Author's response to reviews

Title: Health care workers in southern China are not vaccinated adequately against hepatitis B: a retrospective cohort study.

Authors:

Yu-bao Zheng (guangzhouyb@126.com)
Yu-jie Su (suyuje1987@hotmail.com)
Ke Wang (wangke19821@126.com)
Yu-rong Gu (865576465@qq.com)
Zhan-lian Huang (zhanlian921cn.com)
Chao-shaung Lin (shuangss@21cn.com)
Zhi-liang Gao (zhilianggao@21cn.com)

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Author's response to reviews: see over
Dear Editor,

We are very pleased to learn from your letter about revision for my manuscript entitled “Status of HBV infection and vaccination among health care workers in a Public General Hospital: a retrospective cohort study (Ms. No. 2011913633145142)”. First of all, we wish to thank you and reviewers for your attention and the constructive comments and advice. We have revised the manuscript according to the comments from you and the reviewers.

**Point-by-point reply to Reviewers and Editor as following:**

**Reviewer 1: bahador sarkari**

Reviewers report:

**In abstract:**

**Comment 1:** How many HCWs have been enrolled in the study and how the details have been obtained? by interview, questionnaire, through vaccination records, etc.?  
**Answer 1:** We wish to thank the reviewer#1 for helpful comments and advice which definitely help improve our manuscript. And we agree with reviewer#1 that the number of cohort and should be added to abstract of manuscript. so “A survey of HCWs in a Chinese public general hospital was carried out with a retrospective cohort of 1,420 hospital HCWs (458 males and 962 females). HBV vaccination status was investigated in the cohort from vaccination records from the period of 1988 to 2008” has been incorporated in abstract(METHODS paragraph) of revised version of the manuscript( done highlight section).

**Comment 2:** Results: what was the overall rate of vaccination among HCWs?  
**Answer 2:** I thank reviewer#1 for the constructive comments and advice. The overall rate of vaccination among HCWs was 40.42% in our study. So the overall rate of vaccination among HCWs has been incorporated in Abstract and Results section of revised version of the manuscript( done highlight section).

**Comment 3:** How the natural infections have been evaluated?  
**Answer 3:** We wish to thank the reviewer#1 for helpful comments and advice which definitely help improve our manuscript. And rate of the natural infections was 7.53%(107/1420) among HCWs. And the rate of the natural infections have been
incorporated in Abstract and Results section of revised version of the manuscript according to the comments raised by the reviewers (done highlight section).

Comment 4: How many doses of HBV have been used by HCW and how many of HCWs completed the course of vaccination?

Answer 4: I thank reviewer #1 for the constructive comments and advices. And 10-µg/dose hepatitis B vaccines have been used among HCW. There were 574 HCWs who completed the course of vaccination. So above description about vaccination have been incorporated in Abstract and Results (Status of hepatitis B vaccination in HCW paragraph) section of revised version of the manuscript according to the comments raised by the reviewers (done highlight section).

Comment 5: Conclusion must be based on the findings of the study.

Answer 5: We wish to thank the reviewer #1 for helpful comments and advice which definitely help improve our manuscript. We have revised Conclusion of Abstract section of revised version of manuscript according to the comments raised by the reviewer #1 (done highlight section).

Comment 6: Introduction is too short and not so informative.

Answer 6: We wish to thank the reviewer #1 for helpful comments and advice which definitely help improve our manuscript. We have revised Introduction section of revised version of manuscript according to the comments raised by the reviewer #1 (done highlight section). And the corresponding reference has been incorporated in Introduction and References section of revised version of the manuscript (done highlight section).

Comment 7: How the seroprotection was evaluated in this study?

Answer 7: We wish to thank the reviewer #1 for helpful comments which definitely help improve our manuscript. The seroprotection was evaluated in this study as following: Overall, more HCWs in the present study gained seroprotection against HBV from prior infection than from vaccination. The presence of seroprotection being conferred by vaccination versus natural HBV exposure differed across departments and professions. As shown in Table 2, HCWs working in infectious diseases departments were the most likely to have gained immunity through prior
exposure, as opposed to vaccination. Meanwhile, medical doctors were more likely than technicians and nurses to have gained protection through vaccination (Table 2).

