Author's response to reviews

Title: A descriptive study of reportable gastrointestinal illnesses in Ontario, Canada, from 2007 to 2009

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Author's response to reviews: see over
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Dear BMC Public Health,

On behalf of my co-authors, I am re-submitting the manuscript titled “A descriptive study of reportable gastrointestinal illnesses in Ontario, Canada, from 2007 to 2009”, given the manuscript number 1955675541740579, for publication in BMC Public Health.

We thank all four reviewers for taking the time to review of manuscript and provide comments. The reviewers had some opposing viewpoints on our manuscript and therefore suggested a number of contradictory revisions. It seems that, since our study encompasses a broad variety of data and findings, each of the reviewers has found “something different” in it, and consequently has decided that something else is “not” in it and should be. We have made all requested changes where possible or appropriate, otherwise providing reasons that changes were not made.

As requested by the editor in your email to us on August 10, 2012, we address not only each of the reviewer’s (compulsory and discretionary) revisions, but their overall comments as well.

**Reviewer 1: Franz Allerberger**

*Overall comments:* Typo on page 8 corrected – “cycloporiasis” corrected to “cyclosporiasis”.

*Major compulsory revisions:* The reviewer asks us to change our death definition to include a time period (i.e. died within 30 days after reporting). In Ontario, there is no standardized or mandated follow-up for each disease that requires health units to contact the case to assess their status at, for example, 30 days after diagnosis. We have added the following line in Methods on page 5 to help clarify this: “There are currently no standard follow-up forms or set timelines for initial case contact or follow-up for GI in Ontario”.

*Minor essential revisions:*

- Page 4 - abbreviation “iPHIS” explained on page 4 when it is first used: “integrated Public Health Information System”.
- We thank the reviewer for this astute observation. In order to be consistent with our disease case definitions and the other diseases in our paper, we changed “VTEC” to “VTEC-illness” throughout the entire manuscript: page 2, 3, 5, 8, 9, 10, 11, 13, in the legend of Figure 1 (page 20), in Table 1 (page 21), Table 2, (page 22), Table 3 (page 23), Table 4 (page 25), and Table 5 (page 26), and within Figure 2, and Figure 3.
Reviewer 2: Kevin Pollock

Overall comments: Since this reviewer did not provide any suggested revisions, we will respond to the issues he raised in his comments.

The reviewer stated that our findings are not novel, that the data corroborates what is already known about the epidemiology of GI in Ontario (although the most recent report describes GI epidemiology in Ontario in the year 2003), and presumably elsewhere in Canada or other developed countries. While we agree with the reviewer that the overall incidence of the diseases, as well as the age-specific distribution is somewhat similar to what has been seen in previous reports, there have been changes in the types of sources that GIs are being attributed to based on public health follow-up (e.g. increased suspicion of zoonotic transmission) compared to previous reports. Additionally, previous reports did not characterize incomplete follow-up, multiple exposures, or known/unknown source of infection by individual disease. Finally, multiple different studies publishing similar findings are required to build strength of evidence. Differences between countries may occur because of differences in health care systems.

The reviewer questioned the exclusion of cases with multiple exposures from the analysis. Cases with multiple exposures are only excluded from the “source attribution” part of our analysis, these cases are included in all other analyses. We excluded cases with multiple exposures (totalling 1.5% of the total number of cases) because we wanted to focus on cases where investigators were more confident that they identified the source of the infection. Additionally, we provide for the reader in Table 1, the proportion of cases with multiple exposures excluded listed for each disease. In order to clarify this point, we modified the title of Table 1 to: “Proportion of gastrointestinal illnesses excluded from source attribution analyses”, and added the following (in bold) on page 6 of Methods: “Cases with multiple exposures were excluded from the source attribution analyses...”

The reviewer points out that we include Salmonella serotypes and do not include serotype/strain information for any other disease, which he feels would be much more illuminating. Unfortunately, organism subtype data is not a mandatory field in the Ontario reportable disease information system (iPHIS), and is rarely reported for most diseases, except for salmonellosis. Since we are not able to add subtype information for the other diseases, we have decided to cut out completely the section on Salmonella subtypes throughout our manuscript: we deleted the line “Salmonella serotypes were reported for sporadic endemic, travel-related and outbreak-related cases separately.” from Methods on page 7, and “The most frequently reported Salmonella serotypes over the three years for endemic sporadic (non-outbreak) cases were: S. Enteritidis (24.6%, 1,010/4,107), S. Typhimurium (19.0%,
782/4,107), and S. Heidelberg (8.3%, n=342/4,107); for outbreak-related cases they were: S. Typhimurium (62.5%, 177/183), S. Infantis (7.4%, 21/183), and S. Heidelberg (6.7%, 19/183); for travel-related cases they were: S. Enteritidis (42.2%, 500/1,186), S. Typhimurium (8.5%, 101/1,186), and S. Agona (3.2%, n=38/1,186).” from Results on pages 8-9.

