Author's response to reviews

Title: Waterborne microbial risk assessment: a population-based dose-response function for Giardia spp (E.M.I.R.A study)

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Author's response to reviews:

Sir,

We submit a revised version of our paper MS: 2321256508928143 "Waterborne microbial risk assessment: a population-based dose-response function for Giardia spp (E.M.I.R.A study)"

The parts that were substantially revised are underlined in yellow. We here detail how we answered the comments from the two reviewers.

Reviewer 1.
In his general comment, reviewer 1 questions the difference we found between the slope provided by the Rendtorff model and that we derived from the analysis of our epidemiological data. Indeed, figure 1 shows a great overlap between the 95% confidence intervals of the two series. But this is because we have applied a 20% abatement factor to the cysts counts before computing risk estimates after the Rendtorff model. This was not clear in our text, and we modified it accordingly (page 6 in the Methods section and page 8 in the Results section).

We also modified the abstract and the Method section, to better explain the procedure by which we compared our epidemiological data and risks estimated using the Rendtorff model.

Discussion section: to justify why the risk estimates of the Rendtorff model, not corrected by a cysts count abatement factor, are greater than the risk that we measured after our epidemiological study, we consider a series of explanations (page 10, second paragraph). Reviewer 1 suggests another very interesting explanation, with the idea that population immunity in the study population might be enhanced by the prevalence of Giardia cysts in drinking water; we added this explanation in the discussion, with appropriate recent references.

We also added missing labels on tables and figure

Reviewer 2.
Three main critiques were made by reviewer 2. Regarding recovery rate of the method we used to enumerate cysts, we reckon that the figure of 50 % comes from an assessment study conducted with another water matrix than the ones we had in the study. However, we also compared recovery values published in the literature that used the same U.S.-EPA method, allowing us to add in the text that our figure stands in the low range of the literature values (discussion, p 8). So, while false negative results are of course possible, underestimation should not be as severe as stated by reviewer 2.

The second comment deals with the statistical distribution of Giardia cysts counts over time. We had monthly water samples. We used published data to back our assumption that our samples may represent the water quality (and hence population exposure) during the week that brackets the water samples. We found no other study with short term repeated measurements than the one we had referred to (admittedly with heavy contamination, i.e. different than the water sources we had in our study, as correctly commented by reviewer 2), but several studies have been conducted on monthly or seasonal variability, showing very uneven results.

Monthly analyses for Giardia cysts were conducted in a drinking water supply in Japan that had contamination levels comparable to ours, and showed little time variability (ref 51 added in the discussion, p 9). So we added a sentence to state that the time representativity of our water samples is not fully characterised despite our repetitive sampling.

Thirdly, the difficulty to assign GI conditions to a specific pathogen is recalled by reviewer 2. We are aware of this, and this is why we underwent a complex study, both in its design, data collection and analysis. Despite this care, confounding of the associations by other pathogens (not measured or measured with imperfect microbiological analysis performance) cannot be completely ruled out. Hence, we added a
sentence to make this clearer (discussion p 9), and cited the recent 2006 papers by Robertson et al, as asked by reviewer 2. Also, we substituted the verb suggests to showed in the conclusion, in a way to acknowledge the uncertainties that remain in this quantitative risk assessment work. However, we think this does not downplay the value of our work that, for the first time as regards Giardia, provides epidemiological support to usage of dose-response parameters stemming from a clinical trial, in the task of risk assessment.