PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Effects of exposure to direct and secondhand hookah and e-cigarette aerosols on ambient air quality and cardiopulmonary health in adults and children: protocol for a panel study
AUTHORS	Shearston, Jenni; Lee, Lily; Eazor, James; Meherally, Saher; Park, Su Hyun; Vilcassim, M. J. Ruzmyn; Weitzman, Michael; Gordon, Terry

VERSION 1 – REVIEW

REVIEWER	DAUTZENBERG Bertrand Pitié-Salpêtrière universitary hospital Paris, France, Institut Arthur Vernes Paris, France
REVIEW RETURNED	23-Feb-2019

GENERAL COMMENTS	BMJ Open 2019-029490 This description of a protocol on exposure to direct and second-hand exposure to emission of e-cigarette and Hookah is globally well design and well presented. The interest of this study is high. Remarks are mainly minor and can probably be easily solved by the authors. **Abstract:** The groups are difficult to understand at the first lecture of the abstract (easy to understand with figure page 22) You describe the two control groups (non-smoking/non-vaping) OR cigarette smoking You describe the two exposure groups smoking AND e-cigarette vaping 2 questions • why did you name "exposure group" in the abstract and "test group" in the figure: "Test groups" appear more appropriate int the abstract (and in all the text as in the figure.

	• Why did you use OR to separate control groupe and AND to separate test groups **Ethics consideration** There is no Ethics consideration in the paragraph Ethics and dissemination of the abstract and in the chapter Ethics and Dissemination of the text. Your paper had to present some ethical consideration, mainly for children use in the study. Many parents who smoke or vape don't smoke or vape in the real world in the room where the children are. In the protocol you impose to all children to stay in the room where on a parent use hookah for one hour. In this condition some adverse effects may occurred. For the family who never use Hookah (or cigarettes) in the room were children stay, family have to be inform than it is not an optimal situation for the children to breath this air, but in compensation they will received feedback about this effect and parents could be encourage to better protect children for the future, and this better prevention for the future could largely compensate the effects of one hours of exposure to tobacco emissions. If parents usually use cigarette, hookahs in the same room, such information to parents is not need. **INTRODUCTION** In the literature children under 10 yo are more susceptible to be affected by passive smoking, cigarettes or hookah, and probably passive vaping. I fully agree to include only children 10-18 yo for the study, but a sentence is needed to explain why you don't study the youngers children (for ethical and technical problems?) **Air quality assessment** Page 7: you ask parent to don't smoke in house 48 hours previous the study (OK) Page 11: you write: If you are smoker to refrain to smoke 24 hours before the measure and during the 24 hours of the study. Why you don't ask vaper to don't vape during the same period?

	e-liquide don’t contain tobacco and are not scientifically tobacco product and cannot be included in the sentence (...use tobacco product) If you ask patient to smoke for 24 hours, you may expect a very intensive use of nicotine containing product during the hour of the study, the smoking during this hour will be not representative of the real life 'It is not a severe problem, but conditions of study had to be explained for interpretation of the results. Page 5: you propose 50 minutes of vaping; page 7 you propose 50-60 minutes of smoking. Why you don’t use the same duration of use for the 2 products?? **Comparison of air quality in groups** Page 7 and 9 for control you assess air quality for 60 minutes and you can anticipate few variations of measurement For test group you measure air 15 minute the study (probably to control the blank) but after the initiation of smoking/vaping one may anticipate a linear increase of air pollution until sixty minutes, then a decrease after 60 minutes for the 15 minutes post exposure. Please explain how you plan to compare quality of air in exposed room. Did you plane to use the mean of the 60 minutes or the max exposure during the period (at the end of 60 minutes) or the exposure of the last thirty minute of exposure or others? The decision had to be taken before you start to record data and must be describe in the paper. **e-cigarette is not a tobacco product in EU and in many countries** Table page 17: e-cigarette don’t contain tobacco and are not consider as a tobacco product in EU as also in numerous countries in the world, it would be easy to describe in each case product concerned **Figure** Boxe 4 - 5 and 7-8 as you don’t want to have vaping children or adult in theses boxes is better to write as in the last boxes “non-

	using” (and you may have a footnote "non-using = not using any tobacco product or e-cigarette" Page 23 in the figure it would be better to don’t use the term smoking for e-cigarette Figure 2 Replace pre-smoking by pre-use of study product Smoking by use of study product Post smoking: by post use of smoking product Another solution could be to replace smoking by smoking/vaping in the 3 sentences

