PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (**http://bmjopen.bmj.com/site/about/resources/checklist.pdf**) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	An ecologic analysis of PM2.5 concentrations and lung cancer mortality rates in China
AUTHORS	Fu, Jingying; Jiang, Dong; Lin, Gang; Liu, Kun; Wang, Qiao

VERSION 1 - REVIEW

REVIEWER	C. Arden Pope, III Brigham Young University, USA
REVIEW RETURNED	07-Aug-2015

GENERAL COMMENTS	1. This manuscript reports a population-based, ecological analysis of PM2.5 air pollution and lung cancer rates in China. PM2.5 concentrations were associated with lung cancer mortality rates. The estimates of number of lung cancer deaths were similar to those estimated by using excess risks from the Pope et al. analysis of the ACS CPS-II cohort and the WHO AQGs. Given estimates of excess risk of lung cancer from PM2.5 using U.S. cohorts, there has been concern that the extremely high concentrations of PM2.5 that occur in parts of China could be contributing to substantial lung cancer deaths in China. This type of ecologic analysis in China is very useful and important. 2. The authors seem to have a few misunderstandings regarding the ACS Study. a. These studies were conducted by a research team that included scholars from various institutions including collaborators from ACS. The Pope et al. 2002 JAMA paper that is used primarily in this paper included authors from ACS, Brigham Young University (first author), University of Ottawa, Health Canada, and New York University using the ACS CPS-II cohort data. So for example in page 2, lines 47 and 48, suggest, “A well-known study based on prospective cohort data collected by the American Cancer Society (ACS) [14] reported that . . . “ On page 6, lines 20-21, suggest revising as : “A study based on the ACS CPS-II cohort concluded that . . . “ b. The ACS does not have a “guideline lever for PM2.5” as suggested a couple of times in the paper. For example, on page 2, lines 51-52 it states that “the annual average concentration of 10 ug/m3 was regarded by ACS as a long-term guideline level for PM2.5.” On page 6, lines 18-19 is states that, “As mentioned above, an annual average PM2.5 concentration of 10 ug/m3 was regard by ACS and WHO as the long-term guideline value for PM2.5.” This is stated again in a footnote to Table 1. It is not true. What is true is that the excess risk estimates reported in the research reports are

	based on chances in PM2.5 equal to 10 ug/m3. It is true that the estimates from the Pope et al study that are based on ACS CPS-II cohort data are that for each 10 ug/m3 increase in long-term exposure to PM2.5 concentrations there as an associated increase in the risk of lung cancer mortality of 8%. However, the 10 ug/m3 change in PM2.5 is not a guideline, it is just a conventional increment in exposure that is often used in the air pollution and health literature to express excess risk per some fixed change in exposure. 3. I would suggest that the paper does not need to make such an issue out of the lung cancer mortality estimates being closer to those from the Pope et al. paper versus the WHO estimates. The most interesting finding of the paper is that the ecological analysis reported in this analysis results in excess mortality estimates that are so close to those that would be observed based on using risk estimates from studies of the ACS cohort and WHO estimates. 4. The paper also would be improved if it also referenced recent estimates from the Global Burden of Disease reports. There are specific estimates for lung cancer deaths attributable to PM2.5 in China. How do they compare? Minor comments: 1. The paper is in need of careful editing for style, etc. 2. Page 2, line 21. Suggest, “early 2013, when air pollution reached some of the highest levels in recent years. “ 3. Page 2, line 25. PM needs to be defined, particulate matter (PM). 4. Page 2, line 28. “Several landmark meta-analysis studies. . . “ These studies are not really meta-analysis, but they are “reviews of the evidence”. 5. Page 3, line 44. AOD needs to be defined. 6. Page 4, line 35. “fatalities according to the ACS study and WHO AQGs.” Suggest, “fatalities as estimated using risk estimates from ACS . . . “ 7. Page 10, line 56. Suggest, “fatalities based on excess risk estimates from Pope et al.”

