Reviewer’s report

Title: The cost determinants of routine infant immunization services: a meta-regression analysis of six country studies

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Reviewer: Carol Levin

Reviewer’s report:

Thanks for the opportunity to review this manuscript. The authors use an econometric approach that I am not familiar with, and so my comments are related to better understanding what the authors did and how to interpret the tables, etc. It would be useful for the authors to provide more guidance in the paper for this, if possible.

Abstract

1. Suggest reviewing and revising the conclusion. This paper uses a sophisticated statistical method to estimate cost functions. Yet the conclusion to the abstract isn't really highlighting the paper's results. Rather the conclusion that cost estimates are higher than historical values, could be deduced from earlier papers from the EPIC study. Furthermore, the analysis of determinants does not explicitly include a price variable on the RHS, or an explicit measure of an expanded vaccine schedule—so the conclusion isn't directly tied to the results (albeit there is number of doses on RHS—so yes, more doses delivered). In addition, language such as 'average costs were tightly linked to service volume' is vague. It would be great to focus on how these methods and findings can advance our understanding of immunization costs and how this information can be used to guide program and policy in the future.

Methods

1. Page 5 and Table S3—methods indicates data collected on above site costs, but then Table S3 indicates that these higher level program support costs are omitted from the Total Cost estimate. Authors should explain why these are omitted under section 2.3.

2. Authors should reference again the other EPIC papers where these data are better explained (references 8-11).

3. Authors should explicitly indicate which vaccines and target populations are included in the total cost estimates in the body of the paper. Is it all the vaccines listed in Table S1 or a subset of the vaccines for children 0-12 months? Is TT for pregnant women included? Do the total costs reflect different vaccine schedules across countries? This information is critical for sections 2.4, 2.5 and 2.6
4. If different vaccine schedules influence total costs across countries, is it necessary to include an indicator of the vaccine schedule to capture economies of scope resulting from incorporation of vaccines for children older than 0 to 12 months, and vaccines for adults, etc?

a. In the discussion, the authors note that the expanded vaccine schedules contribute to inter-country differences—not clear to me, why there is no RHS variable to account for this?

5. Section 2.6 Regression analysis—overall I think the authors have to do a better job explaining the implications of using a Bayesian approach in this paper, as it affects how the tables are presented and interpreted compared to standard parametric statistics and Bayesian approaches.

6. Suggest that authors clearly define the dependent variable as total cost on page 7, line 28, before describing explanatory variables (this should have been described fully in section 2.3—taking note of point 3 above). Just to make sure that reader is aware reference to cost means 'Total cost' to distinguish from presentation of unit costs.

7. Did author check correlation coefficients for RHS variables? Seems likely that some are highly correlated with one another. No mention of multicollinearity of RHS variables in discussion.

8. Par 1, page 10—since I'm not familiar wit the statistical approach of WAIC, it was very difficult for me to evaluate the results.

a. I would say in this section to first provide the 5 models and provide the reader with a bit more rationale to why these 5 models.

b. Then also explain better using first differences using results from 2 of the 5 model specifications.

c. I'm not familiar with the output elasticity definition. Page 10, line 17 "We calculated output elasticity as the percentage increase in service volume for a 1% increase in costs, "-shouldn't the output elasticity be a 1% change in output results in an x percent increase in total costs? Maybe this has to do with the Bayesian specification.

9. I have not see sensitivity analysis referred to in econometrics—typically this is used in economic evaluation literature, but this doesn't seem to fit here—the authors aren't testing uncertainty in a parameter estimate, rather isn't the sensitivity analysis just alternative regression specifications?

a. Page 10, line 46—should that read, "We anticipated that Total costs of service delivery would be increasing at higher coverage levels." That is total costs, not unit costs?

10. Table 3—what are the figures in parenthesis? Are they standard errors?
11.  The foot note to table 3 would be better included in the methods section—need to explain how to evaluate goodness of fit, and why there are no indicators of significance for Bayesian regression estimates.

12.  Page 17—Par 1, lines 12-24—this needs to be explained much more clearly and walk the reader through what the output elasticity means (give example for one country—i.e. a 1 % increase in x % results in an ? % in Y…)

a.  Also, help reader get from output elasticity to percentage increases in unit costs shown on row 18/19.  Not clear to me how this was calculated.

13.  Section 3.3, clearly indicate that looking at these predictors on total costs, not unit costs.

a.  Can authors use clear language to explain the 'dedication index'.  i.e. say an increase in the percent of time staff worked on immunization was associated with ….  

14.  Section 3.4  page 18, line 58/59—I wonder if including log catchment population in main regression is stronger than including hospital RHS variable—seems more intuitive that this would increase total costs.

15.  Did authors consider using variables such as frequency of stock-outs or facility wastage rates for a key expensive vaccine for a quality measure?

16.  Section 4.  Discussion—Appreciate that the authors note the different estimates from previous EPIC country studies (reference 7).  Very interesting that for three countries, estimates were very similar, while for Moldova, Uganda and Zambia, they were quite a bit different.  Would be really useful to readers to unpack this more other than just attributing to data cleaning and refinement to cost and outcomes data.  Was it measurement error?  Or methodological differences?  Or some combination?

17.  Page 19—Par 3 is the first time authors refer to 'statistically significant' relationships'.  This terminology was noticeably missing in results section, and my understanding is that using Bayesian prevents assessing statistical significance.  Suggest rewording to be consistent with results section and method.

18.  I would appreciate a discussion on advantages/disadvantages of the choice of functional form/method—since using this Bayesian approach seems new for the health economics literature.  If not, then perhaps make that clearer in methods section.  Also, would appreciate a section on caveats or limitations that includes discussion of possible multicolinearity of RHS variables and omitted variables—that is things that are truly hard to measure that likely influence total costs and estimates.

Minor
1. Page 5, line 29/30—suggest referring to 'above site costs'—this is a recent focus of global health costing, so great that these data include 'above site costs'.

2. Table S3—Should the definition refer to children 0-12 months, rather than 0-12 years? A lot of vaccines in that schedule for adults (pregnant women) and older kids.

3. Page 7—operating environment is a convenient use of words, but I don't see any benefit for lumping, geographic setting, ANC coverage and access to health care using one consolidated term. It isn't intuitive, where the individual variables do make sense when referred to on their own.

4. Page 11, make sure to refer to USD

5. Page 18, what does 'top-coded estimate' of DTP3 coverage mean?

6. Page 18—authors refer to 'statistically significant positive relationship'—did they want to use consistent terminology in previous section 'statistically discernable positive relationship'?

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

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