are reported in the media (or interpreted by readers) as from the same year as the publication of the paper.”

Response: The inflation factors for 2018 are not yet available since it is still 2018. The difference between 2017 and 2016 dollars are minimal (2%) and the data we collected are for 2016, so we think it is better to keep the reported costs in 2016 dollars.

Comments: “3. Page 6, lines 156-158: Please can you explain the rationale for these \$20 and \$400 thresholds? On what basis were these chosen? It is important to know the full details as this affects 59 and 25 labs, as mentioned in line 163. That’s close to half the sample. ”

Response: We selected these thresholds based on information collected and the judgment of subject matter experts. Some of the responses we received clearly indicated misinterpretation of our question and led us to address this as described in the methods. Therefore, we felt strongly that a correction was necessary for conspicuously low reported costs for consumables. However, it does not matter much where exactly we set the threshold. For example, changing the first threshold from \$20 to \$5, and/or the second threshold from \$400 to \$200 resulted in a difference of less than \$15,000 on the total consumable and shared consumable supply costs of almost \$4 million.

Comments: “4. Page 8: Before delving into a regression analysis to predict the missing costs of nonresponding labs, it will be first helpful to know whether the non-response was systematic. It will help if you could show the differences in the characteristics of the non-responding labs from the average of other labs in the country or region. A simple summary stats table of the variables obtained from GPLN management system should work, with t-test of differences for each variable across responding and non-responding labs.”

Response: We did not see any systematic bias in responses, and since we received responses from nearly 90% of the labs surveyed, we did not have any concerns about bias. We added some text to indicate this.

Comments: “5. The Other Findings subsection requires rewriting. There is a lot of information crammed in it, without proper organization. Please consider dividing into more subsections. Also, the Results section of the paper should succinctly present the findings, and not try to explain them or compare with previous estimates.”

Response: Thank you. We significantly revised these sections.

Comments: “6. General comments: Please divide text into more paragraphs throughout the paper. For example, pages 10 and 12 are one entire paragraph each. Much of the text is very hard to follow. There is a lot of great data in the paper – but you need better presentation. Please consider moving some results to the appendix (along with their discussion, e.g. the whole Other Findings subsection). The paper is very heavy in its current form.”

Response: Thank you. We revised the writing accordingly and moved more text to the appendix.

Comments: “7. The Discussion section needs a little more balance. The focus is heavily on sustained external funding. Considering that the study is funded by CDC, a key GPEI partner, with authors who are closely involved in GPEI, this may seem to be a little self-serving. I am not an expert on international polio policy, but I would expect that it may be natural to advocate that nations increase their GPEI funding and eventually become self-reliant. If you don't recommend it or if the nations are not ready (again, I am not an expert), please add some discussion.

Response: Thank you, we edited the tone (see also comments from reviewer 3).

Comments: “Minor comments

1. Abstract line 35 and elsewhere: It will be better to reword “polio-supported staff”. Polio-supported sounds a little strange.
2. Abstract line 39-43: Is there any specific reason you are advocating in favor of continued international funding and not for the countries to increase their government expenditure? I think that the policy advocacy is not fully balanced.
3. Page 3, line 77: Please write the full form of AFP. It is used here for the first time.
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5. Page 5, line 112: Please define ES. First use in the main text.
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7. Methods section: Please divide the text into more paragraphs for ease of reading Especially on pages 6 and 7.
8. Page 7, lines 178-195: The algorithm as written in text is hard to follow. Please consider using equations or some form of algebraic notations for clarity.
9. Page 10, line 272: Please define “concentration-only”.

Response: Thank you, we addressed all of these.

Reviewer: 3

Reviewer Name: Fabian Alvarez, Institution and Country: Sanofi Pasteur, France, Please state any competing interests or state ‘None declared’: FA is employee of Sanofi Pasteur, a polio vaccines manufacturer. Please leave your comments for the authors below

Comments: “The authors objective is to “highlight both the importance of contributions that countries make to the GPLN and the need to sustain external funding to support laboratories worldwide in their

surveillance for polioviruses and other diseases". I believe that they successfully attain their objective. The authors are certainly among the most influential researchers on polio modeling (broad definition of modeling), with tens of papers published around the polio eradication. The current manuscript is an update of a similar analysis published in 2003. As usual, the paper is well written, with clear objectives, methods, and outcomes, and tackles a crucial problem, funding of GPLN in the close to- and post-eradication ages."

Response: Thank you very much for your comments and recognition of our contributions.

Comments: "However, I have a concern regarding the "communication mood" of this manuscript for which I feel is closer to a technical report than to a scientific communication with the above mentioned objective."

Response: Thank you, we edited the text to make the writing feel less like a technical report. Specifically, we moved some methodological details and results to the appendix and long paragraphs into more easily digestible pieces.

Comments: "The results are so deeply described that the key messages may be drowned by the excess of details on how each estimation/extrapolation has been performed. To illustrate my point I mention a couple of examples (I could mention more but "communication mood" is subjective:

- the "one concentration laboratory that responded to the survey" does not have any impact on the global picture (as mentioned by the authors), but its contribution is depicted for each topic. I would prefer to forget about and exclude from the whole analysis to simplify the reading and the resulting messages
- lines 328-352 provides a lot of numbers but it's difficult for the reader to understand which is the message behind"

Response: We moved some of the details to a technical appendix to address this issue. We appreciate that while some readers may want the more technical details, not all will appreciate having them in the main text. We believe that the edits improved the readability of the paper.

Comments: "I would then encourage the authors to simplify the Results section and to illustrate (visually) their messages in order to reach a larger audience:

- simplify/shorten explanations in the Results section
 - merge Figs 2 and 3 which are pretty similar (2a and 2b could be an option, but merging both would be better)
 - provide a figure with a diagram representing of the different laboratories capabilities and funding sources
 - provide a world map accounting for the relative investments on AFP, ES and risks related to polio
- In any case, there is no doubt that this manuscript is an important contribution to the objective of sustaining the funding over the next years in order to succeed the polio eradication"

Response: Thank you, we addressed all of these, except for the world map showing AFP and ES investments and risks. Characterization of risks is beyond the scope of this analysis and the data are not clear-cut enough to map relative AFP and ES investments globally (e.g., it would take multiple paragraphs to describe things like how we handled laboratories that serve multiple geographies, some of which do AFP and ES and others only AFP). We added more information about the GPLN to the text and the list of responding laboratories in the appendix.

Comments: "Minor comments

- line 63: can be updated to mid 2018
- line 77: AFP not defined before (in fact defined line 88)

- line 88 (or 77): could be helpful for naïve readers to mention that AFP could be engendered by other causes than polio.
- line 112: ES not mentioned before (just in the abstract)
- line 133: is geographical area correlated at some point with the corresponding population pool? (even if it does not impact absolute costs it might impact the "cost-effectiveness" of the laboratory
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- lines 304:306: I couldn't understand the reason for "only a fraction... ". Could you please improve your rationale for this?
- page 28, Fig. 4 : I would add something in the legend to make explicit that numbers in parenthesis are response rates, e.g (Resp. rate=). Even if explained in legend it's somewhat disturbing to see different % in the pie and in the legend."

Response: Thank you, we addressed all of these. Assessing cost-effectiveness is beyond the scope of this cost analysis, but we recognized cost-effectiveness analysis as a possible future use of the data in the discussion.

VERSION 2 – REVIEW

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| REVIEWER | Arindam Nandi Center for Disease Dynamics, Economics & Policy, USA |
| REVIEW RETURNED | 17-Sep-2018 |
| GENERAL COMMENTS | Thank you for addressing all my comments. |