Author's response to reviews

Title: Unexpected Decline in Tuberculosis Cases Coincident with Economic Recession -- United States, 2009

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Author's response to reviews: see over
We thank the editors and reviewers for comments. Please see below for responses. Page numbers refer to pages on the track changes document.

**Editorial requirements:**

*Title page:* Please include a title page in the manuscript file. This should contain; Title, Author list, Affiliations (department names, institution name, street name, city, zip code, country), email addresses. The author list and email addresses must be identical in the manuscript file and on the submission system, and it must be clear which affiliation pertains to each author. (Title page needs emails of all authors.)

Updated title page to delete author qualifications and add streets, zip codes, and email addresses.

Please document whether data used in your study is openly available - if not, needs note on ethics.

In Acknowledgements section, we describe ethical considerations underlying the CDC data, “Routine data collected and used in these analyses have been determined to be public health surveillance and not human participants research requiring oversight by an institutional review board.” We added URL links to public use data and technical instructions for data privacy and confidentiality.

**Figures:** We note that the figures have been included in the manuscript file. Please upload the figures as separate figure files using the "upload" form on the submission system only, and delete the figure from the manuscript file. The figure file should not include the title (e.g. Figure 1... etc.) or the figure number. The legend and title should be part of the manuscript file, given after the reference list. Please ensure that the order in which your figures are cited is the same as the order in which they are provided. Every figure must be cited in the text, using Arabic numerals. Please do not use ranges when listing figures. For more information, see the instructions for authors: [http://www.biomedcentral.com/info/ifora/figures](http://www.biomedcentral.com/info/ifora/figures).

Completed.

**Reviewer's report 1**

This article addresses possible explanations for important decline in TB cases in the US in 2009.

The main finding of the paper is to demonstrate that the decline in TB cases is not due to changes in surveillance methods but may be due to several factors that may coincide with economic recession. The article reads well. It provides a good example on how to question trends in TB notification. However, some clarification are needed for a better understanding, in particular for non US readers, and possible limitations of methods should be further discussed.

**Major compulsory Revisions:**

*Background:

At least one sentence on the TB epidemiological situation in the US should be added.

Background added.

*Methods:

Case definition of annual incident cases of TB disease should be added.
URL reference to case definition has been added in this section.

In second paragraph, the definition of high burden counties should be clarified
“High-burden” has been deleted since it may be confusing with respect to international classifications of TB burden. By high-burden, we meant that out of 3143 counties (sub-divisions of a state) in the United States, these 11 areas represent almost a quarter of TB cases reported annually.

Discussion:
In the first sentence, you should summarize what results of your study were used to uncover potential underreporting.
Analyses to uncover potential underreporting included 1) case counts compared to expected by staff loss, type of reporting software, and clinical and laboratory features of cases, 2) use of multiple independent information systems to assess declines, 3) individual line-listed reviews of case reporting, and 4) reports from TB controllers. The first paragraph of the discussion has been revised to better incorporate these aspects, and to refer to an additional detailed assessment in two states that was published after this manuscript was submitted.

Possible limitations of the study should be addressed (including possible limitations of the methods used to calculate expected cases, using clustering as a measure of recent transmission etc.)
Limitations added on p. 18 (clustering) and p. 19 (expected data).

Abstract:
The abstract does not completely reflect the content of the article, especially in the background and result sections and should be revised.

For example:
• The objective in the background section is not exactly the same than the one in the background section of the text. The later seems more to correspond to the content of the article as the article does not only address the issue of underreporting mentioned in the abstract.

Abstract background revised to clarify that analyses were conducted to investigate the unexpected decline rather than a single hypothesis.
• The results section does not include the main findings of the study on which the conclusion is based.

Abstract results revised to include lack of finding of surveillance artifact.

Minor Essential Revisions:
Background:
The change in software systems is difficult to understand (persons outside US may have difficulties to understand what mean change from Universal CDC software, the Tuberculosis Information Management System to a choice of National Disease Surveillance system compliant application. For example, “compliant application” may not be understood, do you mean that the main change was using a National electronic disease surveillance system (used for all disease including TB) instead of a dedicated application for TB? I would suggest to rephrase the sentence for a better understanding.

We clarified that the change was from a single software to choice of any software application that meets U.S. health data transfer standards.

Results:
First paragraph Line 7: What do you mean by modernized TB screening
Modernized overseas TB screening requirements refers to the updated technical instructions for screening applicants for U.S. immigration that began to be implemented globally in 2007 [background and reference 6]. Wording here has been modified, with a brief description of the addition of sputum culture to pre-immigration screening for high-risk persons (those with an abnormal chest radiograph, other signs of TB, or HIV) and tuberculin skin testing of children.

Discussion:

It will be helpful to clarify how could the type of immigration screening impact on the number of reported cases.

I am not sure to fully understand the last paragraph of the discussion. It should be clarified (How does this impact on your result?) or removed.

Clariﬁed how unknown or missing data could impact results.