REVIEWER	Tom Luben U.S. Environmental Protection Agency, United States
REVIEW RETURNED	26-Aug-2015

GENERAL COMMENTS	The authors have conducted an ecologic analysis of province-level lung cancer mortality rates and PM2.5 levels. The use of the annual average surface PM2.5 concentrations is novel, though the fine spatial resolution of the PM2.5 data is lost on the coarser spatial resolution of the mortality data. Still, this is one of the first nationwide studies of PM2.5 and lung cancer mortality in China, and should provide a basis for additional studies.

	Major Comments: Page 6, Table 1: I think the authors have misinterpreted the effect estimate from the Pope et al study. In the Pope et al. study, they find that a 10 ug/m3 increase in PM2.5 is associated with an 8% increase in lung cancer mortality risk. This describes the slope of a linear relationship; that is, any 10 ug/m3 increase will result in an 8% increase in risk. For example, an increase from 25 to 35 ug/m3 would yield an 8% increase in risk, just as an increase from 55 to 65 ug/m3 would yield an 8% increase in risk. In table 1, if seems as though the results from Pope et al. have been interpreted differently. The authors seem to imply no risk at concentrations less than 10 ug/m3 and an additional 8% increase in risk for each 10 ug/m3 increase in PM2.5 concentration. This is not correct. If I am misinterpreting the table, the text should be clarified to help the reader understand the comparison that is being made. Page 10, Table 3: The numbers of lung cancer deaths attributed to Pope et al. and WHO are opposite those reported in the abstract. Similarly the text on page 10, line 56 seems to indicated that the 595,000 deaths are the result of using the Pope effect estimate, which doesn't match up with what is in the table. The bigger problem, however, is that I do not believe that the effect estimate from Pope et al. can be used to estimate lung cancer deaths the same way that the WHO Air Quality Guidelines can (see comment above about misinterpretation of results from Pope et al. in Table 1). Page 11, Conclusions: Need to mention that while you have several years of PM2.5 estimates, this still doesn't match up with the latency period for lung cancer. Is there any evidence that the ranking of PM2.5 concentrations would have remained the same over the past 30 to 40 years? If so, please include that evidence. Either way, please include this as a limitation/uncertainty. Minor comments: Page 7, lines 2 and 3: change to "in this study we assumed that the risk of lung cancer did not increase with long-term exposure...." Page 8, lines 30 and 31: delete "(Sig, <0.01)". Of course these are statistically significant, they are R values. The p-values for these are meaningless.

VERSION 1 – AUTHOR RESPONSE

Reviewer 1:
Major comments:
1. This manuscript reports a population-based, ecological analysis of PM2.5 air pollution and lung cancer rates in China. PM2.5 concentrations were associated with lung cancer mortality rates. The estimates of number of lung cancer deaths were similar to those estimated by using excess risks from the Pope et al. analysis of the ACS CPS-II cohort and the WHO AQGs. Given estimates of excess risk of lung cancer from PM2.5 using U.S. cohorts, there has been concern that the extremely high concentrations of PM2.5 that occur in parts of China could be contributing to substantial lung cancer deaths in China. This type of ecologic analysis in China is very useful and important.
Revision detail:
Thank you so much for your appreciate to this paper. Our paper wants to explore the association between PM2.5 and lung cancer mortality rates and provide an overall estimation of lung cancer deaths by using excess risks from the Pope et al. analysis of the ACS CPS-II cohort and the WHO AQGs in China at a national scale. We anticipate our study can serve as valuable guideline for epidemiology study.

