Author's response to reviews

Title: Incidence and outcome of newly-diagnosed tuberculosis infections in schizophrenics: a 12-year, nationwide, retrospective longitudinal study

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Q1. TB infection is used incorrectly in several places (as you pointed out), and the discussion presents examples of infection and disease together which makes for little cohesiveness. Because they use the terms incorrectly very often, it is difficult to interpret when the terms are being used correctly. Please carefully review each usage of the term and the papers you reviewed to be sure that infection and disease are being used correctly.

A1. Thanks for your remind. TB may infect human beings without causing any symptoms, or diseases. In this study, the end point is newly-diagnosed TB diseases. Therefore, we had replaced the “TB infections” in the text with “TB diseases”.

Q2. They call this a case-control study, but I would refer to it as a retrospective longitudinal study. A case control study would identify TB cases and match controls who did not have TB, and compare proportions of each group with schizophrenia. They did a better study, following schizophrenics and non-schizophrenics to TB, death, or censoring at end of follow-up, and their primary analysis reflects this study design.

A2. Thanks for your comment. We had changed “case-control” to a “retrospective longitudinal”.

Q3. Some p-values in Table 1 should be reviewed (age, dyslipidemia, heart failure, peripheral vascular disease, hemiplegia, AIDS).

A3. Thanks for your careful review. We are sorry for the typo error. We had rechecked the numbers in Table 1 and corrected them.
Q4. Why did multivariate analysis adjust for so many factors? Even those shown to have no crude association?

A4. We are sorry for the unclarity. Only factors with p-value less than 0.1 in the univariate analysis were entered into the multivariate analysis. Not all of the factors in the table 4 were entered into multivariate analysis. We had added explanatory footnotes in the table 4.

Q5. Is table 4 the model that reported the adjusted HR in Table 2? I’m confused as Table 2 states that the HR was adjusted for all of those co-morbidities, but Table 4 suggests that age, sex and hypertension were the only factors in the multivariate model.

A5. We are sorry for the confusion. Table 2 illustrated the incidence of newly-diagnosed TB in the schizophrenics AND control cohort. All possible factors should be adjusted to demonstrate the true impact of schizophrenia. Table 4 showed the risk factors of newly-diagnosed TB in schizophrenics cohort ONLY, not in the control cohort. Because of different purposes and target groups, the factors in Table 4 could not be used for adjustment in Table 2.

Q6. If p-values for table 3 are going to be presented in the text, they should be presented in the table as well.

A6. Thanks for your comment. We had added the P value in the Table 3.

Q7. Why no table for logistic regression? DM was borderline statistically significant? It would be nice to see factors associated with treatment outcomes in a table.

A7. Thanks for your comments. We had presented the result of logistic regression (supplementary table 1) to illustrate the factors associated with treatment outcome. Due to inclusion of age, the number of odds ratio of DM remained the same but 95% CI and p value changed a little.

Q8. Treatment outcomes certainly trended towards being better for schizophrenics. Though not statistically significant, the authors should still discuss why the trend would go in this direction.

A8. Thanks for your careful review. The reason why outcome of TB diseases in schizophrenics trended better than control cohort is undetermined. The outcome of TB diseases depends on host, pathogen and socio-economic factors. Unfortunately, the body weight, initial diseases status, strain type, drug resistance pattern and hence appropriateness of anti-TB regimen are not recorded in the NHIRD. In addition, whether schizophrenics are more accessible to medical attentions and therefore more likely to be diagnosed earlier or whether their compliance is better under government-guided directly observed treatment short course (DOTS) can neither be assessed. The statistical insignificance (p=0.144), limited number of TB cases, and the speculative explanation may arouse more questions. We asked for your permission to interpret the results.
conservatively as we previous did in the discussion section.

If you still suggest that a discussion is required, we will add a paragraph before the conclusion. “The reason why outcome of TB diseases in schizophrenics trended better than control cohort is undetermined. The outcome of TB diseases depends on host, pathogen and socio-economic factors. Unfortunately, the body weight, initial diseases status, strain type, drug resistance pattern and hence appropriateness of anti-TB regimen are not recorded in the NHIRD. In addition, it is undetermined whether schizophrenics are more accessible to medical attentions and therefore more likely to be diagnosed earlier or had better compliance under government-guided DOTS”.