1. Overview: what kind of article is this?
   a. Research Article
      i. Meta-analysis
      ii. Cross-sectional
      iii. Longitudinal

      This is a longitudinal study.

b. Review – This was a longitudinal study done on patients who were never vaccinated with the influenza vaccine before 2009. They were vaccinated in 2010/2011 for the first time and then, yearly after that till 2014.Serum Antibody responses (measured by hemagglutinin inhibition) and/or viral neutralization assays, along with Influenza virus-specific binding activity, HA-specific avidity of Plasmablast derived polyclonal antibodies and Antigen secreting cell numbers were all quantified, charted and reported between 2010-2014. These parameters, all of which indicative of a response to the flu vaccine were reportedly decreased after repeated annual vaccination, even with changes in the seasonal vaccine components during the study.

c. What were the major findings?

There was a decreased B cell response to annual vaccination with seasonal trivalent influenza vaccination

2. Abstract
   a. Does the abstract accurately summarize the article?

      Yes

3. Introduction
   a. Is the review of relevant literature prepared adequately and is it properly sourced?

      They have a sufficient number of articles in their introduction-21 to be exact. However, articles 13,17,20, and 21 are by at least one of the authors on this paper. They are citing themselves too heavily in a widely studied field.

   b. Is the research question clear and does it respond to the gap in the literature?

      The question is implied, but needs to be stated more clearly.

4. Methods
   a. Is the sampling strategy reasonable and sound?

No, we have demographic information on participants, but not information about how they were recruited, compensated, etc. Also, 23 people is not a sufficient sample size. Plus, the

age group (18-30 years old) is not representative of the populations most at risk (infants and older adults). The authors should consider sampling a wider age range since immune function is age dependent.

b. Is the statistical analytic plan rigorous and sound?

   The authors used regression which seems appropriate given that they were measuring multiple variables against each other. However, they made no mention of the power of their study. In the discussion they say they have insufficient power, but they fail to address this in any way.

   We are unable to assess the appropriateness of the Freeman-Halton exact test and would suggest further statistical oversight.

5. Results

a. Are the results presented clearly and comprehensively

   Yes, the results were presented clearly with an adequate number of graphs complementing the written material.

b. Do the results cohere to the research question.

   Yes, the results cohere to the research question.

c. Do the results presented cohere to the tables and figures?

   The tables and figures cohere to the research question, statistically significant results, however, are only seen when the results from 2010/2011 are compared individually to 2012,2013 and 2014.

   Graphs comparing 2012 to 2013 and 2013 to 2014 do not show any statistical significance.

d.. Are the tables and figures clear and precise? Do they respond to the research question?

   The tables are clear and precise, although not all results from the graphs are statistically significant.

6.Discussion/Conclusion

a. Does the article add to existing literature?
   No. There are studies performed on the same topic which have similar results. This study confirms information that has already been established.

b. Do the discussion points appropriately contextualize the findings?

Yes, the discussion covers the topics presented in the article along with its limitations. Further research recommendations are also presented.

C. Are the implications for public health presented beyond “future research is needed”

The major implication of the article was to limit the number of flu shots to just 2 over the course of a persons lifetime instead of taking one every year.

c. What is the overall recommendation for this manuscript?
   i. Reject