REVIEWER	Florian Fischer Bielefeld University, Germany
REVIEW RETURNED	25-Mar-2019

GENERAL COMMENTS	The study protocol adresses an important research question. It is very clear. However, I would like to add the following comments for improvement: - The authors mention a cross-sectional design. This is not true, because it is a pre-post-exposure-design and data collection takes places over four years. - The authors should adress issues related to a selection bias, which may occur due to the recruitment strategy.

REVIEWER	Manfred Neuberger Medical University of Vienna, Austria
REVIEW RETURNED	14-Apr-2019

GENERAL COMMENTS	This is a very well prepared study on acute effects of one ore more adults using tobacco, shisha or e-cigarettes in the home on one or more non-users aged 10 years or older living in the same household. The most challenging task will be the recruitment of participants. Different selection bias in the non-smoking/vaping, hookah and vaping group need to be omitted or corrected. The inclusion items in table 1 are well prepared, but depending on the height of compensation (gift card) wrong answers might occur. Answers of active users and of children or other passively exposed persons should be taken separately and be compared. Some persons could be regarded as eligible from questionnaire, but might have to be excluded from results of lab tests at first visit before exposure. Nicotine addicts might not be able to refrain from smoking or vaping inside the home for 48 hours and this should be verified at first visit. The same applies to possible dual use of tobacco and e-cigarettes or hookah. Problematic is strategy 3 of

	recruitment, because inclusion of tobacco retailers might give tobacco industry and tobacco trade a possibility to influence results. Even after 48 hours without smoking/vaping inside the home, baseline air measurements are expected to show remnants of toxins released from third hand smoke on surfaces, which have a longer half-life than nicotine. Also it has to be taken into account, that persons returning from smoking or vaping on a balcony or a staircase are expected to bring some nicotine, PAH and other toxins with their breath, clothes, hair and skin into the appartment. Limitations are given correctly, however, it will be difficult to disentangle acute effects from chronic effects on passive smokers/vapers.

VERSION 1 – AUTHOR RESPONSE

RESPONSE TO REVIEWERS

Reviewer(s)' Comments to Author:
Reviewer: 1
Reviewer Name: DAUTZENBERG Bertrand
Institution and Country: Pitié-Salpêtrière universitary hospital Paris, France, Institut Arthur Vernes Paris, France

This description of a protocol on exposure to direct and second-hand exposure to emission of ecigarette and Hookah is globally well design and well presented. The interest of this study is high. Remarks are mainly minor and can probably be easily solved by the authors.

- Replace presmoking by pre use of study product Smoking by use of study product Post smoking by pos use of smoking product. Another solution could be to replace smoking by smoking/vaping in the 3 sentences.
    - *The figure has been altered to use the phrase "use of study product" rather than smoking.*

ABSTRACT:

- The groups are difficult to understand at the first lecture of the abstract (easy to understand with figure page 22).You describe the two control groups (non-smoking/non-vaping) OR cigarette smoking. You describe the two exposure groups smoking AND e-cigarette vaping. 2 questions: Why did you name "exposure group" in the abstract and "test group" in the figure: "Test groups" appear more appropriate int the abstract (and in all the text as in the figure). Why did you use OR to separate control groupe and AND to separate test groups
    - *To address this, we have revised the sentence describing the four groups in the abstract to: "This study uses a pre/post design, with four groups: two control groups (non-smoking/non-vaping and cigarette smoking) and two test groups (hookah smoking and e-cigarette vaping)."*
    - *We have also changed "exposure groups" to "test groups" throughout the text of the manuscript.*