Above description on evaluation of the seroprotection have been incorporated in Results (Immunity from vaccination versus natural infection paragraph) of the revised version of the manuscript (done highlight).

M and M:

Comment 8: How the HCW have been reached and how the statuses of vaccination have been evaluated?

Answer 8: We wish to thank the reviewer#1 for helpful comments and advice which definitely help improve our manuscript. Our study: "A large, retrospective cohort of 1420 HCWs (458 males and 962 females) was assembled by recruiting HCWs from the health examination center database (est. 1988). All individuals whose data are in the database have provided written informed consent for future research and analysis of their data; nevertheless, all included subjects also provided written informed consent to participate in this study as well. All of the recruited HCWs had chosen previously to have their routine medical examinations done at the Liver Disease Center of Southern China in a public teaching general hospital; therefore the population is most closely representative of southern China in particular. Their data were analyzed anonymously. Vaccination status was confirmed by routine medical examination reports". Above elaboration of cohort and statuses of vaccination have been incorporated in MATERIALS AND METHODS (Study population paragraph) of the revised version of the manuscript (done highlight).

Comment 9: HBe marker has been evaluated in this study, as stated in M and M section. However there is no detail about this marker neither in the result section nor in the abstract.

Answer 9: We are sorry that our statements on the HBe marker may be misleading. Actually antibody to hepatitis core antigen (anti-HBc) has been evaluated in this study, as described in M and M section. The description of evaluation of the anti-HBc marker has been incorporated in the M and M section of the revised version of the
Results:

Comment 10: How many cases of HCW completed the course of vaccination? What was the overall rate of HBV vaccination in HCWs?

Answer 10: We thank the reviewer#1 for pointing out the important issue on the number of cases of HCW completed the course of vaccination and overall rate of HBV vaccination in HCWs. As requested by the reviewer, we have supplement statement on vaccination of HCWs: “There were 574 HCWs who completed the course of vaccination. And the overall rate of vaccination among HCWs was 40.42% (574/1420)”.

Comment 11: Were there any correlations between anti-HBV/ HBsAg and sex?

Answer 11: We thank the reviewer#1 for pointing out the important issue on correlations between anti-HBV/ HBsAg and sex. And as requested by the reviewer#1, we have supplement the data collection and analysis of correlations between anti-HBV/ HBsAg and sex. And there were higher the rate of anti-HBs positive among males than that of females. However, there was not significantly different in the rate of anti-HBs positive between female and males, that is to say, Vaccination rates were similar between males and females (Table 1).

Comment 12: Having up to 80% anti-HBV in a group by natural infection does not make logical sense?

Answer 12: We are sorry that our statements on the rate of at-HBs positive may be misleading. The rate of Anti-HBV in a group by natural infection refers to the number of HCWs with Anti-HBs produced by natural infection vs the number of HCWs without vaccination(or natural infection). And our having up to 80% anti-HBV included anti-HBcAb positive without positive of HBsAg by natural infection and
those HCWs with anti-HBcAb positive have once been vaccinated before. Of course, the results still need further large sample multicenter validation.

**Comment13**: Quality of written English: Not suitable for publication unless extensively edited.

**Answer13**: We wish to thank the reviewer#1 for the pertinent comments and advice which definitely help improve our manuscript. As recommended by the reviewer#1, we have revised the manuscript, and our manuscript was edited and proofread by Medjaden Bioscience Limited. And some errors in writing of our manuscript have been corrected.
Reviewer #2: Maria Ganczak

Reviewer's report:

Comment.1: In general, there have been many studies surveying this particular topic from all over the world. In my opinion, the subject has already been widely explored, and this survey does not add new input to this field.

Answer.1: We wish to thank the reviewer#2 for helpful comments which definitely help improve our manuscript. And we agree with reviewer#2 that there have been some studies surveying the HCWs being at high risk of infection with hepatitis B viruses all over the world (mainly African origins). However, Few or no studies have been conducted among HCWs who are at an elevated risk of HBV infection due to their exposure to blood and other bodily fluids in the course of their work in any hospital to assess their knowledge base of HBV in China.