2. The authors seem to have a few misunderstandings regarding the ACS Study.
a. These studies were conducted by a research team that included scholars from various institutions including collaborators from ACS. The Pope et al. 2002 JAMA paper that is used primarily in this paper included authors from ACS, Brigham Young University (first author), University of Ottawa, Health Canada, and New York University using the ACS CPS-II cohort data. So for example in page 2, lines 47 and 48, suggest, "A well-known study based on prospective cohort data collected by the American Cancer Society (ACS) [14] reported that . . . " On page 6, lines 20-21, suggest revising as : "A study based on the ACS CPS-II cohort concluded that . . . "
Revision detail:
Thank you for the suggestions. We have revised according to this comment.

b. The ACS does not have a "guideline lever for PM2.5" as suggested a couple of times in the paper. For example, on page 2, lines 51-52 it states that "the annual average concentration of 10 ug/m3 was regarded by ACS as a long-term guideline level for PM2.5." On page 6, lines 18-19 is states that, "As mentioned above, an annual average PM2.5 concentration of 10 ug/m3 was regard by ACS and WHO as the long-term guideline value for PM2.5." This is stated again in a footnote to Table 1. It is not true. What is true is that the excess risk estimates reported in the research reports are based on chances in PM2.5 equal to 10 ug/m3. It is true that the estimates from the Pope et al study that are based on ACS CPS-II cohort data are that for each 10 ug/m3 increase in long-term exposure to PM2.5 concentrations there as an associated increase in the risk of lung cancer mortality of 8%. However, the 10 ug/m3 change in PM2.5 is not a guideline, it is just a conventional increment in exposure that is often used in the air pollution and health literature to express excess risk per some fixed change in exposure.
Revision detail:
Thanks so much for reminding this and we are sorry for that. We agree with that the 10 µg/m3 change in PM2.5 is not a guideline, and any 10 µg/m3 increase will result in an 8% increase in risk. We have changed the methodology to estimate lung cancer deaths based on the study by Pope III et al. according to this comment. In order to analyze the population status within the scope of different PM2.5 concentrations, we classified the PM2.5 concentrations into six levels artificially (0-10 µg/m3, 10-20 µg/m3, 20-30 µg/m3, 30-40 µg/m3, 40-50 µg/m3 and 50-60 µg/m3), taking 10 µg/m3 change in PM2.5 as an increment. We assumed that there was no risk at concentration of 0 µg/m3, thus, an increase from 0 to 10 µg/m3 would yield an 8% increase in risk. So when we estimated the number of lung cancer fatalities on the level of 0-10 µg/m3, we took the mean value of the two increased risks as the increase rate in the risk of lung cancer mortality, which was 4%. Similarly, an increase from 10 to 20 µg/m3 would also yield an 8% increase in risk, and the increase in the risk of lung cancer mortality in the level of 10-20 µg/m3 would be 12%; and the increase in the risk of lung cancer mortality in the level of 20-30 µg/m3, 30-40 µg/m3, 40-50 µg/m3 and 50-60 µg/m3 were thereby 20%, 28%, 36% and 44%, respectively. Based on that, the number calculated by Pope III et al. changed to 614,860, which is also very close to the lung cancer fatalities in China in 2012. Revision details according to this comments in the manuscript are listed below:
On page 1, line 47, ABSTRACT Section, "the number calculated by the American Cancer Society (ACS)" has been changed to 614,860;
On page 2, lines 51-52, the sentence "the annual average concentration of 10 µg/m3 was regarded by ACS as a long-term guideline level for PM2.5." has been deleted;
On page 6, the Paragraphs 2 of the "Statistics analysis" Section has been rewritten, and Table 1 has also been reedited.
On page 10, "Estimates of the potential risk of mortality from lung cancer associated with PM2.5" Section, Table 3 has been reedited, and "the number calculated by the American Cancer Society (ACS)" has been changed to 614,860 in the last paragraph of this part.