ETHICS CONSIDERATION

- There is no Ethics consideration in the paragraph Ethics and dissemination of the abstract and in the chapter Ethics and Dissemination of the text. Your paper had to present some ethical consideration, mainly for children use in the study.
    - *Discussion of ethics has been added to the Ethics and Dissemination sections of the abstract and text.*
        - *Abstract: "This study was approved by the Institutional Review Board at New York University School of Medicine (s16-02226 and s17-01143). Special*

attention was given to the inclusion of children, who are likely significantly impacted by use of these products at home, and thus should be included in research. Results of the study will be distributed at conferences, in peer-reviewed journals, and to relevant public health authorities for use in developing policy."

- *Text: "This study was reviewed and approved by the Institutional Review Board at New York University School of Medicine (s16-02226 and s17-01143). The study design was discussed with the ethics committee extensively during institutional review. During study design and protocol development, special consideration was given to the inclusion of children and the measures that would be obtained from them. Because children are particularly impacted by exposure to secondhand smoke, and potentially to exposure from secondhand e-cigarette aerosols, we feel that it is essential to include them in the study. In order to ensure minimal risk, all data and measures collected from children fall within the range of measures they may be asked to complete in a typical doctor's visit. Additionally, study staff are specially trained on how to interact with children, and to engage children in data collection by explaining every measure, showing the children how to use the instruments, and engaging them in the process of data collection (i.e., showing children how to measure the dimensions of the room as it is done, asking them to participate by pressing the "on" button on the blood pressure monitor). However, after careful consideration, we decided not to include children under the age of five because it would be challenging for them to complete the large range of repeat tests, some of which rely upon participant effort (i.e. spirometry), and would potentially result in fatigue for the children and reduced quality of data collection. Children aged 5-9 are not asked to complete spirometry or heart rate variability, for this reason. Of note, we do not require children involved in the study to stay in the same room as adults while they are using cigarettes, hookah, or e-cigarettes; instead, families are encouraged to behave as they would normally behave, including staying in the portion of the house they would normally stay in during such activities. While this does introduce some additional variability in exposure into the study, it is also more representative of true behaviors and, we believe, more ethically sound.*

- Many parents who smoke or vape don't smoke or vape in the real world in the room where the children are. In the protocol you impose to all children to stay in the room where on a parent use hookah for one hour. In this condition some adverse effects may occurred.
    - *This is an important point and consideration. For ethical reasons, we do not require that children stay in the same room as their smoking or vaping parent. We also want to assess "real-world" exposures, and we agree that many parents do not smoke or vape in the same room as their child. For this reason, we do not place any restrictions on the location of the child, as long as they stay inside the house. We encourage parents and children to do as they normally would during the smoking or vaping session, whether that means staying in the same room or going to a different one. To clarify this in the manuscript, we have added the following sentences in the fourth paragraph of the 'Air Quality Assessment' section: "No restrictions on the movement of the non-smoking/vaping adult and child will be made during the smoking/vaping session; children will not be required to stay in the same room as the smoking or vaping adult. The goal is to assess effects from real world exposures in the home, and many parents do not smoke or vape in the same room as their children, in order to protect them from potential harm."*
- For the family who never use Hookah (or cigarettes) in the room were children stay, family have to be inform than it is not an optimal situation for the children to breath this air, but in compensation they will received feedback about this effect and parents could be encourage to better protect children for the future, and this better prevention for the future could largely compensate the effects of one hours of exposure to tobacco emissions. If parents usually use cigarette, hookahs in the same room, such information to parents is not need.
    - *We agree with your well-made point. We hope the above sentences will make it clear to the reader that children are not required to stay in the room with parents as they smoke or vape.*