Comment.2: The paper would benefit from editing by a native English speaker, who could adjust the grammar and syntax satisfactorily.

Answer.2: We wish to thank the reviewer#2 for the pertinent comments and advice which definitely help improve our manuscript. As recommended by the reviewer#2, we have revised the manuscript, and our manuscript was edited by a professional native English editor at Medjaden Bioscience Limited (done highlight). And some errors in writing of our manuscript have been corrected.

Comment.3: Regarding the contain of the paper, it does not fulfil the basic criteria which allow it to be published in a medical journal.

Answer.3: We wish to thank the reviewer#2 for the pertinent comments. And we have revised the manuscript according to the journal style (http://www.biomedcentral.com/info/ifora/medicine_journals ). We ensure that our files are correctly formatted and our revised manuscript conforms to your journal style (http://www.biomedcentral.com/info/ifora/medicine_journals ).

Major compulsory revisions:

Comment.4: The title is not precisely covering the content of the study.

Answer.4: We wish to thank the reviewer#2 for helpful comments which definitely help improve our manuscript. As recommended by the reviewer#2, we have revised The title of manuscript, “Making up vaccination should be carried immediately out to increase the inoculation of hepatitis B vaccine among health care workers in the south
of China: a retrospective cohort study”. And the revised title have been incorporated in the Title section of the revised version of the manuscript.

**Abstract**

**Comment. 5:** The author should describe the results precisely.

**Answer 5:** We wish to thank the reviewer#2 for helpful comments which definitely help improve our manuscript. We have revised the Result in Abstract of manuscript according to the reviewer#2. And Above describing the results precisely. have been incorporated in the Abstract section of the revised version of the manuscript.

**Introduction**

**Comment. 6:** The Introduction is too short. The authors discuss various issues in only seven lines giving 2 references published in 2002 and 1999. So adding few paragraphs as well as adding at least a number of other, up to date references to support their theses would be of great value.

**Answer 6:** We wish to thank the reviewer#2 for helpful comments and advice which definitely help improve our manuscript. We have revised Introduction section of revised version of manuscript according to the comments raised by the reviewer#2. And we have added some new references in recent 5 years to support background of our research. And the corresponding reference has been incorporated in Introduction and References section of revised version of the manuscript.

**Methods**

**Comment. 7:** The terminology and the methods used should be clarified, e.g. Which study design does this survey represent? I would not say it is a “retrospective cohort study”.

**Answer 7:** We wish to thank the reviewer#2 for helpful comments and advice which definitely help improve our manuscript. And we are sorry that our descriptions on carrying out retrospective observational study were not sufficiently clear. And we have modified the MATERIALS AND METHODS, Study design as follows: Since 1988, a database of Health-care workers (HCWs) with the annual examination had been built up for health observation in the future. Those Health-care workers who
were entered the database were asked to sign a written informed consent for future research and analysis. All data were entered into a computerized database and were analyzed anonymously. The HCWs enrolled in the present study were from this database. The research protocol was approved by the Human Ethics Committee of the Third Affiliated Hospital, Sun Yat-Sen University.

Retrospective study of HCWs vaccinated against hepatitis B from 1988 to 2008. The study was conducted in the Public General Hospital, that is to say, is a teaching hospital in Southern China: The Third Affiliated Hospital of Sun Yet-sen University, a representative General Hospital.

Above the modified METHODS (Study design paragraph) have been incorporated in MATERIALS AND METHODS of the revised version of the manuscript. (done highlight).

Comment 8: The question remains as to why that very hospital was selected for the study. One out of how many? Was it more convenient to obtain such a non-random sample? Was that very hospital more co-operative than the others, more available or more willing to be studied? The authors do not explain how many different hospitals/which types are there in the region in which the study was conducted? How many HCWs live in the country/region? How many of them work at hospitals? In other words, to which extend the study population is representative of the region, of the country? There might be a large generalizability problem. Since the study was conducted among HCWs from university hospitals, the results may not be generalizable to all HCWs in the region/in China. This should be also put into the “Limitations” section which does not appear in the paper.

