Reviewer’s report

Title: Public health value of vaccines beyond efficacy: methods, measures and outcomes

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Reviewer: Eric Weintraub

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Overall I thought it was a very well written manuscript that has an interesting take on how to efficacy/effectiveness pre- and post-licensure studies.

A few minor comments, the paper could be shortened a bit, but overall its a valuable read.

Page 4, line 8 - I think Figure 1 needs inclusion of vaccine safety in the value chain.

Page 7, line 8 - I think its also worth including language on why it is important to repeat effectiveness and safety analysis in particular with infant vaccines, where every year you have a new birth cohort and various changes in the epidemiology of the disease, outbreaks. In addition, vaccination patterns are greatly different than what is completed in pre-licensure trials, there are so many difference vaccination patterns, from delayers to refusers, and thousands of different vaccination combinations of simultaneous vaccinations that need to be accounted for or adjusted for when performing safety and effectiveness studies. Most Post licensure safety studies reassure the safety of our current vaccination schedules and in many cases, while observational studies vs randomized clinical trials add enormous value to the profile of a vaccine because the study was completed on hundreds of thousands of individuals vs just 35,000 in each arm.

Page 7, line 42 - many are observational also because its much cheaper vs a typical randomized trial. Even in the US, there is not enough resources to conduct huge randomized trails post-licensure trials on all newly licensed vaccines. The money just isn't there for these types of studies.

Page 9, line 17, the same concept is true for Vaccine safety, we often taken the inverse of the Risk difference or Attributable risk and look at the number needed to harm - Ie for every 10,000 vaccinated babies, we would expect to see 1 additional seizure case for MMRV vs MMR (just an example of language, not the true number)

Page 11, 35 - with regards to case definition, it is always important to have different case definition, there is a case definition for a physician diagnosis and identifying a potential case in real time, then there is a data case definition, which often can be quite different and require a different level of detail and specificity.

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

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Yes

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Yes

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