INTRODUCTION

- In the literature children under 10 yo are more susceptible to be affected by passive smoking, cigarettes or hookah, and probably passive vaping. I fully agree to include only children 10-18 yo for the study, but a sentence is needed to explain why you don't study the youngers children (for ethical and technical problems?)
    - *Please note, in the time between the original submission of the manuscript and this revision, and amendment to the IRB was submitted to enroll children down to the age of 5, but while asking this subgroup of children to complete less measures.*
    - *You are correct in presuming that children younger than 5 were not included for ethical and technical problems. To clarify, this, the following sentence has been added to the third paragraph of the 'Design, Setting, and Participants' section: "Children under the age of 5 are excluded both for ethical reasons and due to the technical difficulty of having young children complete multiple measures in a small space of time. In addition, children aged 5-9 will not be asked to complete heart rate variability or spirometry."*

METHODS

Air quality assessment

- Page 7: you ask parent to don't smoke in house 48 hours previous the study (OK). Page 11: you write: If you are smoker to refrain to smoke 24 hours before the measure and during the 24 hours of the study. Why you don't ask vaper to don't vape during the same period? e-liquide don't contain tobacco and are not scientifically tobacco product and cannot be included in the sentence (...use tobacco product)
    - *Thank you for catching this. We did in fact mean to include people who vape as well. The sentence has been changed to: "Finally, although participants are asked to refrain from using study products 24 hours before the home visit and between the first and second home visit, it cannot be guaranteed that participants comply."*
- If you ask patient to smoke for 24 hours, you may expect a very intensive use of nicotine containing product during the hour of the study, the smoking during this hour will be not representative of the real life 'It is not a severe problem, but conditions of study had to be explained for interpretation of the results.
    - *This is a great point, thank you. An additional sentence has been added to the 'Limitations' subsection to specify this: "Also of note is that participants who refrain from study product use in the period before the home visit may smoke/vape more intensely during the home monitoring session, particularly if they are suffering from nicotine withdrawal, making the measured air quality and biologic effects not truly representative of a typical smoking/vaping experience."*
- Page 5: you propose 50 minutes of vaping; page 7 you propose 50-60 minutes of smoking. Why you don't use the same duration of use for the 2 products??
    - *Thank you for noting this inconsistency. We intend that individuals use their respective product as many times as they like during an approximately 50 minute window. The language on page 7 has been changed to "approximately 50 minutes."*

Comparison of air quality in groups

- Page 7 and 9 for control you assess air quality for 60 minutes and you can anticipate few variations of measurement. For test group you measure air 15 minute the study (probably to control the blank) but after the initiation of smoking/vaping one may anticipate a linear increase of air pollution until sixty minutes, then a decrease after 60 minutes for the 15 minutes post exposure. Please explain how you plan to compare quality of air in exposed room. Did you plane to use the mean of the 60 minutes or the max exposure during the period (at the end of 60 minutes) or the exposure of the last thirty minute of exposure or others? The decision had to be taken before you start to record data and must be describe in the paper.
    - *We have now clarified how air quality will be compared between the groups in the first paragraph of the 'Data Analysis' section. The addition reads: "Data for all continuous variables will be summarized with descriptive statistics (e.g., mean, SD, median, and 95% CI) for the 15 min control period before the session, the ~50 min session, and the duration of the post-smoking/vaping session."*
- e-cigarette is not a tobacco product in EU and in many countries

- *Thank you for noting this error. The phrase "alternative tobacco products" is no longer used, and has been replaced with "alternative nicotine delivery products." In addition, we have revised "non-smoking" to "non-smoking/non-vaping" throughout the manuscript, where appropriate.*

TABLE 1

- page 17: e-cigarette don't contain tobacco and are not consider as a tobacco product in EU as also in numerous countries in the world, it would be easy to describe in each case product concerned
  - *Table 1 has been revised to consistently say "nicotine or tobacco product."*

