Reviewer's report

Title: Residual risk of transfusion-transmitted infection with human immunodeficiency virus, hepatitis C virus, and hepatitis B virus in Korea from 2000 through 2010

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Reviewer: Sheila O'brien

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This paper presents current residual risk estimates for HIV, HCV and HBV in the Korean blood supply. It is important for residual risk estimates to be published so that physicians in Korea can discuss the risks of transfusion with their patients, and as a basis for policy decision both in Korea and in countries within the region that may wish to compare their own estimates. There are several important areas of revision that the authors should address in order to maximize the value of their work for these purposes.

Major Compulsory Revisions

1. Confidence intervals for the risk estimates are essential to be able to compare between time periods and to be able to compare the estimates with those of other blood programs. I suggest that 95% confidence intervals be provided for the incidence density and for the window period estimates, and that the confidence interval for the residual risk estimate consider both of these.

2. P-values should be included when making comparisons between time periods.

Minor Essential Revisions

1. The window period estimates require references. The window period for HCV NAT is very long and should be similar to that of HIV unless you are using a different mini-pool size. If it is truly 23 days, some justification should be provided.

2. Once NAT was implemented the window period for NAT should be used in the residual risk estimate. It is not clear if this was done and needs to be stated clearly in the methods. However, since NAT was not used until 2005, the window period for HCV at least should be that of the EIA for the first two time periods (2000-2001 and 2002-2003). This means that some of the reduction in residual risk for that marker was due to the change in window period with the new assay. This should be stated clearly in the discussion.

3. How did the authors handle the 2004-2005 estimate? For half of the time NAT was used (with a shorter window period). They should state which window period they used, and mention in the discussion that this transition period may be an under-estimate of the true risk (if the NAT window period was used) or an over-estimate (if the EIA widow period was used).
4. How many HIV and HCV NAT yield donations were identified per year (NAT positive but antibody negative)? Many countries that implemented NAT found that the NAT yield was very low, in fact so low that they continue to use the method of Schreiber even though it may over-estimate the incidence density. It is very important to readers and policy makers to be clear as to the true yield of NAT, and of course if it is low it would also explain why the NAT yield method was not used.

5. There may be some false positive donations included in the HBV incidence density estimates. I suggest that the authors examine their data based on the sample to cutoff ratio. If they have HBV NAT supplementary testing (which I suspect they do not) it would be ideal, but nevertheless the issue of false positivity can be addressed by re-analysing the data using only those samples that had a s/c ratio above a certain level. At their discretion, they could report both estimates. See the paper by Zou (Transfusion 2009;49:1609-20).

6. How was the incidence density in first time donors calculated?

7. The odds ratios in the abstract are better stated as “The odds ratios for HCV and HBV positivity in first time donors compared to repeat donors were 11.8 and 19.6, respectively”.

Discretionary Revisions

1. The assays have changed several times over the years that data were analysed. It would be very helpful to readers if the authors could comment on what effect this may have had on their estimates. With NAT there was definitively a reduction in window period, but is there any evidence that the sensitivity of the other assays changed?

2. Should consider mentioning that residual risk estimates are used by physicians to counsel their patients about the risks of transfusion.

3. Should provide more details of testing in the methods, especially the pool size used for NAT.

4. The lack of difference in HIV rates between first time and repeat donors may also be because the risk questioning does not capture the risk. For example if risk is more in the heterosexual population, it can be very difficult to capture with screening questions.

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

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests