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Atmospheric Chemistry and Physics Discussions
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Interactive comment on "Effects of AIR pollution on cardiopuLmonary disEaSe in urban and peri-urban reSidents in Beijing: protocol for the AIRLESS study" *by* Yiqun Han et al.

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Response to referee #1

Overall: Thank you for your comments and useful suggestions to improve our manuscript. We acknowledged that despite this is an overview paper of AIRLESS project with the focus on methodology, more results are warranted for the readers to understand the studied participant, including their demographic characteristics, and the levels of exposure and health outcomes. Therefore, we have restructured the paper and added more preliminary results accordingly. Please find below the point-to-point response. Detailed table and figures will be finalized and added in the updated

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manuscript.

Comment 1: For the health part, it's important to know the basic demographic statistics of the participants in both urban and peri-urban sites. E.g. the attended clinical visits, distributions of age, gender, socioeconomic status, baseline exposure status, etc. Is there any significant difference between the two groups? Are you going to compare to the two groups of participants or treat them as two different cohorts? In addition, it would be useful to have some descriptive results related to the measurements of health outcomes.

Thank you for this suggestion. We have added more analysis to summarize the key characteristics (age, BMI, gender, smoking, annual income, education level), health biomarkers, with an exemplary table as attached. Detailed table and figures will be finalized and added in the updated manuscript. Generally, we treated the residents in urban and peri-urban area of Beijing as two different groups of participants. The characteristics of both ambient air pollution/sources, health conditions, and baseline demographic characteristics are different. Generally, compared with peri-urban participants, urban residents were older, had a lower BMI, and a higher educational and income level at the baseline, as shown in the attached table.

Comment 2: For personal exposure, it's crucial to have some results to validate the performance of PAM with reference instruments. How did you calibrate the instruments, and how well they agree with the reference instruments? What's the measurement range and error? What's the performance of PAM for different microenvironments (i.e. indoor and outdoors)? It's also important to know the completeness of personal exposure monitoring (e.g. how many validate days for the personal dataset, etc), as carrying personal monitors for 7 days is not common in an epidemiological study which would cause a lot burden.

Thank you for this comment. We have added a summary of a previous publication which characterised the performance of the sensors integrated in the PAM thoroughly.

Briefly, the collocation experiment has considered different scenarios (outdoor, indoor, transportaiton)ïijŇand the statistics of measurement range and error were also reported under different microenvironment. The corresponding changes in the method section of the manuscript is as below: All PAMs were calibrated with two outdoor co-location deployments at the PKU urban site after the winter and summer deployments to participants. The performance of the NO2 and PM2.5 sensors was additionally characterised in an indoor microenvironment next to commercial instruments. Overall, the air pollution sensors showed high reproducibility (mean adj R2= 0.93, min–max: 0.80–1.00) and excellent agreement with standard instrumentation. In the winter co-location deployment adj.R2>0.84 for all sensors, while in the summer adj R2>0.71. There were some indications that the EC sensor performance is less reliable at high temperatures (>40°C); however, such extreme thermal conditions were not recorded during the deployment to participants. Further work showed that the error of the PAM was negligible compared with the error introduced when deriving exposure metrics from fixed ambient monitoring stations close to the participants' residential addresses. Hence, novel sensing technologies such as the ones used here are suitable for collecting highly resolved personal exposure measurements in large-scale health studies.

Comment 3: A summary of key air pollutants in both urban and rural sites during the health campaign periods in two seasons would lead the readers with a better understanding of the background AP settings, which can be useful to compare with other health studies around the world.

Thank you for this comment. We have added in the manuscript a whisker box plots illustrate ambient concentrations of CO and PM2.5 measured at the reference monitoring stations and personal concentrations at the urban and peri-urban sites during the winter (Nov-Dec 2016) and summer (May-June 2017) campaigns. Detailed statistics of other pollutants measured concurrently in PAM and fixed monitoring station will be summarized in a supplement table.

Comment 4: Comparison of personal exposure with examples from certain participants, and capture rate of personal exposure data.

We appreciated this comment. An exemplary plot of personal exposure to multiple pollutants of a certain participant (U123) was added in our manuscript, as attached. The plot also includes the ambient concentration of the corresponding pollutant, along with the time-activity (i.e. indoor vs. outdoor) to illustrate the difference between personal and ambient exposure. âĂČ

Response to referee #2

Overall: Thank you for taking the time to provide valuable feedback. This paper presented the methodological framework for the collection of detailed medical biomarkers and exposure estimates as part of the AIRLESS project (Beijing, China). The comments are extremely relevant as the reviewer has a clear understanding of current gaps in our understanding of the effects of air pollution on health and the potential of projects like AIRLESS to address such issues. Regarding the reviewer's comment, we have added more tables and figures into the results and discussion session. The manuscript has also been restructured and certain sections has been revised accordingly. Please find below the point-to-point response.

Comment 1a: "The association, if identified, may not directly reflect the true toxicity of health effect for a pollutant but an alternation of source-related effect."

This comment hits the nail on the head. We have re-written parts throughout the manuscript to stress this point. We have modified the background section to stress the four wider research gaps this project aims to address: a) To investigate the interactive effects of air pollution and hypertension. b) To establish more reliable links between air pollution and health effects by reducing exposure misclassification. c) To differentiate source-related health effects of air pollution. d) To investigate the underlying mechanism of air pollution on health. Using novel sensor technologies, we capture personal exposure at high spatial and temporal resolution and break the correlation between traffic related pollutants such as PM2.5 and NO2 often observed at fixed monitoring

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sites (due to common emission sources). By reducing the correlation between individual pollutants, we can assign specific health effects to individual pollutants (or to different sources, i.e indoor NO2 has different sources than outdoor NO2 and therefore is a proxy for different pollutants).

