Author’s response to reviews

Title: Conventional and Molecular Epidemiology of Tuberculosis in Manitoba

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Re: BMC Infectious Diseases ID – 2059401606175084 Revised Manuscript  
Conventional and Molecular Epidemiology of Tuberculosis in Manitoba  
Kym S Blackwood, Assaad Al-Azem, Lawrence B Elliott, Earl S Hershfield and Amin M Kabani

Thank you for your comments. Please find the revised manuscript attached. We have found the suggestions very helpful in improving our manuscript and hope that our revisions are satisfactory. In response to whether the study was approved by the local ethics committee or that formal ethical review was waived, lines 92 – 98 have been clarified to indicate that patient confidentiality was not violated, therefore, the ethics committee did not need to be consulted. I have stated below, point by point to each reviewer’s comments, the changes that have been made.

Replies to reviewer 1: No comments had been made upon which a reply was deemed necessary.

Replies to reviewer 2:

1. 72 (44%) of FP1 data could not be linked by conventional contact tracing.

This has been addressed in lines 232-239, supported by a new reference [19] in which only 10% of cases could be linked. The authors interpret this as being due to three factors commonly discussed in epidemiology publications, a) an inherent limitation in contact tracing is that transmission between casual contacts is likely missed i.e. transmission of disease on a bus, train, crowded bar, etc., b) cases with identical fingerprints may not be due to recent infection, but rather, reactivation and c) the strain may be innate to the population, with no identifiable source case.
2. Almost all of the culture positive Canadian-born treaty cases (159/163) outside of Winnipeg seem to be coming from a small number of northern reserves (9) and of the FP1 strain. The same strain is dominating in Winnipeg. Can the authors shed any light on the relationship between these reserves and Winnipeg that might explain the distribution? Do the nine hyperendemic reserves account for a disproportionately large fraction of the CB treaty reserve population? Is the CB treaty population of Winnipeg known?

Figure 4 indicates that there were 163 culture positive cases on the reserves. In fact, 90.8% (148 out of a total of 163 reserve cases available for typing) were clustered, as seen in figure 4. Of that, 64 of these clustered strains are attributed to FP1. It is highly likely these 64 strains of FP1 are from these 9 reserves, since these 9 contain most (159/189) of the total TB cases found on reserves. With 148 of the isolates clustering, the cases on these hyperendemic reserves are clustered, by FP1 as well as some of the lesser predominant FP types, i.e. 2, 5, 72 (figure 5).

Since there is 162 isolates of FP 1 (with 64 cases in reserve land) the dominance of FP1 strain in both Winnipeg and the reserves reflect the horizontal transmission of these strains through travel of individuals from reserve to the city and vice versa. This was proven with contact tracing data and social network analysis (line 199-201, data not shown).

The Canadian-born treaty population of Winnipeg is not known, only the population for the province (line 82), however, as noted on line 223, it would most likely underrepresented due to a proportion of individuals not claiming status.

3. Minor suggestions:
   a) Added in text, lines 298-300, with appropriate references, the elimination goals of 5% reduction per year and elimination date of 2010.
   b) Needed to indicate the year of population estimates given at the beginning of Methods. Added 1996 at Line 81, also at line 116.
   c) Added in text (lines 166-167) the amount of bands in the RFLP pattern (12) and that it was completely sensitive to first line antituberculoid drugs. Also, the fingerprint data, in general, is from initial isolates (line 100-104).

Thank you for your consideration. If you have any questions, please do not hesitate to contact me by phone (204) 789-6039, by fax (204) 789-2306 or email at kym_blackwood@hc-sc.gc.ca.

Sincerely,

Kym Blackwood