Reviewer’s report

Title: Screening of post-mortem tissue donors for Coxiella burnetii infection after large outbreaks of Q fever in The Netherlands.

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Reviewer: Wim van der Hoek

Reviewer’s report:

The Q fever epidemic in the Netherlands has been described extensively in a large number of publications. The present paper focuses on screening of tissue donors, a topic that has not been dealt with before and that was listed as of public health importance by the Health Council of the Netherlands and by the European Centre for Diseases Prevention and Control. This is therefore a relevant addition to the existing knowledge base.

Major Compulsory Revisions:

1. The main conclusion listed in the abstract is that the used assays are sufficiently specific for use on post-mortem samples. This seems difficult to reconcile with the main text under ‘Serological testing’ where serious problems with false-positivity are described.

2. One would expect a statement in the abstract about the sensitivity of the assays used, as high sensitivity of the screening test would be important to avoid harm to recipients of tissue. This bears on the sensitivity of the EIA. It has been shown that sensitivity of the EIA is good for diagnosis of acute Q fever but much lower than IFA in seroprevalence surveys (Blaauw et al. 2011 in Epidemiol Infect). The authors argue in the discussion section of the paper that low sensitivity is not a major problem, which seems reasonable in the case of tissue donation, but they also claim to provide “the first estimate of the general seroprevalence of antibodies against Coxiella of 3.0% after the recent outbreaks of Q fever in The Netherlands”. In order to arrive at a reliable estimate of seroprevalence, the authors should have tested a random sample of EIA negative sera in order to be able to correct for the low sensitivity of EIA. This was the procedure used in the study that the authors refer to for comparison (Schimmer et al. 2012). In the study by Schimmer et al, the corrected prevalence was 2.4% instead of the 1.5% based on EIA only. As the 3% seroprevalence is likely to be an underestimate of the real seroprevalence, I would suggest that the authors do not list this as their major finding under ‘Conclusions’ on page 13 and mention the limitations of the EIA-based estimate.

3. The paper is not clear on the role that donor characteristics and Q fever incidence should play in a screening algorithm. The authors could expand the discussion section with their opinion on (1) the general need for screening of tissue donors after an outbreak; (2) how long such screening should continue; (3) should screening be implemented in the entire country or only in the high
incidence / outbreak area? There will be no definite answers but if the authors feel that there is insufficient evidence for a complete screening algorithm, they should say so.

Minor Essential Revisions:
1. Page 3: Airborne transmission from INFECTED goats and sheep
2. Page 3: culling of PREGNANT goats at infected farms
3. Page 4: Give the reference to the report of the Health Council of the Netherlands
4. Page 7-8: What is the origin of the (1) Q fever incidence data; (2) bulk tank milk positive farms; (3) farms with abortion wave?
5. Page 8: the authors found a “strong correlation” between notifications and seroprevalence, but no increased prevalence among donors living within a five-kilometre radius from an infected farm. One would expect a bit more information on how ‘living within a five-kilometre radius from an infected farm’ was determined, i.e. a sentence on geographical analyses under ‘Statistics’ (maybe rephrase this to ‘Data analysis’).
6. Page 11: I do not understand the sentence “Risk assessments are hampered by limited knowledge about the magnitude of the outbreaks”. The Dutch outbreaks have been described extensively, including estimates of under ascertainment, underreporting etc.

Discretionary Revisions:
7. Page 5: a number of exclusion criteria are mentioned but from the results section it is not clear how many were excluded. What were the occupations that were considered ‘hazardous’?
8. Throughout the paper: maybe better to describe the antibodies as “IgG antibodies against phase 2 of C. burnetii”
9. Page 5: what were the criteria for EIA positivity?
10. Page 9: a reference to the Dutch Q Fever Consensus Group guidelines on diagnosis chronic Q fever, as described in the literature would be appropriate.
12. Table 1: I fail to understand this table; it gives the number of donors tested, no results of testing? If all samples were negative, why not simply report this in the main text?

Level of interest: An article of importance in its field

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.