Comment 1b: "For the health outcomes, the multiple biomarkers from the same pathways may generate an issue of multiple comparison (or not)."

Thanks for the comment from the reviewer. We reckon the number of biomarkers in the study will increase in the difficulties in explaining the biological mechanisms, as some of the biomarkers may share similar pathways or be regulated in a more complicated biological network (eg. Cytokines). The fast development of omic-related analysis, which could generate thousands of biomarkers, will be helpful but meanwhile add more challenge in understanding the biological mechanism. We have considered this issue for the analysis of multiple biomarkers. Specifically, to investigate the associations between the exposure to air pollutant and the changes in metabolome and transcriptome, false discovery rate (FDR) adjusted p-value will be applied to detect the statistical significance. Pathway enrichment analyses based on the changes in multiple biomarkers will be used to investigate potential mechanisms.

Comment 2: regarding to low-cost sensor technologies, "sensor technology is complex and requires careful calibration both internally within device and externally across the devices and with other standard instruments under various environmental circumstances. The current study only reported the specifications and performances of the PAM monitor, but did not include detailed descriptions on how to ensure the accuracy of the monitors in the real world measurements."

Thanks for the comment from the reviewer. We understand the importance of the validation of the personal monitor (PAM) we used in this study. The performance of the sensors integrated in the PAM has been characterised extensively in a previous publication. To clearly describe the performance of PAM and the collocation experiment,

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a paragraph has been added in the manuscript as below: All PAMs were calibrated with two outdoor co-location deployments at the PKU urban site after the winter and summer deployments to participants. The performance of the NO2 and PM2.5 sensors was additionally characterised in an indoor microenvironment next to commercial instruments. Overall, the air pollution sensors showed high reproducibility (mean adj R2= 0.93, min–max: 0.80–1.00) and excellent agreement with standard instrumentation. In the winter co-location deployment adj.R2>0.84 for all sensors, while in the summer adj R2>0.71. There were some indications that the EC sensor performance is less reliable at high temperatures (>40°C); however, such extreme thermal conditions were not recorded during the deployment to participants. Further work showed that the error of the PAM was negligible compared with the error introduced when deriving exposure metrics from fixed ambient monitoring stations close to the participants' residential addresses. Hence, novel sensing technologies such as the ones used here are suitable for collecting highly resolved personal exposure measurements in large-scale health studies.

Comment 3: The results are relatively simple. At least, the demographics of the study population and the exposure and outcome measurement statistics are needed, so that it is good for readers to understand the overall differences of exposure and outcomes between the two study sites. The results will also help support the proposed hypothesis of the study.

Thanks for the comment, apart from the recruitment summary in the manuscript, we have added more analysis to summarize the key characteristics (age, BMI, gender , smoking, annual income, education level), health biomarkers, as well as a boxplot to compare the exposure level between urban and peri-urban subjects in the manuscript, with an exemplary table as attached. Detailed table and figures will be finalized and added in the updated manuscript.

Comment 4: Only the outdoor monitoring sites include detailed air pollutant species as compared to the personal exposure. Thus, the importance of the contributions of the

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species to the personal exposure seems to be attenuated. Will it be possible to use the GPS data to split outdoor and indoor exposure in the health analysis, so that the comparisons are relatively fair? Thanks for the comment, this is really an important question to understand the health effect of pollutant species. Currently, personal sensors were not applicable to a wide range of pollutant species, especially considering the performance of measurement at a high time-resolution. The common commercial portable monitors used in most of the epidemiological studies are usually targeted on either particles (PM2.5, BC, etc), or gaseous pollutants (NO2, CO etc). The personal monitor we used was developed ourselves which is unique to include both PM and gaseous sensors in one device. This enable PAM to measure PM in different size fraction, and four species of gaseous pollutants, which will help us to understand the health effect of the most concerned pollutants. We have updated Table 2 in the manuscript to describe the physical and chemical parameters of both ambient and personal exposure measurement. Apart from that, we have also considered the suggestion the reviewer of splitting indoor/outdoor exposure to give a more accurate exposure assessment. A automated model was developed to classify time-activity-location patterns based on parameters collected with the PAMs (GPS, background noise, acceleration)2, which has been described in our newly published paper. The classifications include core location categories: “home”, “work”, “other indoor static”, “other outdoor static”, “ travel”, as well as activities “cooking”, “sleeping” and modes of transport (“walk”, “cycle”, “motorbike”, “car/bus”, “train/tube”). We have now created a new subsection to highlight this methodological element of the project.

References: 1 Chatzidiakou, L., Krause, A., Popoola, O. A., Di Antonio, A., Kellaway, M., Han, Y., ... & Fan, Y. (2019). Characterising low-cost sensors in highly portable platforms to quantify personal exposure in diverse environments. Atmospheric measurement techniques, 12(8), 4643. 2. Chatzidiakou, L., Krause, A., Popoola, O. A., Di Antonio, A., Kellaway, M., Han, Y., ... & Fan, Y. (2019). Characterising low-cost sensors in highly portable platforms to quantify personal exposure in diverse environments. Atmospheric measurement techniques, 12(8), 4643.

Please also note the supplement to this comment:
https://acp.copernicus.org/preprints/acp-2020-208/acp-2020-208-AC1-supplement.pdf

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