Answer 8: We wish to thank the reviewer#2 for pertinent comment and advice which definitely help improve our manuscript. And we are sorry that our descriptions on study population were not sufficiently clear. Our study was conducted in the Public General Liver Disease Hospital, and our hospital is a Liver Disease Center in Southern
China. So there were many Medical workers of most Health care center in south of China who have selected our Liver Disease Center(hospital) for routine physical examination including hepatitis B inspection and vaccination. The HCWs enrolled in the present study can represent Local area of the HCWs in the south of China to a certain extent. Even so, the results of the research can not be completely generalizable to all HCWs in China or the south of China. Hence, HCWs vaccination should be further assessed by future large-scale retrospective studies. So this elaboration have been put into the “Limitations” section in Discussion of the revised version of the manuscript. (done highlight).

Comment.9-1: What was the number of HCWs at the hospital at the time of the study? The numbers might vary in 20 year period? So how nominators and denominators were calculated year by year? Through those 20 years were the data collected on the same basis, with the use of the same system?

Answer.9-1: We wish to thank the reviewer#2 for pertinent comment which definitely help improve our manuscript. And we are sorry that our descriptions on Study design and Study population of MATERIALS AND METHODS were not sufficiently clear.

Although the numbers might vary in 20 year period, the data collected on the same basis from a database of Health-care workers(HCWs) with the inclusion criteria and exclusion criteria. Despite the data collected was not based on the same system or standard in 20 year period, all unit of result of data collected in research have been standardized according to the international standard.

Comment.9-2: What does “753 of them had no precise material on vaccination” mean?

Answer.9-2: 753 of them had no precise material on vaccination” mean that those HCWs material on vaccination was ambiguous. And our study was based on a large, retrospective cohort that included 1420 HCWs (458 males and 962 females) were recruited from the Liver Disease Center in Southern China, that is to say, is also the
Public General Hospital and a teaching hospital in Southern China. We collected information of vaccination status of subjects by the routine medical examination every year. The exclusion criteria were: those HCWs had no precise material on vaccination, declined the questionnaire and declined written informed consent (as figure).

2338 HCWs from Third Affiliated Hospital, Sun Yat-Sen University between 06/1988 and 02/2008.

918 HCWs excluded:
- Vaccination record incomplete (753)
- Declined questionnaire (98)
- No written informed consent (65)
- Other causes (2)

1420 HCWs included

Figure 1. A flow diagram of study participants.

Above the modified description of Study design and Study population (including Figure 1 flow diagram of study participants) have been incorporated in MATERIALS AND METHODS of the revised version of the manuscript.

4. Part of the Results section is put to the Methods.

Results

Comment 10-1: The Results section is too short. The authors discuss various issues in only half of the page. Some Results are located by the authors in the Discussion section.

Answer 10-1: We wish to thank the reviewer#2 for helpful comments and advice which definitely help improve our manuscript. As recommended by the reviewer#2, we have supplemented some result and also removed some result from the Discussion section. And we have modified the descriptions on Result of the manuscript (in Result of our revised version of the manuscript, modified sections have been done highlight).
Comment.10-2: What was the reason to compare “status of antibody produced by natural infection versus vaccination”?

Answer 10-2: We wish to thank the reviewer#2 for helpful comments and advice which definitely help improve our manuscript. The cause of comparing “status of antibody produced by natural infection versus vaccination” is to detect how many gained seroprotection against HBV from prior infection than from vaccination in the present study. And above descriptions have been incorporated in Result of the revised version of the manuscript.

Discussion

Comment 11: Some comments should be placed in the Results section. The discussion section is too brief. Eleven out of 19 references were published ten and more years ago and are insufficient to support the theses described in this paper. Only one of those was published in the last five years.

Answer 11: We wish to thank the reviewer#2 for pertinent comment which definitely help improve our manuscript. As recommended by the reviewer#2 we have modified discussion of our manuscript: Some comments in discussion have been placed in the Results section. And we have supplemented related reference of recent 5 years to replace corresponding reference which were published ten and more years ago. Modified sections has been incorporated in Discussion and References section of revised version of the manuscript.