FIGURE 1

- Boxe 4 - 5 and 7-8 as you don't want to have vaping children or adult in theses boxes is better to write as in the last boxes "non-using" (and you may have a footnote "non-using = not using any tobacco product or e-cigarette") Page 23 in the figure it would be better to don't use the term smoking for e-cigarette
  - *Thank you for these suggestions; both have been implemented. "Non-Smoking" has been changed to "Non-Using" and a footnote has been added, in the 'Figure Legends' section.*

FIGURE 2

- Replace pre-smoking by pre-use of study product, Smoking by use of study product, Post smoking: by post use of smoking product. Another solution could be to replace smoking by smoking/vaping in the 3 sentences.
  - *The figure has been altered to use the phrase "use of study product" rather than smoking.*

Reviewer: 2
Reviewer Name: Florian Fischer
Institution and Country: Bielefeld University, Germany

Please leave your comments for the authors below:
The study protocol addresses an important research question. It is very clear. However, I would like to add the following comments for improvement:

- The authors mention a cross-sectional design. This is not true, because it is a pre-post-exposure-design and data collection takes places over four years.
  - *The term "cross-sectional" is no longer used to describe the overall study design, and instead "pre/post exposure" is used. The title has been revised to "Effects of exposure to direct and secondhand hookah and e-cigarette aerosols on ambient air quality and cardiopulmonary health in adults and children: protocol for a panel study."*
- The authors should address issues related to a selection bias, which may occur due to the recruitment strategy.
  - *In the 'Limitations' section we note that selection bias may occur and that the results of the study may not be generalizable. In addition, we have added the following sentence: "However, demographic information from the study participants can be compared to that of smokers and vapors from the NYC Hanes surveys to determine comparability (nychanes.org)." Also, we have added an additional paragraph to the 'Data Analysis' section to describe the handling of differential selection bias among groups.*

Reviewer: 3
Reviewer Name: Manfred Neuberger
Institution and Country: Medical University of Vienna, Austria

Please leave your comments for the authors below:

- This is a very well prepared study on acute effects of one or more adults using tobacco, shisha or e-cigarettes in the home on one or more non-users aged 10 years or older living in the same household. The most challenging task will be the recruitment of participants.

Different selection bias in the non-smoking/vaping, hookah and vaping group need to be omitted or corrected.

- *We agree that selection bias is likely to be an issue. To ensure selection bias is not different between study groups, we will compare the groups on demographic characteristics. This has now been noted in an additional paragraph in the 'Data Analysis' section: "All groups will be compared on demographic characteristics, including gender, age, race, education, and household income, to ensure there is not differential selection bias. This will be assessed part way through the study, so that selective recruitment of under-represented groups can be completed to re-balance study groups if needed."*