3. I would suggest that the paper does not need to make such an issue out of the lung cancer

mortality estimates being closer to those from the Pope et al. paper versus the WHO estimates. The most interesting finding of the paper is that the ecological analysis reported in this analysis results in excess mortality estimates that are so close to those that would be observed based on using risk estimates from studies of the ACS cohort and WHO estimates.
Revision detail:
We agree with that study about excess mortality estimates from PM2.5 using risk estimates from studies of the ACS cohort and WHO estimates would be more interesting, especially in China, the concerns about the health impact of such a high PM2.5 concentration are increasing. It appeared that knowing the chemical carcinogen of PM2.5 responsible for the lung cancer was more important to estimate excess mortality estimates from the PM2.5 since the composition of that varied dramatically over space. Thus, this study was undertaken to explore the association between PM2.5 and lung cancer mortality rates and investigate the spatial variation of the relationship between them using the geographically weighted regression models, for the preliminary design; then to present the ecological analysis reported in the analysis results in excess mortality estimates where strong correlations appeared. However, this study was limited by its ecological nature and data deficient. Firstly, PM2.5 dataset was not comprehensive enough to carry out statistically robust studied in China since the refined PM2.5 data were not reported until 2012 and the national monitoring data has been deficient so far; Secondly, population-based cancer registries were not well established and epidemiologic data for cancer were limited in China. Thus, we just estimated the number of lung cancer fatalities by using excess risks from the Pope et al. analysis of the ACS CPS-II cohort and the WHO AQGs in China at a national scale. If more accurate and perfect datasets can be obtained, systematic studies will be given in the future.

4. The paper also would be improved if it also referenced recent estimates from the Global Burden of Disease reports. There are specific estimates for lung cancer deaths attributable to PM2.5 in China. How do they compare?
Revision detail:
Many thanks for your suggestion. In this paper, we referenced the latest WHO assessment of deaths by lung cancer (cancer country profiles 2014), and cited the Global Cancer Country Profiles (Profiles) 2014 (WHO http://www.who.int/cancer/country-profiles/en/) that includes the estimated absolute number of cancer deaths for 2012 in the last paragraph in “Estimates of the potential risk of mortality from lung cancer associated with PM2.5” Section. The cancer mortality data presented in the Profiles was obtained from the WHO Global Health Estimates which is the latest WHO assessment of deaths by cause for the year 2012. Therefore, we referenced it as a criterion for evaluating performance of the rough estimate of lung cancer fatalities in this study. Excess mortality estimates from PM2.5 using risk estimates from studies of the ACS cohort and WHO estimates were not given in this paper by its ecological nature and data deficient. Therefore, the comparison with the GBD data has not been conducted here.

Minor comments:
1. The paper is in need of careful editing for style, etc.
Revision detail:
This manuscript has been spell-checked and grammar-checked by American Journal Experts (www.journalexperts.com). Those awkward sentences also have been revised according to the reviewers’ valuable comments.

2. Page 2, line 21. Suggest, “early 2013, when air pollution reached some of the highest levels in recent years. “
Revision detail:
Thank you for the suggestion. We have revised the sentence according to this comment.

3. Page 2, line 25. PM needs to be defined, particulate matter (PM).
Revision detail:
We have revised it according to this comment, and the "PM" has been defined in the manuscript.

4. Page 2, line 28. "Several landmark meta-analysis studies. . . " These studies are not really meta-analysis, but they are "reviews of the evidence".
Revision detail:
Many thanks for reminding and we are sorry for that. We have revised this sentence according to this comment

5. Page 3, line 44. AOD needs to be defined.
Revision detail:
We have revised the word according to this comment, and "AOD" has been defined when it was first used in the manuscript.

6. Page 4, line 35. "fatalities according to the ACS study and WHO AQGs." Suggest, "fatalities as estimated using risk estimates from ACS . . . "
Revision detail:
Thank you for the suggestion. We have revised the sentence according to this comment.

7. Page 10, line 56. Suggest, "fatalities based on excess risk estimates from Pope et al."
Revision detail:
Thank you for the suggestion. We have revised the sentence according to this comment.