Comment.12: What are general practical recommendations? A “recommendations” section in the final part of the manuscript would be of value.

Answer.12: We wish to thank the reviewer#2 for helpful advice which definitely help improve our manuscript. As recommended by the reviewer#2, We have supplemented A “recommendations” section in the final part of the manuscript. “It is our view that HCWs who have a reasonable expectation of being exposed to blood on the job should be offered the HBV vaccine as a matter of course. Furthermore, HCWs should be informed that vaccination is not always effective and serological testing should be
performed to confirm vaccine effectiveness. HCWs should be counseled regarding what steps they should take to protect their health in cases of vaccine non-responsiveness”. So above supplement about recommendations have been incorporated in Discussion section of revised version of the manuscript according to the comments raised by the reviewers (done highlight section).
Reviewer #3: Hisham Ziglam

Comment 1: Poor English (Not scientific language).

Answer 1: We wish to thank the reviewer #3 for pertinent comment. As recommended by the reviewer #3, we have revised the manuscript, and our manuscript have been edited by a professional native English editor at Medjaden Bioscience Limited (done highlight). And some errors in writing of our manuscript have been corrected.

Comment 2. Did not mention the size of cohort. Only presenting percent in the abstract.

Answer 2: We wish to thank the reviewer #3 for pertinent comment. And we agree with reviewer #3 that Number of cohort and should be added to abstract of manuscript. so “the number of cohort including 1420 hospital HCWs and Information details of vaccination status of subjects were collected by vaccination records” has been incorporated in abstract of revised version of the manuscript (done highlight section).

Comment 3. Line 83. Mentioned the size of cohort is 1420. Not clear are these the whole number of HCWs in that hospital. If no how did he select the sample?

Answer 3: We are sorry that our descriptions on the size of cohort of our study were not sufficiently clear. Our study was based on a large, retrospective cohort that included 1420 HCWs (458 males and 962 females) were recruited from the Liver Disease Center in Southern China, that is to say, is also the Public General Hospital and a teaching hospital in Southern China. Since 1988, a database of Health-care workers (HCWs) with the annual examination had been built up for health observation in the future. Those Health-care workers who were entered the database were asked to sign a written informed consent for future research and analysis. All data were entered into a computerized database and were analyzed anonymously. The HCWs enrolled in the present study were from this database.

Comment 4: How did he conduct the survey? Interview survey, through the mail or self-reporting and what are the questions included in his survey.

Answer 4: We wish to thank the reviewer #3 for pertinent comment and advice which definitely help improve our manuscript. And we are sorry that our descriptions on
conducting the survey of study were not sufficiently clear. Our study was conducted in the Public General Liver Disease Hospital, and our hospital is a Liver Disease Center in Southern China. So there were many Medical workers of most Health care unit who have selected our Liver Disease Center (hospital) for routine physical examination including hepatitis B inspection and vaccination in south of China.

We collected information of vaccination status of subjects by the routine medical examination every year and the questionnaires about vaccination previously. The exclusion criteria were: those HCWs had no precise material on vaccination, declined the questionnaire and declined written informed consent (as figure 1).

And the modified description on Study design and Study population (including Figure A flow diagram of study participants) have been incorporated in MATERIALS AND METHODS of the revised version of the manuscript.

Comment 5: In line 90. He mentioned that the HCW were aged from 24-51 and then on line 92 he mentioned that 146 below age 24 and many over age 51. Therefore, data is conflicting and I am not sure which is which is correct?

Answer 5: We are sorry that our descriptions on ages of objects may be misleading. “And only 1182 HCWs were aged from 24 to 51 years”. And the final cohort consisted of 1420 HCWs had a mean age of 37.72 ± 13.37 years (only 1182 HCWs}
ages range, 24–51 years). By age band, there were 146 subjects ≤25 years old, 788 that were 26–39 years old, 394 that were 40–59 years old, and 92 that were ≥60 years old.

Above modified sections have been incorporated in the M and M section (Data collection paragraph) of the revised version of the manuscript (done highlight).