Finally, the reviewer states that while we mention some forms of bias [in relation to our source attribution analyses], we do not discuss investigator bias. We have modified two sentences on page 13 of the Discussion as follows (changes in bold): “Factors that likely influence this percentage include: the number of days from exposure to investigation and the associated recall bias, the investigators’ bias and knowledge of the sources as well as the transmission modes for the various pathogens, the case’s understanding or bias pertaining to their illness and its cause or source, and the effort made by the investigator. It should be recognized that with these limitations, the source is frequently unknown. Notably, the “known” sources of GI in our study are not systematically supported with information such as positive food samples or a statistical association through the use of case-control study methods, and are therefore highly susceptible to the various biases described above.”

Reviewer 3: Karin Nygard

Overall comments: While the reviewer finds our paper well-written, she thinks it is too ambitious in scope and that it should be shortened to emphasize the main interesting findings. While we agree with the reviewer that the scope of our manuscript is large, we do not think it is appropriate to cut any of the results (except for the Salmonella serotype results, see our response to Reviewer 2). Supporting this, is that two other reviewers felt the opposite (i.e. Reviewers 2 and 4), stating that they in fact wanted more analyses (e.g. organism subtypes, trends) instead of less.

Major compulsory changes: See “Overall comments” above for this reviewer.

Minor essential revisions:

- Point #1: Acronym iPHIS explained on page 4 (see Minor essential revisions for Reviewer 1)
- Point #2: The reviewer states that more information on the source attribution methods and evidence base for using it is needed.
  - We have modified a line in the Methods (page 5-6) to address the questionnaire and follow-up time information (additions/changes in bold): “There are currently no standard follow-up forms or timelines for initial case contact or follow-up for GI in Ontario; each exposure reported by a case and deemed relevant by the investigator is recorded in iPHIS. Because these exposures are assigned by public health professionals who may have additional information including food testing results and food premise investigation records, local public health authorities use this information to establish links between cases. These exposures can be used to perform source attribution, being similar to “expert elicitation” source attribution methods (Pires et al., 2009).”
  - On page 13 of the Discussion, we added the following line “While the level of evidence for this type of source attribution is considered to be low, we believe these findings are nonetheless useful in describing the exposures identified and investigated by local public health authorities.”
  - For additional changes relevant to this reviewer’s concerns, see the last point in response to Reviewer 2.
Point #3: In order to better define “travel-related” cases, on page 6 of the methods we added the following (additions in bold) “travel, if out-of-province travel was recorded in any of the exposure fields (travel information is to be entered into iPHIS only if the investigator deems it relevant, i.e. travel occurred within the incubation period)”.

Point #4: Whether or not cases are related to outbreaks is information that is also collected in iPHIS – to clarify this, we added the following (addition in bold) on page 7 of Methods: “Outbreak-related cases were those linked to a reported outbreak in iPHIS”.

Point #5: We thank the reviewer for pointing out this issue; we have altered the sentence on page 9 as follows (changes in bold): “Endemic sporadic cases that were successfully followed up by public health accounted for 44.6%...”.

Point #6: Typo (Paratyphoid Fever) in table 4 fixed.

Point #7: We agree that structure would help the reader with the Discussion, and to that end have added subheadings to the Discussion section: Incidence, Outbreaks, Demographics, Seasonality, Travel, Source Attribution and Risk Setting, and Case Reporting.

Point #8: Limitations: See added lines in Discussion outlines in Point#2 above.

Discretionary revisions:

Point #1: We agree with the reviewer that domestic is a better word than endemic, and have changed this terminology throughout the paper, all of the Tables, as well as Figures 1, 3, and 4.

Point #2: While we agree that some of the pathogens that cause the illnesses described in our paper, namely botulism and listeriosis, may not necessarily cause gastrointestinal symptoms, signs and symptoms of listeriosis may include diarrhea, nausea and vomiting; similarly, foodborne botulism cases may present with vomiting, diarrhea, constipation abdominal swelling and nausea. The main reason we wanted to include these two diseases in our study is because they are foodborne illnesses, and therefore share many of the features in common with the other GI included in the study.