Reviewer 2:
The authors have conducted an ecologic analysis of province-level lung cancer mortality rates and PM2.5 levels. The use of the annual average surface PM2.5 concentrations is novel, though the fine spatial resolution of the PM2.5 data is lost on the coarser spatial resolution of the mortality data. Still, this is one of the first nationwide studies of PM2.5 and lung cancer mortality in China, and should provide a basis for additional studies.
Major comments:
1. Page 6, Table 1: I think the authors have misinterpreted the effect estimate from the Pope et al study. In the Pope et al. study, they find that a 10 ug/m3 increase in PM2.5 is associated with an 8% increase in lung cancer mortality risk. This describes the slope of a linear relationship; that is, any 10 ug/m3 increase will result in an 8% increase in risk. For example, an increase from 25 to 35 ug/m3 would yield an 8% increase in risk, just as an increase from 55 to 65 ug/m3 would yield an 8% increase in risk. In table 1, if seems as though the results from Pope et al. have been interpreted differently. The authors seem to imply no risk at concentrations less than 10 ug/m3 and an additional 8% increase in risk for each 10 ug/m3 increase in PM2.5 concentration. This is not correct. If I am misinterpreting the table, the text should be clarified to help the reader understand the comparison that is being made.
Revision detail:
Many thanks for the suggestions and we are sorry for that. We agree with that the Pope et al. study describes the slope of a linear relationship, and any 10 µg/m3 increase in PM2.5 will result in an 8% increase in lung cancer mortality risk. We have changed the methodology to estimate lung cancer deaths based on the study by Pope III et al. according to this comment (Table 1 has been reedited). Firstly, we took 10 µg/m3 change in PM2.5 as an increment and classified the PM2.5 concentrations into six levels artificially (0-10 µg/m3, 10-20 µg/m3, 20-30 µg/m3, 30-40 µg/m3, 40-50 µg/m3 and 50-60 µg/m3) for analyzing the population status within the scope of different PM2.5 concentrations. Then, we assumed that there was no risk at concentration of 0 µg/m3, thus, an increase from 0 to 10

µg/m3 would yield an 8% increase in risk. So when we estimate the number of lung cancer fatalities on the level of 0-10 µg/m3, we took the mean value of the two increased risks as the increase rate in the risk of lung cancer mortality, which was 4%. Similarly, an increase from 10 to 20 µg/m3 would also yield an 8% increase in risk, and the increase in the risk of lung cancer mortality in the level of 10-20 µg/m3 would be 12%; and the increase in the risk of lung cancer mortality in the level of 20-30 µg/m3, 30-40 µg/m3, 40-50 µg/m3 and 50-60 µg/m3 were thereby 20%, 28%, 36% and 44%, respectively. Based on that, the number calculated by Pope III et al. changed to 614,860, which is also very close to the lung cancer fatalities in China in 2012. Revision details according to this comments in the manuscript are listed below:
On page 1, line 47, ABSTRACT Section, "the number calculated by the American Cancer Society (ACS)" has been changed to 614,860;
On page 2, lines 51-52, the sentence "the annual average concentration of 10 µg/m3 was regarded by ACS as a long-term guideline level for PM2.5." has been deleted;
On page 6, the Paragraphs 2 of the "Statistics analysis" Section has been rewritten, and Table 1 has also been reedited.
On page 10, "Estimates of the potential risk of mortality from lung cancer associated with PM2.5" Section, Table 3 has been reedited, and "the number calculated by the American Cancer Society (ACS)" has been changed to 614,860 in the last paragraph of this part.

2. Page 10, Table 3: The numbers of lung cancer deaths attributed to Pope et al. and WHO are opposite those reported in the abstract. Similarly the text on page 10, line 56 seems to indicated that the 595,000 deaths are the result of using the Pope effect estimate, which doesn't match up with what is in the table. The bigger problem, however, is that I do not believe that the effect estimate from Pope et al. can be used to estimate lung cancer deaths the same way that the WHO Air Quality Guidelines can (see comment above about misinterpretation of results from Pope et al. in Table 1).
Revision detail:
Many thanks for reminding, it was a mistake in Table 3, and we are sorry for that. We have reedited Table 3, and the correct number of lung cancer fatalities calculated by the WHO AQGs ranged from 531,036 to 532,004, whereas the correct number calculated by the American Cancer Society (ACS) reached 614,860.
We have changed the methodology to estimate lung cancer deaths based on the study by Pope III et al.. On page 6, the Paragraphs 2 of the "Statistics analysis" Section relating to the methodology has been rewritten, and Table 1 has also been reedited.

