Author's response to reviews

Title: Community-level Risk Factors for Notifiable Gastrointestinal Illness in the Northwest Territories, Canada, 1991-2008

Authors:

Aliya Pardhan-Ali (apardhan@uoguelph.ca)
Jeff Wilson (jeff_wilson@novometrix.com)
Victoria L Edge (victoria_l_edge@gmail.com)
Chris Furgal (chrisfurgal@trentu.ca)
Richard Reid-Smith (rreidsmi@uoguelph.ca)
Maria Santos (maria_santos@gov.nt.ca)
Scott A McEwen (smcewen@uoguelph.ca)

Version: 2 Date: 21 December 2012

Author's response to reviews: see over
Answers to Reviewers Questions

Thank you for your feedback. I have used line numbers and yellow highlighting for revisions. Aliya

Referee 1

1. The authors should add the n value in tables 2, 3 and 4 to each variable

   APA: ok please see revised Table 2

Referee 2

1. The table 1 data is therefore community based data. Tables 2 to 4 are fine but a large table with the results (case numbers) for the three pathogens and the community risk results needs to precede these so that people can understand the results more easily. In addition Figures 2 to 4 should be put in a single table (emphasizing the three different models).

   APA: ok please see revised Table 2

2. I am not suggesting the authors re-do the study. However, the authors do need to indicate in the paper how the ascertainment bias issue is to be regarded and dealt with in this study.

   APA: please see lines 335-342

2. While I am sure some of the Giardia derives from wildlife there is a need to provide a balanced discussion in which human sources are also an issue.

   APA: Please see lines 215-234

3. The use of the term sparing effect is slightly ambiguous and another term might help reader understanding.

   APA: ok have changed it to protective effect or decreased risk

4. The two figures look a bit badly drawn and simplistic. If these are to be included then it would be useful to add a bit more explanation to the descriptions on page 26 and to re-do the figures.

   APA: ok please see revised Figures 1 and 2 and corresponding title and descriptions

6. The report shows an association (negative) with food price and Campylobacter, but also indicates that prices are higher the further north the communities are. Is the association really to do with the price or the latitude?

   APA: my mistake – it should say that prices are considerably higher in rural and remote communities not necessarily communities that are further north in NWT. Please see lines 253-256 for correction.
7. The use of the term underreporting bias is not adequately explained.

APA: Please see lines 241-245

8. There is no discussion of the giardiasis cases and moving around. Is this a function of greater exposure to natural waters or untreated drinking water?

APA: Please see lines 215-221 and 317-321

Referee 3

General Comments

1. However, the attempt to bring the two together in an ecological study, the weakest of all epidemiological studies, is fraught with potential for misinterpretation and overinterpretation. Authors may wish to reconsider this statistical approach*, which attempts to link two completely separate data sources, and instead note some interesting spatial patterns in the incidence of GIT disease, and go back to the community survey results to look for biologically plausible clues to explain observed patterns.

APA: I respectfully disagree and stand by my current approach because we are interested in examining contextual community-level factors (social, economic and other aspects of the environment - some of which genuinely operate at the population-level, directly or indirectly) and between-population differences. The literature suggests that while ecological studies do have limitations, so do other designs and we have not ignored these in our work (please see lines 327-349). Equally, ecological studies are not susceptible to certain biases that can affect associations among individuals (eg. recall bias, reverse causality). Ecological approaches have been successful in generating hypotheses about illnesses/conditions such as cancer, asthma, rhino conjunctivitis and eczema. As per your suggestion, interpretation of results should be done with care and I have made the requested changes (eg. relationship vs. statistical correlation). I have already published a paper on spatial and temporal patterns of NGI in the NWT– Please see Pardhan-Ali A, Berke O, Wilson J, et al. A spatial and temporal analysis of notifiable gastrointestinal illness in the Northwest Territories, Canada, 1991-2008. International Journal of Health Geographics 2012, 11:17

2. Overall, it feels like authors are trying too hard to tie everything back to country food consumption and zoonotic risks. There is sound microbiological and epidemiological evidence to link the 2 bacterial GIT diseases in question to consumption and handling of retail poultry, eggs, and pork (NOT wild game), and to suggest that giardiasis in people is very often of human origin – i.e. daycare outbreaks and human sewage contamination of water supplies.

APA: I examined 18 community-level variables (collected by the NWT Bureau of Statistics and were considered by the government to be most relevant to the NWT population) of which only 3 were related to traditional activities – traditional foods, hunting/fishing, and trapping. We were unbiased in our analytical approach and traditional activities only appeared in 1 of the 3 models. In the background, I am simply
stating that other studies that have looked at areas with aboriginal populations have examined social and economic variables but few studies have included traditional activity variables. I have revised the paragraph on giardiasis. Please see lines 215-234.

3. The results of this study focus on the potential risks of infectious diseases associated with country food consumption, based on tenuous statistical correlations*. That said, we cannot ignore these results – but we should be VERY careful not to overinterpret them. Phrasing throughout the paper should emphasize that these are statistical correlations NOT risk factors or “relationships”.*

APA: Please see lines 47-54, 204-214, 248-252, 325-327

4. If the study population of interest is Aboriginal, it is not clear why this study is focused in the NT, which has a relatively large non-Aboriginal population as compared to Nunavut, Nunavik, Labrador, and the northern half of most provinces in Canada.

APA: This study was part of a larger study that I conducted about NGI in the NWT for my PhD Thesis. Please see lines 58-61 where I have now specified that my research interests are about NWT rather than Aboriginal populations alone. However it is important to note that 28 out of 33 communities in the NWT have ≥85% Aboriginal population.

