Author’s response to reviews

Title: Demographic characteristics of transfusion-transmitted infections among blood donors in China

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BMC Infectious Diseases
Demographic characteristics of transfusion-transmitted infections among blood donors in China

Dear Professor W. van Leeuwen,

Thank you very much for your attention and suggestions about our manuscript entitled “Demographic characteristics of transfusion-transmitted infections among blood donors in China” (No: INFD-D-19-00443R1).
We revised the manuscript (by highlighting the changes within the document by using colored text) and responded point by point to the comments as listed below. The manuscript English language had been greatly improved.

We would like to resubmit this revised manuscript to BMC Infectious Diseases, and hope it is acceptable for publication in the journal.

Looking forward to hearing from you soon.

With kindest regards,

Yours Sincerely

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Response to reviewer 1 (Professor Trinks).

Thanks for your careful reading and valuable comments on the manuscript. According to your suggestions, the review has been revised carefully and seriously.

For your comments and suggestions, we make the following responses.

The revise details are listed below.

1. English grammar must be checked throughout the manuscript. Some sections of the manuscript are poorly written and are difficult to understand.

Response: The manuscript English grammar had been checked throughout the manuscript.

2. The phrase "Among which there were..." should be in the results section.
Response: Line 133-136. The phrase "Among which there were..." has been removed to the results section.

3. In Table 1, different brands of ELISA kits were used for each TTI. Do these kits differ in their sensitivity and specificity?

Response: Dear Professor Trinks, different brands of ELISA kits used for each TTI may have different sensitivity and specificity, but all kits were FDA-approved for blood screening in China. Therefore, all kits meet the requirement of sensitivity and specificity for the detection of TTIs in China. To avoid false results caused by the limitation of sensitivity and specificity of reagents, all samples from blood centers or blood banks were sent to our lab (National Center for Clinical Laboratories) for TTIs confirmation.

4. Was there any difference in the prevalence of the TTIs and the demographic characteristics analyzed in this study regarding the geographic location of the blood bank?

Response: Dear Professor Trinks, the prevalence of the TTIs was not analyzed in our study, because the prevalence of the TTIs was calculated by the number of TTIs reactive samples and total screening samples during study period. We did not get the total screening samples of each blood bank. Hence, we did not perform the analysis of TTIs prevalence among every geographic location of the blood bank.

Furthermore, the number of blood donors with TTIs differed in each geographic location of the blood bank, some blood banks had larger sample sizes, while others had fewer samples, which may lead to the bias in analysis of TTIs demographic characteristics between different blood banks. So, we also did not analyze the demographic characteristics of each blood bank.

We look forward to your understanding that we did not evaluate the difference in the prevalence of the TTIs and the demographic characteristics regarding the geographic location of the blood bank in this study. Thank you very much for your kind suggestion. We will focus on them in our next research among Chinese blood donors.

Response to reviewer 2 (Professor Jacquot).

Thanks for your careful reading and valuable comments on the manuscript. According to your suggestions, the review has been revised carefully and seriously.
For your comments and suggestions, we make the following responses.

1. The manuscript is difficult to read due to English grammar and syntax issues. It needs to be proofread and edited so the reader can better understand the findings and conclusions.
Response: The manuscript English language had been greatly improved.

2. It is unclear to me why the control group for this study consists of donors with negative TTI testing but elevated ALT. Why were donors with normal ALT not selected for comparison?
Response: Dear Jacquot. As you suggested, the donors with normal ALT were better choices for comparison. But, in China, the blood donations with elevated ALT (>50 U/L) will be discarded and not transfused. Only these discarded samples can be enrolled in the scientific research and sent to National Center for Clinical Laboratories for further confirmation. Furthermore (line 231-234), according to China Report on Blood Safety 2016 [3], the samples that tested non-reactive for TTIs (ALT >50 U/L) were enrolled in the study as TTIs negative controls that showed the high agreement of demographic distribution with normal voluntary blood donors. So we selected the elected ALT samples (tested non-reactive for TTIs) for comparison.

3. This test is no longer used to screen donors in the United States due to poor sensitivity and specificity
Response: 1) ALT test may detect the donations in window period and detect occult hepatitis infection. The different prevalence hepatitis virus (HBV and HCV) in China and US may result in the different blood screening strategy. China is the high epidemic area of hepatitis, has large number of hepatitis virus carriers. ALT test is helpful to improve blood quality. 2) Elevated levels of ALT may indicate the occurrence of hepatitis or other diseases. It is controversial for Chinese blood donors to cancel ALT test. Therefore, the ALT test among blood donors has not been abolished by the Chinese government.

4. The three month duration is very specific - what is the reason for these three months in 2015?
Response: Dear Jacquot. Between March 2015 and September 2015, this six month duration was our evaluation duration. This evaluation research consisted of demographic characteristics analysis of transfusion-transmitted infections (This study) and comparative evaluation between chemiluminescence immunoassay (CLIA), electrochemiluminescence immunoassay (ECLIA)
and ELISA for HIV screening among blood donors. This study is a part of the big project. Besides, automated CLIA and ECLIA had been used in clinical laboratories but not applied to screen HIV in blood donors. Hence, we want to supervise the demographic characteristics among blood donors and evaluate the performance of ELISA, CLIA and ECLIA for blood screening. So we chose these 6 months in 2015.

5. It appears to nucleic acid testing (NAT) is not performed up front. Is that correct? Without NAT, the window period for detecting TTI is higher and this can compromise blood supply safety.

Response: Dear Jacquot. Maybe, I made confusing statements in section “Materials and methods”. According to Blood Donation Law of the People’s Republic of China, blood donations are firstly screened using one or two ELISA kits of each serologic marker (HBsAg, anti-HCV, anti-HIV and anti-TP). The donations that tested serologically non-reactive for TTIs must be performed by multiplex nucleic acid assays to detect HBV, HCV and HIV DNA/RNA. However, NAT will not be performed when the blood donations were screened as serologically reactive for TTIs and elevated ALT level >50 U/L in blood bank.

The blood donations that tested serologically reactive for TTIs or serologically non-reactive for TTIs (elevated alanine aminotransferase [ALT] level >50 U/L) were not transfused and enrolled in this study. Due to the limitation of specificity of ELISA, the samples that tested initially reactive for TTIs may be nonspecific reaction, so these samples were enrolled in this study and sent to our lab (NCCL) for retesting.

6. Please use brackets [] instead of parentheses with parentheses (on page 9 for example) - avoid (age(18-25):____) and use (age[18-25]:____).

Response: Line 150-153,174-175, 179-180, 183-184, 211. Parentheses with parentheses () have been change to brackets and brackets [].

7. I would change "donor times" to "previous donation history" to clarify that you are comparing first-time to repeat donors.

Response: We have changed "donor times" to "previous donation history" throughout the paper. The "previous donation history" was highlighted in the paper.

8. This histogram images are blurry and hard to read with the grey scale.
Response: The histogram image had been revised. We revised all tables and figures in the manuscript to make them easier to read.

We have to sorry for giving you so many troubles because of those confusing statements. Your comments and suggestions really helped me a lot. We have put great effort to this manuscript. I wish it can be satisfactory.

If there is any information I can provide and revise, please don’t hesitate to contact me.

Thank you again for your time and patience and looking forward to hearing from you soon.

Best regards

Yours sincerely

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