- The inclusion items in table 1 are well prepared, but depending on the height of compensation (gift card) wrong answers might occur.
  - *We agree that this is particularly challenging; while some potential participants have suggested that the gift card amount is not high enough, other callers have seemed inconsistent in their reporting of nicotine/tobacco product use, perhaps because of the amount. Overall, we feel that we have struck a balance in the middle. The sentence on gift cards has been revised in the manuscript to reflect this, in the 'Recruitment and Identification' subsection: "All participants will be compensated with a gift card, in the amount of $100. We have chosen this amount because we feel it fairly reimburses participants for the extensive time required to participate, without being irresistibly high."*
- Answers of active users and of children or other passively exposed persons should be taken separately and be compared.
  - *For screening, both active and passively exposed persons are interviewed via phone separately. At the home visit, each participant is interviewed separately (except for younger children who may need parental assistance with some questions), where they are asked again about their tobacco/nicotine product use. This has been clarified in the 'Screening' and 'Survey' subsections:*
    - *Screening: "Both actively and passively exposed individuals in a potential study household are screened."*
    - *Survey: "…survey will be conducted with each participant *independently* to assess the following…"*
- Some persons could be regarded as eligible from questionnaire, but might have to be excluded from results of lab tests at first visit before exposure. Nicotine addicts might not be able to refrain from smoking or vaping inside the home for 48 hours and this should be verified at first visit. The same applies to possible dual use of tobacco and e-cigarettes or hookah.
  - *We agree this is possible. We do measure exhaled carbon monoxide, which could biologically confirm smoking vs non-smoking status for some people. However, it does not assess compliance with not vaping before or after the first study visit. This is mentioned in the 'Limitations' section, and we have added further clarification: "Finally, although participants are asked to refrain from using tobacco study products 24 hours before the home visit and between the first and second home visit, it cannot be guaranteed that participants comply. However, as exhaled carbon monoxide will be assessed in all participants, it will be possible to determine exposure to smoke (but not to e-cigarette aerosol) before the smoking session and to remove participants from select analyses as needed."*
- Problematic is strategy 3 of recruitment, because inclusion of tobacco retailers might give tobacco industry and tobacco trade a possibility to influence results.
  - *This is an interesting point, but fortunately is not problematic in the case of this study. We can think of no way in which this recruitment strategy would enable the tobacco industry and the tobacco trade to influence the results of the study. All that tobacco retailers do as regards our study is to have flyers in their stores describing the study, discuss the possibility of hookah smokers and e-cig vapers contact our staff to be screened for eligibility by our staff, and if the customer is interested, the customer takes the telephone number of a member of our staff who then screens the customer for eligibility and if appropriate, enrollment in the study. All participants must meet stringent eligibility criteria to enroll in the study. All recruitment, data collection, analyses, interpretation and crafting of manuscripts for publication and presentation exclusively are conducted by the study principal investigators and the research staff*

working with them, with no input whatsoever of the tobacco industry or tobacco retailers.

- Even after 48 hours without smoking/vaping inside the home, baseline air measurements are expected to show remnants of toxins released from third hand smoke on surfaces, which have a longer half-life than nicotine. Also it has to be taken into account, that persons returning from smoking or vaping on a balcony or a staircase are expected to bring some nicotine, PAH and other toxins with their breath, clothes, hair and skin into the apartment.
    - *We agree that individuals who do not smoke or vape inside a home may still bring in third hand smoke/vape remnants on their person and personal effects, which could impact the baseline air measurements of nicotine and organic carbon but not the other measures of air quality. A sentence has been added to the 'Limitations' section expressing this: "Fifth, it is possible that individuals who do not smoke or vape inside a home, but who do so outside of it, can bring toxins and remnants into non-smoking/non-vaping homes, potentially altering baseline air measures of nicotine."*
- Limitations are given correctly, however, it will be difficult to disentangle acute effects from chronic effects on passive smokers/vapers.
    - *We agree this may be challenging.*

VERSION 2 – REVIEW

REVIEWER	Dautzenberg, Bertrand Sorbonne University, Paris France
REVIEW RETURNED	17-May-2019

GENERAL COMMENTS	Bmjopen 2019 029490 R1 This article describes a prospective study of housing pollution and the effects of passive exposure to hookah and e-cigarette with a control of unexposed group and a control of exposed to cigarette smoking group. The reason that led to the study of two very different products in the same study, the hookah which is a tobacco product with a significant amount of smoke and a not-tobacco product, the e-cigarette which does not produce smoked, but an aerosol of composition close to that of the e-liquids used to produce it. It is interesting to do the study on each product, but it is necessary to explain why the choice was made to include theses so different products in the same study. The paper is clear and minor remark and questions. Titre • The title does not mention the measured respiratory effects that will be measured, but this is acceptable because tittle is already very long Abstract • Introduction line 5 : An aerosol is by definition "a colloidal suspension of particles dispersed in air or gas" remove "and gases" at the end of the sentence because gas is a component of aerosol. Introduction • Nicotine delivery product: A small number of electronic cigarette consumers use e-liquids without nicotine. Does not it make sense to formally exclude them from the study and specify that you