Comment 6: in line 97 the ELISA kit provided by Shanghai Industrial Division Biotechnology Limited Company made in China. What is the sensitivity of the kit and supporting references for this kit?

Answer 6: We are sorry that our descriptions on conducting the sensitivity of the kit and supporting references were not sufficiently clear. “The kit with gold-standard method for the detection of hepatitis B surface antigen has high sensitivity and specificity, and enzyme immunoassay in line with the rate of 99.0%, and no special equipment, simple and fast, with a wide range of application value[22]”. Above the supplement of kit has been incorporated in the M and M section (Data collection paragraph) of the revised version of the manuscript (done highlight). And the corresponding reference was also incorporated in the M and M and Reference section of the revised version of the manuscript (done highlight).

Comment 7: What about the ranges of used- kit in this survey? Was there the same range in brochure of the kit?

Answer 7: We wish to thank the reviewer#3 for helpful comment which definitely help improve our manuscript. The ranges of used-kit in this survey was from 0 to 250IU (standardization unit). There was the same range in brochure of the kit in this survey by Unit standardization.

Comment 8: How many times they run test. Once or twice?

Answer 8: We wish to thank the reviewer#3 for helpful comment. All tests in this survey were carried out two times. This description on test has been also incorporated in the M and M (Data collection paragraph) section of the revised version of the manuscript (done highlight).

Comment 9: Line 122- 126 about Status of antibody produced by natural infection versus by vaccination.
Comment 9-1: My comment is it reliable?
Answer9-1: We are sorry that our descriptions on Status of hepatitis B vaccination in HCW were not sufficiently clear. Antibody produced by natural infection was diagnosed as subjects who had positive of anti-HBs with or without positive of anti-HBc and had no vaccination before. Antibody produced by vaccination was diagnosed as subjects who had positive of anti-HBs without positive of anti-HBc and have once been vaccinated before. Our study showed that the vaccination status was different among different departments, and the difference was considered statistical significant. Moreover, from status of natural infection, we can see the HCWs who have a reasonable expectation of being exposed to blood on the job should be offered hepatitis B vaccine. The HCW should be counseled that non-response to the vaccination series most likely means the HCW is susceptible to HBV infection. Above the supplement of status of natural infection and vaccination has been incorporated in the Result and Discussion section of the revised version of the manuscript.

Comment.9-2: did all the staffs remember been vaccinated or no? Or it was written in their vaccination card?
Answer.9-2: We collected information of vaccination status of subjects by the routine medical examination every year and the questionnaire about vaccination previously. Those Health-care workers who were entered the database were asked to sign a written informed consent for future research and analysis. All data were entered into a computerized database and were analyzed anonymously. The HCWs enrolled in the present study were from this database. The research protocol was approved by the Human Ethics Committee of the Third Affiliated Hospital, Sun Yat-Sen University. Above modification has been incorporated in the M and M (Study design and Study population paragraph) of the revised version of the manuscript.

Comment.9-3: If there is vaccination card then why the rate of hepatitis B vaccination in HCW is low in the Public General Hospital?
Answer.9-3: We wish to thank the reviewer#3 for helpful comment which definitely help improve our manuscript. We are sorry that our descriptions on status of the rat of
hepatitis B vaccination in HCW were not sufficiently clear.

The present study demonstrated that HCWs in southern China, overall, had a disappointingly low rate of HBV vaccination (near 40%). Furthermore, approximately one-fifth of vaccinated HCWs lacked serological evidence of protection. Vaccination rates differed in relation to HCWs’ department of employment and profession. And the main reason for it is weak consciousness of HCWs for preventing the hepatitis B virus infection by hepatitis B vaccination. And non-response to the vaccination series means for that non-responder is chronically infected with HBV. So the HCW should then be counseled to discuss what non-response to the vaccination series means for that specific HCW and what steps should be taken in the future to protect his/her health.

Above modification has been incorporated in the Discussion of the revised version of the manuscript (done highlight).

Comment 10: Line 134 when mention the rate of contracting HBV in needle stick injury is about 6-30% which is scientifically wrong because it can be even more higher than this in patient with very high viral load. Reference must be included.