3. Page 11, Conclusions: Need to mention that while you have several years of PM2.5 estimates, this still doesn't match up with the latency period for lung cancer. Is there any evidence that the ranking of PM2.5 concentrations would have remained the same over the past 30 to 40 years? If so, please include that evidence. Either way, please include this as a limitation/uncertainty.
Revision detail:
Many thanks for the suggestion. We agree with that these several years of PM2.5 estimates couldn't match up with the latency period for lung cancer. There is no evidence that the ranking of PM2.5 concentrations would have remained the same over the past 30 to 40 years in China since the refined PM2.5 data were not reported until 2012 and the national monitoring PM2.5 data was still deficient so far. Thus, we include this as an uncertainty here and have revised in the last paragraph of "Conclusions" Section in Page 11.

Minor comments:
1. Page 7, lines 2 and 3: change to "in this study we assumed that the risk of lung cancer did not increase with long-term exposure...."
Revision detail:
Thank you for the suggestion. We have revised the sentence according to this comment.

2. Page 8, lines 30 and 31: delete "(Sig, <0.01)". Of course these are statistically significant, they are R values. The p-values for these are meaningless.
Revision detail:
Many thanks for the reminding. "(Sig, <0.01)" has been deleted according to this comment.

VERSION 2 – REVIEW

REVIEWER	C. Arden Pope, III Brigham Young University, Provo, Utah
REVIEW RETURNED	16-Sep-2015

GENERAL COMMENTS	The reviewer completed the checklist but made no further comments.

REVIEWER	Tom Luben United States Environmental Protection Agency
REVIEW RETURNED	17-Sep-2015

GENERAL COMMENTS	While the authors have made a few minor revisions to address reviewers' comments, they continue to grossly misinterpret the results from the Pope III et al. study. The 8% increase in risk associated with a 10 ug/m3 increase in PM2.5 represents a beta coefficient from the regression model of 0.077. This describes the slope of the line characterizing the association of PM2.5 and lung cancer mortality in this study. Because this relationship is characterized as linear, the risk is constant for any 10 ug/m3 increase in PM2.5 concentration. That is, if PM2.5 increases from 0-10, the risk is 8%. If PM2.5 increases from 50 to 60, the risk is STILL 8%. The way the authors have determined risk in Table 1 is wrong. It is not appropriate to use the results from the Pope III et al. study in this way. Due to this misinterpretation, the text on page 5, lines 18-33 is wrong. The authors should not use the results of Pope III et al. in this type of analysis. I recommend that the authors delete any reference to the results of Pope III et al. in this part of the manuscript, and instead focus only on the WHO AQG analyses. Additionally, the authors should acknowledge the discrepancy in spatial resolution between the PM2.5 exposure estimates and the lung cancer mortality rates. While the PM2.5 estimates they use come from a model with fine spatial resolution, the benefit of this is lost when it is paired with lung cancer mortality data that is available at the province level.

VERSION 2 – AUTHOR RESPONSE

Reviewer 1 comments:
1. The authors have been reasonably responsive to previous comments and suggestions.
Revision detail:
Thank you so much for your appreciate.