5. There is a lot of undefined jargon used in this paper. Authors need to ensure that terms that have a very specific meaning are well defined*. (i.e. environmental, ecological, notifiable, and even Aboriginal all have specific epidemiological and Canadian meanings that may not be accessible to a broader international audience.)

APA: ok I have provided definitions throughout the paper

Specific comments

Abstract

1. Background: Is “notifiable” universally understood?

APA: I have defined it. Please see line 33

2. Methods: be specific about the different data sources. Why were these models used, and why different models for campylobacteriosis than the other two diseases? Explain in accessible terms to a general scientific and medical audience what “Rate ratios” mean.

APA: These details have been explained in the Methods-Statistical Analyses. In my opinion, I don’t think this information is suitable for an abstract with limited word count. I have also defined rate ratios in this section. Please see lines 149-159.
3. Results: Give directions of “community level risk factors”, not just the variable name*. i.e. Higher percentage of internal mobility as well as having a health centre (vs a hospital) were associated with increased risk of giardiasis at a community level, whereas increased health expenditure per capita was associated with decreased risk of giardiasis at a community level”.

APA: ok please see lines 34-40 and 44-47

4. Conclusion: It is possible that the results regarding campylobacteriosis and traditional activities are indeed spurious, and mention should be made of the benefits of traditional activities far outweighing the risks, if they actually exist*. The conclusions about traditional knowledge, genetic adaptation, and acquired immunity come out of left field in the abstract.

APA: ok I have revised those sentences. Please see lines 47-53

Background:

1. Define “Contextual community level risk factor”.

APA: ok please see line 59

2. There seems to be a pre-existing agenda to focus in on country foods instead of looking for general risk factors from a broad array of demographic and behavioural variables*.

APA: As mentioned above, I examined 18 community-level variables (collected by the NWT Bureau of Statistics and were considered by the government to be most relevant to the NWT population) of which only 3 were related to traditional activities – traditional foods, hunting/fishing, and trapping. We were unbiased in our analytical approach and traditional activities only appeared in 1 of the 3 models. In the background, I am simply stating that other studies that have looked at areas with aboriginal populations have examined social and economic variables but few studies have included traditional activity variables.

Materials and Methods

1. Subheading “Data sources and database development” – no mention is made of databases?

APA: You are right, it was an error. “Databases” has been removed from the subheading

2. How were these 18 variables selected? Were any tests done to determine covariation/collinearity and surrogacy*?

APA: Please see lines 139-141
3. NWT communicable disease registry: was anything done with the age, gender, community, and food and water history data for individual cases? This could help address individual level risk factors.

APA: Yes, please see –


Statistical Analyses:

1. Why include variables that resulted in a change in the measure of effect by greater than or equal to 20%? (ie why this number?)

APA: The literature recommends that if we see a >20-30% difference between the crude and adjusted odds ratio/risk ratio this indicates confounding and can be controlled analytically by including the confounding variable in the model.

Results:

1. Why use a relaxed p value of greater than or equal to 0.20?

APA: If we use a stricter p-value (eg p<0.05) an important predictor/risk factor might be excluded if its effect is masked by another variable (ie the effect of the risk factor only becomes evident once a confounder is controlled) so using a liberal p-value helps prevent this problem.

Campylobacteriosis:

2. How is it possible to have two variables that individually are associated with an increased incidence of disease at the community level, and yet together lead to a decreased incidence?* Could these paradoxical results reflect a sample size issue? - for example, how many people both trap and consume country food?

APA: When there is an interaction term, the main effects of the interacting variables become obsolete. The main effects should be reported but only the interaction should be used for interpretation. I have explained this further in lines 169-176. In general, the power for estimating individual-level regression coefficients depends on the total sample size whereas the power for group-level effects depends more strongly on the number of groups.
Giardiasis:

3. It seems quite likely that health centre vs hospital is directly linked to community size (not included in the variables examined).

   APA: Since this is a community-level study, the power for group-level effects depends more strongly on the number of groups than on sample size.

Discussion:

1. “relationship” is misleading. Statistical correlation perhaps?

   APA: ok please see line 204.

2. Define “environment”.

   APA: ok please see line 212

3. In the discussion, lines are often blurred by use of terms like “raw meat” without specifying if the authors are implying retail meat or wild game*.

   APA: I have revised my discussion and the term raw meat does not appear anywhere

Campylobacter.

4. This is compatible with the results that show that high food prices (ie in remote communities) are associated with decreased risk of campylobacteriosis, but incompatible with the findings that country food consumption (which should be higher in remote communities) was associated with increased risk of campylobacteriosis. This seems contradictory.

   APA: As mentioned above, when there is an interaction term, the main effects of the interacting variables become obsolete. The main effects should be reported but only the interaction should be used for interpretation. I have explained this further in lines 169-176. Both models are giving us the same information.

5. The parabolic association of salmonellosis with core need is not explained. Why would risk increase up to 42%, then decrease with increasing proportion of households in core need past 42%?*

   APA: Please see lines 196-202 and 286-289
6. There are no rats in the NT, and insect vectors are limited as compared to Vancouver and London (references 31 and 32).

APA: I have found more suitable references. Please see references 24 and 25.

Conclusions:

1. Explain “nondifferential exposure misclassification”

APA: ok please see lines 331-332

2. Be cautious when making blanket statements about communities, especially Aboriginal communities.*

APA: Sorry I do not know which statements you are referring to – please specify.

Editorial Staff

1) Include aims of study in abstract

APA: Please see line 30-34