Author's response to reviews

Title: A large community outbreak of waterborne giardiasis- delayed detection in a non-endemic urban area

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Author's response to reviews: see over
Dear Editor,

Thank you for your letter with the reviewers’ comments. The comments were very useful, and we have added some text in the manuscript to address these points. Please find below our point-by-point response to the reviewers’ comments. Our responses are presented separately for each reviewer and written in italics.

I hope this will make the manuscript clearer and ready for publication. Please do not hesitate to contact me again if there is something more that needs to be addressed.

Best wishes,

Karin Nygård

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**Reviewer 1**

**Minor Essential Revisions:**

Note: all minor concerns

- Figure 2 not Figur 2; changed
- Figure could be redone slightly—maybe risk ratio or relative risk instead of risk rate—and move RR and CI just above the last two lines; *changed to risk ratio, and headings moved*
- Under Environmental Investigations, I would not say that A is cross-connected to B—just that it is interconnected since both are potable supplies (cross-connection usually implies a connection with a possible source of contamination); *changed*
- under clinical presentation respectively) not respectively2); *changed*

**Discretionary Revisions**

Several questions came to mind when reading this. If the authors can add brief explanations, it might be helpful to readers. In the catchment areas, especially for A,
were there grazing animals and water animals (perhaps beaver or similar water animals living there?) I am not familiar with such animals in Norway, but we have lots beaver here that become infected and contaminate water supplies.

- Added a sentence about this: The catchment area is used for recreational activity, grazing of sheep and there are also some residential areas located close to the water intake. **There are no water-animals (i.e beavers) in the area.**

Controls that had travelled outside the country were excluded; were there any cases that had traveled outside the country. I presumed not but should you say something about that?

- None of the cases included in the case-control study had travelled to a high-endemic area. To avoid confusion, we have changed the sentence to: **Cases and controls that had travelled to a highly endemic country for giardiasis during the incubation period were excluded.**

I was also interested in the prescriptions for metronidazol. There was an excess of some 2500 but could you add a brief statement about the usual number (about 2000) and speculate on why these are prescribed. Is it due to cases associated with foreign travel?

- Unfortunately, indications for treatment is not included in the NorPD. We have added an explanation: **NorPD is a national health register containing information on prescriptions from pharmacies in Norway, however indications for treatment is not included in the register. Metronidazol is normally prescribed for a variety of indications such as bacterial vaginosis, gingivitis, part of the combination treatment for H. pylori, infections with Clostridium difficile and other anaerobic bacteria, amoebiasis, giardiasis, and prophylactically for colorectal surgery.**

**Reviewer 2**

**Major revisions**

1. Please can the authors be explicit about recruitment and analysis of the case control study, and discuss non-response biases. 27 cases and 54 controls were included in the matched analysis. However in Table 3 it becomes apparent that 83 cases were recruited. (i) This is a big loss to the study (ii) I can see why cases without controls were excluded but it is surprising that there are exactly 2 controls for each case. I would have expected a substantial proportion of cases to have 1 control and also to be included in the analysis. (iii) I did not see mention of the number of cases who met the case definition for the case control study nor of the number of controls approached.

- Many cases were interviewed regarding exposures where we did not pick controls. We only interviewed controls for the first 27 cases and stopped there due to the urgency of the outbreak. I have now included a sentence about this in the Methods – data analysis part: To assess risk of giardiasis associated with quantity of water consumed, we later did a group matched analysis in order to include information available from cases that were interviewed regarding exposures, but where we did not interview individually matched controls.

- Controls were telephoned after a list of randomly selected persons as described in the article, until we acquired two controls per case. Unfortunately we have not complete register of number of controls contacted, but the controls were mainly
very positive and the response rate was high. We have added a sentence: **Potential controls were contacted by telephone until we had two controls interviewed per case.**

2. A comment on the amount of water consumed from a Norwegian survey (with a reference) is now included in the discussion: In a Norwegian survey from 1997 women and men in the age-group 16-29 years drank on average 390g and 323g water/day respectively compared to 338 g and 276 g for all adult women and men respectively [11].

Cases were correctly asked about water consumption before illness but was this emphasised strongly? Could they have been reporting a high current consumption if they had been advised to drink more water during their diarrhoeal illness?

− There will always be a possibility of recall bias, however they were explicitly asked for the period before they fell ill – what they normally do – as explained in the text. It seemed more part of their lifestyle to drink a lot of water. We may actually have underestimated the total consumption, as our category stopped by >5 glasses, while some cases actually drank litres of water a day. A sentence to emphasize this is now included: Persons who drank a lot of water had a much higher risk of illness. Close to two thirds of the interviewees drank more than 5 glasses of water daily, and many reported drinking several litres daily. **To avoid recall bias they were asked explicitly for the period before falling ill, and they stated this was what they normally would drink – many mentioned this as part of dieting, healthy living or exercising.**

**Minor revisions**

The different shading of the map is not clear in black and white.

− Need to get some advice regarding the figure from the editors

In the abstract more than 90% acquired infection abroad, in the background this figure is more than 80%.

− Discrepancy on percent acquired abroad is due to the fact that for between 5-10% information on place of infection is missing. Wording in Background is changed to: More than 90% of the 300-500 annual cases with information on place of infection have been acquired abroad

In the case definition, for residence in Bergen during incubation period, please define period used for the study and whether residence was required for some or all of the time.

− Have included the timeframe used in brackets (one month). In the text we have written: who **had been** in Bergen during the incubation time for giardiasis. This is now changed to **visited or stayed**

For estimate of excess prescriptions, it would help to state (if true) that there was no seasonal variation in prescribing outside the outbreak period.

− Since the NorPD was established January 1st 2004, there is not enough data to establish possible seasonal variation. We have now added this date to the Methods section: **Since the NorPD was established January 1st 2004**, the average monthly
number of prescriptions during January 1st to August 31st 2004 was used as the baseline, ..

There are different time periods and different definitions used for different analyses. This is a bit confusing. Please could the authors check carefully e.g. water supply attack rates are Aug – Nov in text and Sept – Nov in Table.

− Changed to Aug – Nov in Table

Discretionary Revisions (which the author can choose to ignore)

Supermarket A has a high level of statistical significance in the univariate analysis. Presumably this disappears in the multivariable analysis. Is there an obvious explanation?

− We did not match on zip-codes in selection of controls. Many of the first cases were young adults living in student housing, leading to a confounding effect.

As early warning another measure might be to suggest that laboratories test for rare organisms such as Cryptosporidium and Giardia in the event of an outbreak of diarrhoeal illness that is not explained by the usual pathogens.

− That should be the routine procedure.