Author’s response to reviews

Title: Farming, Q fever and public health: agricultural practices and beyond

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Author’s response to reviews:

Reviewer reports:

Reviewer #1: This is a nice review of the basic features of Coxiella burnetii, a description of ways that outbreaks have occurred, and some discussion of ways to prevent outbreaks. I have 2 comments:

1. The manuscript should be reviewed extensively for language issues. There are numerous unusual word choices and grammatical mistakes that make the manuscript a little difficult to read and understand.

The manuscript has been revised.

2. A suggestion is to expand the last section on One Health a bit more (maybe with reduction of some of the more basic information). I think readers would be more interested in details of "one health" efforts in the Netherlands and specific accomplishments. Have there been policy changes? Have farmers cooperated willingly? Have there been efforts to reduce Coxiella in the environment? Et cetera.

That is a good suggestion. We added the following paragraph to the One Health section:

The collaborative action, however, was not evident from the start of the outbreak. As Q fever abortions have only been notifiable since 2008, the exchange of information about abortion and farm data before that date were restricted by privacy legislation. This frustrated the exchange of information between the animal and human domain and hampered the identification of sources of human Q fever cases. It also became clear that the mode of action and the consequences of measures were different in the public health and animal domains. Public health control is focused on advising both public bodies and private individuals, whereas in the animal sector control measures are imposed on farms i.e. on enterprises. These enterprises have a legal status and can litigate the government for the imposed control measures. Therefore these measures have to be
risk and science based. This difference in approach between the public health and animal health domains lead to misunderstandings in the willingness to control the disease. However, during the course of the ongoing epidemic this risk-based approach failed to show the desired result. A change in approach towards the precautionary principle was needed to implement drastic measures like the culling of pregnant goats on infected farms so that the Dutch Q fever epidemic could finally be overcome.

Reviewer #2:

The authors state, that Coxiella burnetii can function as a model organisms to better understand dynamics of outbreaks/epidemics. Factors contributing in spreading of Cb are manifold from environmental conditions, farming/housing conditions, surveillance and governmental policies. Strict rules have to be implemented to register early signs and to prevent epidemics.

Minor comments:

English needs to be corrected. Some sentences are too long and hard to understand.

The manuscript has been revised.

Page 8: The authors state, that at least six animals (cattle) that have aborted should be tested. Later for small ruminants two to six animals. Please clarify, same for serological testing. The number of animals to be tested depends on the size of the herd/flok and the prevalence of Cb within the region.

We included a figure (Figure 1) to summarize the harmonized passive schemes and interpretation of results in endemic regions or countries so as proposed by Sidi-Boumedine et al., 2010.

Page 3, Line 45-46: 1 bacterium is the infective dose via the aerosolic route

It has been changed as suggested.

Line 48: Please clarify the term "assist to abortion storm".

It has been rephrased as such “it is possible to create conditions for abortion storms which increase the likelihood for human epidemics”.
Page 4, Line 4: Do you mean that after large state owned animal facilities and cooperatives for cattle and sheep were closed down, farmers switched to goat farming, which coincided with an increase in human Q fever cases? Please clarify.

It has been rephrased as such ‘In Bulgaria, a collapse of the of state-owned and cooperative cattle/sheep farms in the 1990s opened doors to the caprine business sector. This change in the agricultural sector was associated with an increased incidence of human Q fever cases’.

Page 4, Line 16: Do you mean the animals are passing through villages and small towns on a daily basis to reach the pastures? Please clarify.

It has been rephrased as such ‘goats were reared in close vicinity to farmers and their family and daily passing through villages and small towns to go pastured’

Line 33: Please clarify "high propagation of the bacteria in the environment"

It has been rephrased as such ‘In these contexts, infection with endemic and/or imported C. burnetii leaded to abortion waves and excretion of high numbers of bacteria in the environment, and ultimately dissemination to the general population.’

Line 52-56: Do you mean the receiving herd =buying herd is at high risk of an infection? Please clarify.

Yes, if the prevalence of Q fever in the country is low, trading will provide the likely risk factor for introduction of infection. In case of high prevalence, trade will have a minor contribution.

Line 60: wet or soaking wet/drenched

It has been changed.

Page 6 line 4: see above

It has been changed as suggested.
Reviewer #3:

This review about Q fever is original in the way it considers Q fever as an ideal example of the implementation of the One Health approach in the context of global change. The manuscript is well written and provides an overall analysis of the disease epidemiology, microbiology, and evolution, before discussing current surveillance systems and control options.

