Reviewer's report

Title: Active surveillance of Q fever in human and animal population of Cyprus

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Reviewer: Sally Cutler

Reviewer's report:

General
The authors report the acquisition of Q fever in a cohort of both villagers and their livestock followed over one year, together with a countrywide effort to identify acute cases. The study is of value as it is of paramount importance to heighten awareness of this neglected yet significant pathogen. The findings highlight the problem of subclinical seroconversion. Whether these cases will develop later complications or merely reflect exposure and possible immunity, remain open questions. Although epidemiological data is severely lacking for Q fever in many countries, this study choose to use a very low serological cutoff limit that could flaw the interpretation of the authors findings. In general a single IgG titre of 1:200 or a four-fold increase in titre would be required for serological diagnosis. Variation in titre has been reported with the use of different antigens, but the source of the diagnostic antigen was not disclosed. Was this a local strain or reference strain such as Nine Mile? If this was a reference strain, were parallel tests done with a local strain? Other criteria were also applied for diagnosis, however, details of these were not given. How was the differential diagnosis achieved?

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
The monthly follow up of seronegative villagers was presumably both clinical and serological (this needs clarification in the text), yet single point IgG titres were used rather than four-fold increases. The authors should clarify this point further.
The higher seroprevalence in humans when compared with livestock is worthy of discussion. Could this indicate another source of exposure, maybe rats or other reservoir host?
The aim of explaining the small number of acute clinical cases despite high seroprevalence is not achievable with a study design such as this. This is best deleted.
Serological and clinical case finding criteria must be detailed.
IgM results are described, but only serological tests without specification of whether these were IgG or IgM is given in the materials & methods.
Discussion is needed outlining the problems of serodiagnosis for Q fever, including poor standardisation, variation with different antigens, detection of only about a third of acute cases as seropositive and lack of harmonised testing approaches.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
The causative agent of Q fever, Coxiella burnetii, is spelt in three different ways within this manuscript!
Reference for the shell vial culture technique should be provided.
Q fever continues to be a public health problem beyond the Mediterranean.
A better and more up-to-date reference could be used to replace reference 1 for the significance of Q fever as a public health problem.
Page 5: delete "rickettsial" as C. burnetii is phylogenetically distant from the rickettsiae.
It was confusing to see "three phases" in the introduction when two phases were discussed in the abstract. The reference for phase 1 results should be included in the introduction after "reported
elsewhere” (presumably this is reference 7). What samples were used for cultivation attempts (blood, bone marrow, respiratory secretions)? Were the culture positive cases also seropositive?

Discretionary Revisions (which the author can choose to ignore)

**What next?:** Reject because scientifically unsound

**Level of interest:** An article of limited interest

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

**Statistical review:** No

**Declaration of competing interests:**

I declare that I have no competing interests.