	include only consumers of electronic cigarette using e-liquids with nicotine. Exclusion criteria • Smoking cannabis us may produce effects close to tobacco. Are cannabis users clearly excluded from the study or reported by questionnaire? Session • There is no clear description of what is a “session” and what happens before and the next 24 hours. It is understood from reading the text that the session which lasts about 50-60 minutes includes a 15-minute phase during which nothing is consumed, a final phase of 15 minutes after the end of the consumption, it is deduced that consumption lasts 20-30 minutes. For shisha it's a short time but possible. For cigarettes, is it possible to consume one, two or three cigarettes during this phase explain if the user is free to consume ad libidum or propose limits. For the e-cigarette, are you going to estimate the liquid consumption or the number of puffs? or do you allow in any case the consumer to use e-cigarette at libidum? Please precise. • Open fires and other household parameters are mentioned, but there is no clear evidence of consumption or exposure to the products concerned 24 hours before and 24 hours after exposure. For many, the session is only a small part of the exposure, so collecting the minimum amount of exposure information during the 48 hours of the study would help interpret the results. Cotinine before and 24 hours • You measure the level of cotinine in the urine before exposure and at 24 hours, but if the 20-30-minute session of active exposure will represent the only exposure, for others it will represent only a small part of exposure. Is there an organized questioning on the exhibition the 4 hours before and after the exhibition session? otherwise explain why you neglect this parameter. Bibliography OK Table OK Figure OK

VERSION 2 – AUTHOR RESPONSE

Reviewer: 1
Reviewer Name: Bertrand Dautzenberg
Institution and Country: Sorbonne University, Paris France

This article describes a prospective study of housing pollution and the effects of passive exposure to hookah and e-cigarette with a control of unexposed group and a control of exposed to cigarette smoking group.

The reason that led to the study of two very different products in the same study, the hookah which is a tobacco product with a significant amount of smoke and a not-tobacco product, the e-cigarette which does not produce smoked, but an aerosol of composition close to that of the e-liquids used to produce it. It is interesting to do the study on each product, but it is necessary to explain why the choice was made to include these so different products in the same study.
The paper is clear and minor remark and questions.

- *We have added the following clarifying sentence to the first paragraph of the Introduction section: "Both hookahs and e-cigarettes were chosen to be included in this study as they are the leading contributors to the new epidemic of use of non-cigarette, alternative nicotine products, and because they both lend themselves to near identical methodologies to investigate their influences on in-home air pollution and cardiopulmonary function."*

Title

- The title does not mention the measured respiratory effects that will be measured, but this is acceptable because tittle is already very long
    - *We agree.*

Abstract

- Introduction line 5 : An aerosol is by definition "a colloidal suspension of particles dispersed in air or gas" remove "and gases" at the end of the sentence because gas is a component of aerosol.
    - *We have changed the text to read "particles and gases."*

Introduction

- Nicotine delivery product: A small number of electronic cigarette consumers use e-liquids without nicotine. Does not it make sense to formally exclude them from the study and specify that you include only consumers of electronic cigarette using e-liquids with nicotine.
    - *We do not exclude consumers that use nicotine-free e-liquids for 2 reasons:*
        - *1. As e-cigarettes are not well regulated, we are unsure if e-liquids that claim to have no nicotine actually have no nicotine, or if they instead contain a much smaller amount.*
        - *2. It is important to test if there are health effects from using e-cigarettes that do not contain nicotine, as these products also deliver some chemicals (such as metals from the coil or chemical constituents of flavorings) that are harmful to health.*

Exclusion criteria

- Smoking cannabis us may produce effects close to tobacco. Are cannabis users clearly excluded from the study or reported by questionnaire?
    - *We have struggled with the question of whether to exclude cannabis users but decided against it as its use is so prevalent and individuals often are reluctant to admit to its use, as it remains illegal in New York State, where we are conducting the study. Rather than exclusion, we do ask in a questionnaire whether or not the individual has smoked or vaped any products other than tobacco products. To address this in the manuscript, we have added the following: "Cannabis use is not included as an exclusion criteria, but individuals are asked if they smoke or vape products other than tobacco or e-liquid, so that sensitivity analyses can be completed." In addition, smokers/vapers are asked not to 'smoke or vape' in the home for 48 hours before the smoking/vaping session.*