Main comments

I mainly have comments about the surveillance and control sections.

Regarding active surveillance, the authors made the choice to present the strategy existing in Belgium: I wonder if it would be possible/relevant to discuss different systems (input versus drawbacks, costs, ...); should an harmonized scheme be recommended, as for passive surveillance? the OIE position could perhaps be mentioned?

We decided to describe the active surveillance in Belgium and the Netherlands because it is well known to the authors and as we know so far are the only implemented active surveillance systems in use. Other active surveillance schemes are fairly or not described in the literature. This hampers the possibility to have a throughout overview on effectiveness, costs, ect ect.. No harmonized scheme is put into practice in Europe or advocated by the OIE. EFSSA has not provided suggestion either in these terms.

The paragraph presenting options to control Q fever needs some clarifications (the context of the prevention/management measures suggested is sometimes ambiguous). For instance, what is the difference between notification as “a measure to identify infected farms” and “active surveillance schemes” presented in the previous section? Why is vaccination/culling/manure management discussed for goats and not other ruminant species? Also, I am surprised that the removal of risk material (placentas, aborted foetuses) is not mentioned (although I am aware that this measure is difficult to implement in the field). Finally, should a few words be included about the daily risk of exposure of professionals (breeders, vets, etc.)? Overall, I think that it would be relevant to cite the EFSA 2010 Scientific Opinion, in which the sustainability and limitations of various control options are deeply discussed.
We understand the confusion. For that reason we generalised the text from goats to ruminants and added the hygienic measures like the removal of risk material. Examples from the Dutch Q fever outbreak are mentioned as in this outbreak all measured were implemented to control the outbreak. In our opinion the control measures as mentioned in the EFSA opinion are covered. The EFSA opinion as well as the publication derived from the opinion are in the reference list.

Minor comments

Page 3, line 11: remove coma after “C. burnetii”

It has been changed as suggested.

Page 3, lines 43-44: I suggest rephrasing the first part of the sentence (“knowing that the estimated infective dose is slightly above to 1 bacterium”) so that it becomes clearer that, although there are a few publications on this topic, knowledge about the infective dose remains sparse

It has been changed as suggested.

Page 3, line 47: add an “s” to represent (subject = exposition)

It has been changed as suggested.

Page 3, line 56: I suggest replacing this reference in French, or at least add another reference (for instance the 2010 EFSA scientific opinion?)

We included the EFSA reference as well and kept the French reference since a more up-dated outlook on recent outbreaks is included in the latter.

Page 5, line 14: I suggest specifying that the transmission routes focused here are transmission routes “to humans”; overall, I think that it would be relevant to rephrase lines 14-20 to clearly distinguish suspected/potential and well established transmission routes.

Page 5, line 16: I suggest rewording the reference to egg consumption; indeed, to my knowledge, the com1 gene of C. burnetii has been detected in eggs and mayonnaise, but human contamination through the consumption of eggs has never been reported
Page 5, line 16: references are needed to illustrate the possibilities of tick bite and human-to-human contamination, respectively.

The entire paragraph has been rephrased as such’ Transmission routes of C. burnetii to humans are various. These includes well established and effective routes such as inhalation of aerosolized bacteria spread from infected reservoirs [9] and other seldom recorded including food consumption (unpasteurized milk and derivatives[22]), tick bite [23], and human-to-human [24, 25]. C. burnetii can persist for long in the environment, resist to physical and chemical stresses, and easily dispersed due to a pseudo-sporulation process [26]. Outbreaks or cluster cases related with aerosolized transmission route are frequent and often associated with specific environmental conditions favoring the diffusion [27-32], including windy days [27-29, 32, 33], landscape [33] or artificial circumstances [30]. ‘. This reference on eggs was not included in the rephrased new sentence.

Page 5, line 18: the word “vector” seems inappropriate to me (unless I do not understand the message of the authors); would “fomite” be more suitable?

It has been changed with ‘reservoirs’.

Page 5, line 24: a reference about C. burnetii environmental persistence and its ability to sporulate would be welcome

The reference is added:


Page 5, lines 27-51: this enumeration of events for which wind was associated with Q fever human cases is a bit fastidious to read: I would suggest citing all references in an introduction sentence and then detail only 2-3 specific examples

It has been changed as suggested.

Page 5, line 55: add an “S” so that it reads “limits”

It has been changed as suggested.
Page 6, lines 10-19: because the examples cited are essentially European, I suggest referring also to studies performed in the United States about environmental persistence and spread of C. burnetii (for instance, Kersh et al. 2013 Presence and Persistence of Coxiella burnetii in the Environments of Goat Farms Associated with a Q Fever Outbreak)

It has been changed as suggested.