Answer 10: We are sorry that our descriptions on risk of blood-borne Infections of HBV in Health Care Workers were not sufficiently clear. And we agree with reviewer#3 that it is wrong which the rate of contracting HBV in needle stick injury may be even more higher than this in patient with very high viral load. “Estimates of the rate of HBV infection of HCWs following a one-time needle prick with an HBV-exposed needle range widely from 6% to 30%. [3]” And as recommended by the reviewer#3 the supplementary reference (as following) has been incorporated in the Reference section and corresponding position in Discussion of the revised version of the manuscript (done highlight).

11. Discussion

Comment.11-a: Must be started by giving the main finding of the present survey in brief.

Answer.11-a: We wish to thank the reviewer#3 for helpful comment which definitely help improve our manuscript. The present study demonstrated that HCWs in southern China, overall, had a disappointingly low rate of HBV vaccination (near 40%). Furthermore, approximately one-fifth of vaccinated HCWs lacked serological evidence of protection. Vaccination rates differed in relation to HCWs’ department of employment and profession.

And Vaccination rates are disappointingly low among HCWs in southern China, with large portions of HCWs, especially HCWs working in infectious diseases departments, showing serological evidence of a natural infection history. HCWs should not only be more broadly encouraged to be vaccinated, they should be made aware that a single inoculation may not confer protection. When HCWs contract an HBV infection, they place coworkers and patients at risk of infection as well.

Above the concise main finding has been incorporated in the Discussion(first paragraph) and Conclusion of the revised version of the manuscript(done highlight).

Comment.11-b: This part must be revised. It s not well managed.

Answer.11-b: We wish to thank the reviewer#3 for helpful advice. As recommended by the reviewer#3 the Discussion part has been revised and managed well in Discussion of the revised version of the manuscript(done highlight).

Comment.12: References must be updated and used more article to compare the results and findings. Several recent articles reviewed the same subject not included in this study.

Answer.12: We wish to thank the reviewer#3 for helpful advice which definitely help improve our manuscript. Some references have been updated, And we have supplemented related reference of recent 5 years to replace corresponding reference which were published ten and more years ago according to the comments raised by the reviewers. Modified sections have been incorporated in Discussion and References section of revised version of the manuscript(done highlight section).
Comment.13: What is the strength and weakness of this study and why not mentioned in the text.

Answer.13: We wish to thank the reviewer#3 for helpful advice. And the strength and weakness of this study have been incorporated in the final part of the manuscript as following:

1) The strength of this study: HCWs are at an elevated risk of HBV infection due to their exposure to blood and other bodily fluids in the course of their work. Vaccination rates are disappointingly low among HCWs in southern China, with large portions of HCWs, especially HCWs working in infectious diseases departments, showing serological evidence of a natural infection history. HCWs should not only be more broadly encouraged to be vaccinated, they should be made aware that a single inoculation may not confer protection. When HCWs contract an HBV infection, they place coworkers and patients at risk of infection as well. Hence, HCWs should be vaccinated not only early, but also regularly. HCWs with undetectable or low anti-HB levels in particular should receive booster vaccinations.

2) Weakness of this study: This study has the limitation of being largely limited to enrollment of HCWs in southern China. This geographical limitation limits the generalizability of these findings. Additional studies involving HCWs in other regions are needed to determine whether the patterns of data observed here are common throughout China and Asia at large, and larger retrospective studies are needed to confirm the present results.

Above modification has been incorporated in the final part of the manuscript.

With many thanks for your cordially help and patience, we are looking forward to your positive response as soon as.

With kind regards,
Yours sincerely

Yu-Bao Zheng, PhD, MD. Associate Professor. Master's Supervisor. Department of Infectious Diseases The Third Affiliated Hospital of Sun Yat-Sen University No. 600 Tianhe Road, Guangzhou 510630, China Telephone: +86-20-85252372 Fax: +86-20-85252250 Mobile phone:(0)13631361926;
Email: zhybao@mail.sysu.edu.cn ; guangzhouzyb@126.com .