Reviewer’s report

**Title:** How useful is a history of rubella vaccination for determination of disease susceptibility? A cross-sectional study

**Version:** 2 **Date:** 1 August 2012

**Reviewer:** Wilhelmina Ruijs

Reviewer’s report:

The authors assessed the test characteristics of a history of rubella vaccination in order to offer women who are susceptible to rubella post partum vaccination. The test characteristics are correctly described, however in the evaluation of the test the context is missing. The manuscript needs essential revisions before publication.

Major essential revisions:

**Abstract:**

1. The conclusion should be adapted according to the comments below.
   The cost constraint mentioned is the background is not addressed in the conclusion.

**Main Text:**

**Introduction:**
In the Introduction essential information is missing:

2. What is the extent of the problem?
   - What is the incidence of CRS in Malaysia nowadays?

3. At the end of the first paragraph it is stated that “To prevent CRS women need to be vaccinated to reduce their susceptibility”. However, women can also acquire natural immunity (by infection in childhood) that protects against CRS.
This should be mentioned in the Introduction, because it also explains the high seroprevalence of rubella IgG in unvaccinated women. Moreover it should be mentioned that rubella in childhood in about 50% of the cases goes without symptoms, thus women can be protected without knowing this.

4. When was rubella vaccination introduced in Malaysia, and on what scale?
   - In the Introduction is stated that the rubella vaccination program was started in 1988, while in the Discussion is stated that Malaysia has implemented a vaccination program since 2002. Please clarify.
   - What is the uptake of rubella/MMR vaccination in Malaysia?
   - Is rubella still prevalent among children?

Methods:

Statistical analysis:

5. The aim of the “test” is to correctly identify women who are susceptible to rubella.

It is confusing that in the text a positive test is a negative history of vaccination. For clarity I would suggest that sensitivity is defined as the percentage of all susceptible women that indeed report not to be vaccinated. Specificity is then defined as the percentage of all protected women that indeed report to be vaccinated. Positive predictive value of the test is the chance that a woman who reports not to be vaccinated is susceptible to rubella.

Results:

6. The results could be presented more clearly:

The majority of the women (66.6%) had a positive vaccination history. Of these women with a positive vaccination history 92.2% were immune.

A third (33.4%) of the women had a negative vaccination history, nevertheless 81.4% of them were immune to rubella.

(Followed by sensitivity, specificity and predictive value of the test)

Discussion:

7. In the evaluation of the test characteristics the context of the application of the “test” is missed. The aim of the test is to identify women who are susceptible to rubella in order to offer them vaccination to prevent rubella in possible future pregnancies. For this purpose the sensitivity is the most important test characteristic.

The sensitivity of the test is 54%, this means that almost half of the susceptible women are missed and not protected against rubella. On the other hand, compared to no testing at all, half of the susceptible women are identified.

The specificity of the test is 69%, however, it is no real problem that woman turn out to be protected while they report not to be vaccinated.
The predictive value of the test is only 19%, but again it is no real problem that women turn out to be protected while they report not to be vaccinated.

Serological testing—as the gold standard—is of course superior in correctly identifying women who are susceptible to rubella, however this test is expensive compared to asking about the vaccination history. A cost-utility analysis is needed to determine which test is preferable from a public health point of view: a history of vaccination “test” or a serological test.

Minor essential revisions:

Main Text:

Introduction:
8. In public funded hospitals pregnant women are routinely asked if they are vaccinated for rubella. What is the policy for unvaccinated women?
Are they simply vaccinated after delivery, or are they tested for rubella IgG?

9. “Exposure to rubella vaccine / vaccination” can be shortened to “rubella vaccination”.

10. The last two sentences “Thus it would be….rubella susceptibility” can be shortened: “The aim of this study is…”

Methods:
11. “This was a cross-sectional study carried out” should be “A cross-sectional study was carried out”

12. Check of reported vaccination status:
- Did you check the reported vaccination status, e.g. in a vaccination register or by asking for a vaccination card?
- Did you check if the reported vaccination status was according to age? As you state that rubella vaccination was introduced in 1988 for school girls (of what age?) it seems unlikely that older women are vaccinated.

Results:
13. The median age of the respondents is more informative than the mean age, because different age groups were offered a different vaccination program.

14. “None of them had a previous history of rubella infection” is misleading, because according to the additional file only documented rubella infections were registered.

Discussion:
15. In the second paragraph the first part of the first sentence (A total of
18.6%......had unknown vaccination status and) should be deleted as these women are correctly identified by using vaccination history as test.

Discretionary revisions:

Main Text:

Methods:

16. It would be interesting to compare the “test” characteristics in various age groups e.g. women born before and after introduction of vaccination

Discussion:

17. “7.8% of the vaccinated women were found to have low antibody titers and are considered not to be protected.” In recent literature it is suggested that the screening cut-off level for rubella IgG needs to be adapted to an immunized antenatal population. See Byrne et al. Seroprevalence of low rubella IgG antibody level among antenatal women in England tested by NHS Blood and Transplant: 2004-2009. Is rubella susceptibility increasing? Vaccine 2011.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have no competing interests.