Point #3: Since our study was focused on Ontario, we defined as travel-related, all cases with travel outside of Ontario. Canada is a large country, and we do not think it is appropriate to assume risk factors for all GI are the same across the country. While it is likely that some disease risk factors may be similar across Canada, risks may also be similar with other neighboring regions, namely the North-Eastern United States.

Point #4: We think that all of the tables and figures currently included are necessary to convey the results of this study to the reader. Table 1 shows novel data for Ontario as well as addresses comments by reviewer 2, Tables 2 and 3 show standard incidence and outcome information, Table 4 illustrates the differences between diseases and what is known about their sources, and Table 5 gives the results of the source attribution analysis; Figure 1 shows the inclusion/exclusion criteria for the analyses, Figure 2 shows age-specific incidence, with Figures 3 and 4 showing the seasonality in all of the various diseases.

Reviewer 4: Gordon Nichols

Discretionary revisions: Point #2: The level of detail requested by the reviewer on current and past control policies and programmes is beyond the scope of this paper. The title of the paper is “A descriptive study of reportable gastrointestinal illnesses in Ontario, Canada, from 2007 to 2009”.
Our objective was not to evaluate the effectiveness of policy or control programmes using the data we provide – this would necessarily be a very different study, one that would need to focus on specific groups of GI that would be more likely to be targeted by a specific intervention (e.g. requiring the industry to test shell eggs for *Salmonella* spp. would be expected to affect only rates of salmonellosis).

**Major compulsory revisions:**

- **Point #3:** We agree with the reviewer that a more complete analysis of temporal trends between our study years (2007-9) and previous years (1997-2003) would be very interesting. However, this is not possible with the data that we had available for this study. As a result, we compared our incidence rates and case counts to those reported in the earlier studies, however, due to differences in study design and analysis, these comparisons are limited by the information available in the various papers. A separate study on temporal trends in GI would need to be designed that would obtain data from 1997 to 2009 inclusive, and analyse all the data in the same study. The US CDC does such an analysis using laboratory data from their sentinel sites (e.g. Preliminary FoodNet Data on the Incidence of Infection with Pathogens Transmitted Commonly Through Food – 10 States, 2009. 2010. MMWR, 59(14):418-422). Note that the CDC study does not report on seasonality or perform any source attribution analyses; its main objective is to look at trends. This was not our objective.

- **Point #4:** This point is very much related to the point above: since we are not comparing our data to data in previous years (i.e. this is not a paper focused on trends over long periods of time), we feel that the current sentence on page 15 captures all that is needed for the manuscript at this point in time. Currently the sentence reads: “A full discussion of these factors is beyond the scope of this paper; however, in Ontario some of the factors included: changes in laboratory testing, changes in case definitions, and a change in the reporting system in 2005 from the Reportable Diseases Information System (RDIS) to iPHIS.” If we included comparisons across time in our analyses (i.e. where these factors would have affected the data actually in this study), then it would be very appropriate (and in fact necessary) to expand on all of these changes and how they could have influenced case reporting.

- **Point #5:** We added the following on page 5 of Methods: “Case definitions for all of these diseases are available online (Ontario Ministry of Health and Long-Term Care, 2009).”

- **Point #6:** GI caused by viruses are not reportable diseases in Ontario; only institutional GI outbreaks (often caused by viruses) are reportable. Therefore, it was not possible for us to include viruses in our analyses. This study is not a burden of illness study, we are not suggesting that the reportable GI that we describe are responsible for the greatest GI burden in Ontario. We have added the following line in the Discussion on page 11 to address this point: “It should be noted that since our study is based on reportable disease data, we could not include viruses that cause GI including the noroviruses, which are estimated to be responsible for 58% of GI caused by known pathogens in the United States, followed by nontyphoidal *Salmonella* spp. at 11% (Scallan et al., 2011).”

- **Point #7:** We agree with the reviewer that there are great differences in reporting for various pathogens, and in fact the current line in our Discussion addressing this reads: “While underreporting varies by pathogen, for every GI reported, there are an estimated 10-49 cases in the community that are not reported [13].” The differences in reporting by pathogen is more in-line with a paper on the burden of illness, such as the one done by Scallan et al (2011).

- **Point #8:** We thank the reviewer for pointing out how the data in our tables may be mis-interpreted. We have made the following changes/additions to our Discussion section (changes in bold):
o Page 14: “For the 26% of cases with a known exposure source, we identified food as the primary exposure source for 54.2% of GI reported in Ontario...”

o Page 14: “In previous Ontario studies the overall proportion of GI attributed to food (when the source was known) was higher,...”

We hope our revisions meet with your approval and look forward to your response.

Sincerely,

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