Reviewer’s report

Title: Cost-Effectiveness of Increasing Vaccination in High-Risk Adults Aged 18-64 Years: A Model-Based Decision Analysis

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Reviewer: Litjen (L.J) Tan

Reviewer's report:

This is a nicely written manuscript detailing the cost effectiveness of implementing the authors' 4 Pillars program in adults 19-64 years of age with chronic condition predisposing them to increased risk of complication from adult VPDs. The authors restricted their analysis to ACIP-recommended vaccines.

I find the authors' choice to use a Delphi panel analysis to assign a 0% percent effectiveness to PPSV protection against NBP interesting when they used literature to assign VE for the other vaccines that they looked at. It is clear that while controversy exists, several publications assign effectiveness to PPSV with respect to NBP. I refer to a more recent review by Fedson in 2015 (Human Vaccines & Immunotherapeutics 10:5, 1322-1330), as well as the 2013 Cochrane review from Moberly et al. This will likely improve the cost effectiveness of the program while complicating the decision tree by adding the difficulty of having to consider a single dose of PPSV vaccine separately. This should be addressed in the manuscript.

While I believe that the impact of the 4 Pillars program is substantial, I also believe that there will be challenges to the complete implementation of all four components for many facilities. Indeed, many report that the immunization champion, followed by system-based changes such as standing orders provide the best yield. It would be useful to see a breakdown of the cost and the effectiveness of each component of the 4 Pillars program. Many facilities may indeed choose to simply implement vaccination champions if that proves to yield the best cost effectiveness. If that is not possible, I think some discussion on this is necessary. More widespread implementation of the 4 Pillars may be facilitated if we can understand whether all 4 components need to be put into practice simultaneously.

How are opportunity and indirect costs factored in? For example, costs associated with maintaining a IZ champion? Is that person assuming more responsibilities or being compensated for their work? Costs of maintaining and updating software for office-based systems, the costs of patient outreach including reminder-recall. If these costs and others like them are not considered, that should be addressed within the discussion, since that would increase the authors' cost of implementation of $1.78/eligible patient, which seems low to this reviewer.
I wonder why the authors did not measure baseline rates from non-intervention facilities from when trial started and also two years later, to match with intervention facilities? It appears to me that even in non-intervention facilities, vaccination rates can still increase due to external pressure, such as increased education on adult VPDs in adult with chronic illnesses? This way that possibility can be addressed.

While I believe that much of this manuscript addresses specifically the 4 Pillars program, and questions do arise as to the ability to generalize the results to other similar programs, I think that there are important components of cost that are discussed here that are worthy of publication. Additionally, if the authors are able to break apart the cost of each of the 4 "pillars," that is, improving access, increasing patient recall/outreach, office-based systems to improve operationalizing vaccinations, and establishing an immunization champion, the implication of the paper will be more extensive and valuable.

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

Yes

**Does the work include the necessary controls?**
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Yes

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Yes

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I am able to assess the statistics

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