Page 6, line 24: is “parasitic” a relevant word here? Intra-cellular?

It has been changed as suggested.

Page 7, line 11: suggestion to refer also to the recent review from Qiu & Luo on Legionella and Coxiella effectors (Nature Reviews Microbiology)

It has been changed as suggested.

Page 7 lines 18-22: this sentence is poorly in line with the rest of the paragraph and rather ambiguous; (i) perhaps a reference is needed to better explain why the authors refer to “large-scale drug distribution or vaccination”? (ii) given the fact that C. burnetii has a broad spectrum of host species and is largely distributed, it seems unlikely to me that it will succumb in response to large scale drug distribution or vaccination: could the authors better explain their idea?

This sentence has been removed.

Page 7, line 58: add an “S” to the word “strain” (cf. all strains)

It has been changed as suggested.

Page 8, lines 2-3: why is the sentence written using a future tense?

It has been changed as suggested.
Page 8, line 13: the verb “allow” does not seem appropriate to me; I suggest rephrasing the end of the sentence

The sentence has been rephrased.

Page 8, lines 14: “harmonized schemes have” instead of “harmonized scheme has” (the plural is used in the cited publication)

It has been changed as suggested.

Page 8, lines 40-41: I suggest removing “from the same flock” because “of the affected herd” is written in the same sentence

It has been changed as suggested.

Page 8 lines 19-41: the paragraph is rather dense and a bit hard to read: perhaps a figure could help better understanding the suggested scheme?

It has been changed as suggested.

Pages 8, lines 44-58 and page 9 lines 1-12 (cf my previous comment): I wonder if it would be possible/relevant to discuss different systems and the relevance of suggesting harmonized schemes

That is an interesting point to rise. Only in general terms surveillance schemes are discussed. Not many active schemes are really implemented. As far as we know only in Belgium and the Netherlands active schemes are implemented. The EFSA report on this give guidelines for this and we based our figure 1 on this report. Further on country dependent schemes will be used to coop with specific situation. So in our opinion it is difficult to discuss and compare different systems and their relevance.

Page 8, line 8: is there any financial compensation for the compulsory measure?

It has been rephrased as such ‘Compulsory control measures (supported financially by the national authority)’.

Page 8, line 12: reference 50 is unclear in the bibliography section

It has been changed.
Pages 9, lines 29-33: could “measures to identify infected farms” be presented as the implementation of an active surveillance scheme within a limited area after the detection of an outbreak?

Yes, we specified the measures like wise.

Pages 9, lines 45-50: to my view, the sentence “in most countries, Q fever is a notifiable disease in humans as well as animals” and the discussion about the availability of diagnostic tests would better fit in the paragraph about surveillance systems.

We understand this consideration and is depending on the perspective. Also in the scientific opinion on Q fever notification and diagnostics is discussed in the control part.

Pages 9, lines 50-51: “for animals, notification of abortion is included”: this sentence is ambiguous, I suggest rephrasing

We understand the confusion; rephrased as: Notification criteria may vary per country, but notification of abortions is always one of the criteria.

Page 9 line 55 to page 10, line 9: why is this paragraph focused on goats? What could be said about vaccination/culling for other ruminant species?

We generalized this paragraph and gave examples from the Dutch Q fever outbreak as in this outbreak most of the control measures were broadly implemented.

Page 10, lines 5-9: I suggest slightly rewording this sentence because, although modelling studies are helpful to test the potential impact of diverse control strategies, they only “suggest” (rather than “indicate”) which options are likely more effective because they rely on various hypotheses and input data.

We agree with this and changed as suggested.

Page 10, line 12: add an “S” to measure (1st word)

It has been changed as suggested.
Page 10, lines 12-19: again, the paragraph is focused on goats: what would be different for sheep/cattle herds?

See next comment

Page 10, lines 48-52: and for sheep/cattle herds?

Less is known about the effectiveness of control measures on sheep farms. Vaccination is shown to be effective to prevent shedding of Cb in dairy herds shown by Guatteo et al. this is now added to the text.

Page 10, lines 55: reference 16 is quite ‘old’ (2011): any reference with more recent data about human Q fever in the Netherlands?

The mentioned ref is indeed quite old and many publications followed on Q fever in humans; however the epidemic ended in 2010 so all relevant data on acute, direct to the exposure related human Q fever cases were included in this paper.