You do not discuss possible impact of changes in TB control. Does this mean that no changes have occurred in the study time period?

We added a statement p. 20 that steady declines in TB rates over the study period are evidence of continued progress in TB control; however, we have no evidence of programmatic improvements affecting the unexpected 2009 decline.

Reference : references 2 to 4, 10, 11, 12 should include the author (individuals or organisation)

Updated references.

Discretionary revisions:

For clarification, I would suggest to summarize the possible reasons of the decline in TB cases that you have investigated in the beginning of the second paragraph.

Added a summary statement.

Reviewer’s report 2

An excellent and interesting paper

Minor essential revisions

Page 12, last para: 855 rather than 8-55

Thank you, corrected to 855 as well as correction to .8% from Chin reference.

Discretionary revisions

My main concern in this very good paper is that the abstract doesn’t adequately reflect the conclusions of the investigation. In particular, that a real decline in reported cases may not reflect a real step up in the effectiveness of control measures. Rather, it may reflect a combination of reduced immigration (eg from Mexico) and the very real possibility of decreased presentation for health care consequent on the recession.

We updated the abstract and concluding sentence (p. 20) as requested.

While it is not reasonable for the authors to delay submission of their paper until data from the next year is available, they may wish to mention the potential usefulness of the subsequent year’s data in assessing the extent to which the downturn in one year is a ‘one off’ or sustained.
We have added provisional 2010 results for overall case counts, and our interpretation of those data, to the discussion on p. 20. We do not yet have a final 2010 data set with corresponding variables for comparison.

**Reviewer's report 3:**
The manuscript describes a decline in tuberculosis cases in the United States in 2009 using time series analysis of reported tuberculosis cases according to multiple surveillance systems. Overall it is a well-written study with a clear hypothesis and the results are intriguing.

**Minor Essential Revisions**
The manuscript shows only the difference between observed and expected numbers of cases. The reader has to trust the authors that the deviation between observed and expected numbers in 2009 cannot be attributed to a poor fit of the model. I would strongly recommend including a graph showing the original data with the observed number of cases, as well as the best fit of the ARIMA model, such that the reader can easily check the goodness of fit of the model and the magnitude of the deviation.

We used the Akaike information criterion and Schwarz criterion to evaluate goodness of fit and select best ARIMA models (p. 10). To avoid redundancy in publication since the modeling approach is being considered for publication elsewhere, we did not include the graph of observed TB cases with the ARIMA model and prediction for BMC Public Health readers, however we include it for reviewer interest. Values of $R^2$ for the ARIMA models ranged from 0.93 to 0.96, indicating excellent model fit (p. 15).

![Graph of observed and ARIMA model fitted TB cases](image)

(2) I would also recommend describing explicitly in the methods section how the ARIMA model was selected that was used in the forecasting. It would be helpful to the reader to provide the details of this best fitting model in the methods section.
Added a sentence in the methods (p. 15) to reflect criteria for selecting best models for 2000-2007 data. The 2008 data were then used to validate model forecasting by examining a t-test for the errors (\( p=0.90 \)) on results p. 14.

(3) Please explain why there is no correction for multiple testing in examining differences between observed and expected cases, whereas there is correction for multiple testing in the identification of time trends. There are a large number of tests performed for the difference between observed and expected cases with \( P<0.05 \) as a criterion. The few significant findings may arise as a consequence of performing this large number of tests.

Observed versus expected cases in Table 1 were examined to screen TB patient and surveillance reporting characteristics for hypothesis generation. Statistical significance is less meaningful for these analyses than examination of prediction intervals and the magnitude of the deviations. We present both prediction intervals and P-values for readers interested in the number of individuals affected by a given characteristic, and the decline within that stratum. Many strata showed declines that were significant at \( P<0.001 \), suggesting declines across a broad swath of characteristics. While some of the strata are associated, such as demographic and social risk factor variables, others such as reporting software type represent independent hypotheses. In contrast, the multiple testing in Joinpoint regression analysis in identification of time trends for monthly TB data reflects the internal process of detecting changes in trend across 120 months of data using permutation tests. In responding to the reviewer, we updated P-values in Table 1 to reflect model-based standard errors for the expected value based on a t-distribution with 7 degrees of freedom (9 data years 2000-2008 in the model – 2 parameters for intercept and year), or critical value of 2.36, whereas previously we calculated expected value standard error using a Z critical value of 1.96. We also updated ARIMA and Joinpoint results on p. 14-15 where we identified typographical errors in P-values and confidence limits that corresponded to provisional analyses rather than final data. We confirmed that the Figures correspond to final data. Findings were materially unchanged as a result of these updates.

(4) Please provide some explanation of the Joinpoint linear regression (including flexion points). Most of the prospective readers of this article have never heard of this method. We added a sentence regarding Joinpoint to p. 10; Joinpoint begins by assuming no change in trend over the period of data and assesses potential changes in trend using permutation. We deleted “controlling the error probability for multiple tests” to avoid confusion for readers unfamiliar with the method, and added the URL reference to the Joinpoint website.