Session

- There is no clear description of what is a "session" and what happens before and the next 24 hours. It is understood from reading the text that the session which lasts about 50-60 minutes includes a 15-minute phase during which nothing is consumed, a final phase of 15 minutes after the end of the consumption, it is deduced that consumption lasts 20-30 minutes. For shisha it's a short time but possible. For cigarettes, is it possible to consume one, two or three cigarettes during this phase explain if the user is free to consume ad libidum or propose limits. For the e-cigarette, are you going to estimate the liquid consumption or the number of puffs? or do you allow in any case the consumer to use e-cigarette at libidum? Please precise.
    - *The smoking/vaping session lasts for approximately 50-60 minutes. Air measurements, however, occur for approximately 80-90 minutes, to also allow for pollution measurements for 15 minutes before smoking/vaping*

starts, and 15 minutes after smoking/vaping ends. While we agree with the reviewer that a tightly controlled session may yield more reproducible results, because of ethical reasons and to better mirror real-world exposures, the user of the product was instructed to use their product at libidum, "taking as many or as few puffs as they would normally do over that time period" (page 7, app line 41). We have revised the last paragraph on page 7 to add more precision: "Air measures will occur for a total of approximately 80 minutes: 1) for a baseline period of approximately 15 minutes before smoking/vaping begins to allow for measurement of background air quality; 2) during smoking/vaping; and 3) for a cool-down period of approximately 15 minutes after smoking/vaping ends. Participants will be asked to smoke/vape as they normally do over the course of approximately 50 minutes (referred to as the smoking/vaping session), taking as many or as few puffs as they would normally do over that time period, in order to assess impact on air quality from the "typical" exposure in that home. No restrictions on the movement of the non-smoking/non-vaping adult and child will be made during the 50 minute smoking/vaping session; children will not be required to stay in the same room as the smoking or vaping adult. The goal is to assess effects from real world exposures in the home, and many parents do not smoke or vape in the same room as their children, in order to protect them from potential harm."

- Open fires and other household parameters are mentioned, but there is no clear evidence of consumption or exposure to the products concerned 24 hours before and 24 hours after exposure. For many, the session is only a small part of the exposure, so collecting the minimum amount of exposure information during the 48 hours of the study would help interpret the results.
    - *We agree with the reviewer, but because of the addictive nature of nicotine-containing products, we cannot expect the participants to truly refrain from smoking/vaping, at home or otherwise, for long periods before or after the home session. Our assessment of exhaled carbon monoxide and saliva cotinine levels will partially address this concern. We do ask study participants not to smoke or vape any products within 48 hours of the home visit and between the two visits, but we are aware that many individuals will do so anyway and that this is a limitation. To clarify in the text, the following sentence at the end of the "Air Quality Assessment" paragraph has been edited to read: "In addition, participants from all households are asked to ensure that no one smokes or vapes any type of product inside the home for 48 hours before the first home visit, and between the first and second home visit, although due to the addictive nature of nicotine, it is reasonable to expect that some participants will not comply."*

Cotinine before and 24 hours

- You measure the level of cotinine in the urine before exposure and at 24 hours, but if the 20-30-minute session of active exposure will represent the only exposure, for others it will represent only a small part of exposure. Is there an organized questioning on the exhibition the 4 hours before and after the exhibition session? otherwise explain why you neglect this parameter.
    - *In the questionnaire, we ask participants if anything has been smoked or vaped inside the home on the day of the first home visit. We also ask questions about nicotine and tobacco use in the past 7 days, 2 weeks, and 30 days, for a variety of different products. This is briefly summarized in the "Survey" section on page 7.*