Reviewer 2 comments:
1. While the authors have made a few minor revisions to address reviewers' comments, they continue to grossly misinterpret the results from the Pope III et al. study. The 8% increase in risk associated

with a 10 ug/m3 increase in PM2.5 represents a beta coefficient from the regression model of 0.077. This describes the slope of the line characterizing the association of PM2.5 and lung cancer mortality in this study. Because this relationship is characterized as linear, the risk is constant for any 10 ug/m3 increase in PM2.5 concentration. That is, if PM2.5 increases from 0-10, the risk is 8%. If PM2.5 increases from 50 to 60, the risk is STILL 8%. The way the authors have determined risk in Table 1 is wrong. It is not appropriate to use the results from the Pope III et al. study in this way. Due to this misinterpretation, the text on page 5, lines 18-33 is wrong. The authors should not use the results of Pope III et al. in this type of analysis. I recommend that the authors delete any reference to the results of Pope III et al. in this part of the manuscript, and instead focus only on the WHO AQG analyses.
Revision detail:
Many thanks for your suggestions. We agree that Pope III et al.'s study describes the slope of the line characterizing the association of PM2.5 and lung cancer mortality, and the risk is constant for any 10 ug/m3 increase in PM2.5 concentration. However, in Table 1, "50-60 μg/m3" does not refer to the concentration of PM2.5 increase from 50 μg/m3 to 60μg/m3. It means the concentration level (range from 50 μg/m3 to 60μg/m3) which human long-term exposures to. The mortality risk under the level of 50-60 μg/m3 won't be 8% obviously. In this study, we classified the PM2.5 concentrations into six levels artificially [Level 1 (0-10 μg/m3), Level 2 (10-20 μg/m3), Level 3 (20-30 μg/m3), Level 4 (30-40 μg/m3), Level 5 (40-50 μg/m3) and Level 6 (50-60 μg/m3)]. We assumed that there was no risk at concentration of 0 μg/m3, thus, an increase from 0 to 10 μg/m3 would yield an 8% increase in risk according to the study by Pope III et al.. So when we estimated the number of lung cancer fatalities in Level 1, we took the mean value of the two increased risks as the increase rate in the risk of lung cancer mortality, which was 4%. Similarly, an increase from 10 to 20 μg/m3 would also yield an 8% increase in risk, and the increase in the risk of lung cancer mortality in Level 2 would be 12% and so on. This assumption was supported by both the study of "Lung Cancer, Cardiopulmonary Mortality, and Long-term Exposure to Fine Particulate Air Pollution" and Reviewer 1. In order to make the assumption more clear for understanding, we made some revisions in Table 1 and in the Paragraph 2 of the "Statistics analysis" Section according to Reviewer2's comment. We think that our research based on the ACS study of Pope III et al. and WHO AQGs can serve as a valuable reference for the risk evaluation of PM2.5 air pollution related diseases. The estimation of potential risks of mortality associated with lung cancer caused by exposure to high PM2.5 concentrations based on the ACS study of Pope III et al. is a good contrast to the estimation based on the WHO AQGs. So, we recommend that reference to the results of Pope III et al. should be involved in this part of the manuscript.
We are sorry for vague statement and we have revised the manuscript according to this comment for better understanding.

2. Additionally, the authors should acknowledge the discrepancy in spatial resolution between the PM2.5 exposure estimates and the lung cancer mortality rates. While the PM2.5 estimates they use come from a model with fine spatial resolution, the benefit of this is lost when it is paired with lung cancer mortality data that is available at the province level.
Revision detail:
Many thanks for reminding. We agree that the benefit of fine spatial resolution of PM2.5 dataset is lost when it is paired with lung cancer mortality data that is available at the province level. However, this dataset still provides a continuous surface of concentrations (micrograms per cubic meter) of PM2.5 for health and environmental research. In addition, population-based cancer registries are not well established and the epidemiologic data for cancer are limited in China. Li et al. (Li et al., 2011) produced the dataset of estimated mortality from lung cancer based on the population coverage and accuracy of the available mortality for provinces. We adopted the data in this study due to its reliability for mortality from lung cancer by province and it can well provide a valuable scientific reference for epidemiology until a new and more accurate lung cancer mortality report is published in China. If more accurate and perfect datasets can be obtained, systematic studies will be given in the future. The limitation of lung cancer mortality at the province level was stated in the Section of "Strengths and

limitations of this study”. We also made some revisions according to this comment in Paragraph 3 in Section “Data acquisition” for better understanding of the dataset.