Dear Reviewer,

We thank you for your comments on our opinion article, which significantly improved the paper. Below we provide our point-by-point response to the reviewers' comments. We have added one coauthor 'Petros Vasilakos', who supported addressing the comments and improving the quality of the paper. Comments are in *italic grey typeset*, responses are in regular black typeset, and changes to the manuscript are in blue regular typeset.

***General comments***

**Comment:** *This paper addresses an important topic: how to improve the evidence base to allow the effective targeting of air pollution interventions to improve public health. It includes some useful, relevant information and some interesting examples. However, it reads rather as a series of disjointed sections which aren't drawn together in a clear narrative, and sometimes appear inconsistent. I think the paper would benefit from some redrafting. In particular, it would be helpful to include an introductory section explaining the main purpose of the paper, what it covers, and the authors' view of what it adds to the literature already published on this topic. Some information on how the literature cited was selected would be useful, too.*

**Response:** We thank the reviewer for his comment. We have made the following changes:

- We redrafted the paper to better connect between the sections and reflect the main focus on the importance of including PM chemical composition in epidemiological assessments. These changes could be best seen in blue color throughout the manuscript.
- We have presented existing literature reviews on the topic of each section.
- We have added an introductory section explaining the main purpose of the paper, what it covers, and our view of what it adds to the literature already published on this topic. This section reads as follows:

## 1.4 Introductory overview

In this account, we discuss how the broader atmospheric science community can inform policies and interventions to mitigate sources of PM components that pose risks to human health (Figure 1). We advocate for a foundational shift towards considering PM deferential toxicity in epidemiological health assessments, made possible through improved air quality modelling suitable for exposure assessment, and present the key milestones within aerosol science that, in our view, are necessary for this shift. Section 2 introduces the concept of PM differential toxicity and its potential as an exposure metric. Section 3 critically examines recent advances in modelling tools for estimating fine-scale exposures to specific PM components. In section 4, we identify the type of ambient observations we think are essential for developing and validating exposure models. In section 5, we highlight remaining gaps in our understanding of PM component emissions, their atmospheric transformation and associated health effects and identify research opportunities. Section 6 delves into the need for strong collaboration between research communities to elucidate biological mechanisms underlying the health impacts of specific PM components.

- We have updated the section titles to reflect the common theme of the article centered around PM differential toxicity. The article new table of content is as follows:

## 1.	Preamble

### 1.1	A brief chronology of air pollution

**Comment:** *The abstract gives the impression that the paper focuses on the differential toxicity of particulate air pollution; in fact much of the detailed information relates to aspects such as monitoring, modelling, emissions sources, atmospheric chemistry etc. Pulling out some of the conclusions, or specific recommendations for future research, from these sections and including them in the abstract might be useful to the audience. Perhaps the intended focus of the paper is to comment on how improved monitoring and modelling of components / metrics of particulate air pollution could contribute to informing policies and interventions to maximise health improvements? If so, then some of the information included is perhaps not really relevant.*

**Response:** The focus of the paper is on the differential toxicity of PM and how improved monitoring and modelling of PM components could contribute to informing policies and interventions to

maximize health improvements. We have rewritten the abstract to better reflect the paper focus. The abstract reads as follows:

**Abstract.** Air pollution, with high levels of particulate matter (PM), poses the greatest environmental threat to human health, causing an estimated seven million deaths annually and incurring 5% of the global GDP. While PM health impacts are influenced by the toxicity of its individual chemical constituents, the PM mortality burden is solely based on its total mass concentration. This is because of a lack of large-scale, high-resolution PM chemical composition data needed for epidemiological assessments. Identifying which PM constituents are harmful for health has been the 'Holy Grail' of atmospheric science, since the seminal six US cities study that first linked PM to mortality in 1993. Ever since, atmospheric scientists have focused on understanding aerosol composition, emission sources and formation pathways, while longitudinal epidemiological studies needed individual level exposure data, using land use regression models for the prediction of exposures at fine resolutions. In this opinion article, we argue that the time has now come to shift focus towards considering PM chemical composition in epidemiological health assessments, laying the foundation for the development of new regulatory metrics. This shift will enable targeted guidelines and subsequent regulations, prioritizing mitigation efforts against the most harmful anthropogenic emissions. Central to this shift is the availability of global long-term, high resolution PM chemical composition data obtained through field observations and modelling outputs. In the article, we underscore key milestones within aerosol science integral for advancing this foundational shift. Specifically, we examine emerging modelling tools for estimating exposure to individual PM components, present the type of ambient observations needed for model developments, identify key gaps in our fundamental understanding of emissions and their atmospheric transformation and propose a forward cross-disciplinary collaboration between aerosol scientists and epidemiologists to understand the health impacts of individual PM components. We contend that aerosol science has now reached a pivotal moment in elucidating the differential health impacts of PM components, as a first step toward their incorporation into air quality guidelines.

**Specific comments**

**Comment:** *Controllable vs noncontrollable /anthropogenic vs natural sources: There is some inconsistency in the discussion in different sections of the paper regarding PM from natural/uncontrollable sources. The inclusion in the paper of Table 1, outlining evidence gaps and needs related to the health effects of natural PM, suggests that some of the authors consider that these are priorities for research. Other parts of the paper seem to regard these as sources to be dismissed. For example, the paper calls for the exemption from guidelines of components from uncontrollable sources, and recommends collaboration with WHO to achieve this. WHO air quality guidelines are health-based, and do not reflect achievability. Instead, the extent to which sources can be controlled through policy or operational interventions is one of the factors taken into account by legislators when developing national (or regional) regulation or legislation. Whether the lack of control over a source necessarily means that it should be exempted from compliance assessments is a topic of debate - there are health-based reasons that might suggest that it should not – and some discussion of these issues could be included in the paper.*

**Response:** We agree with the reviewer that regulations are health based and do not reflect achievability. Therefore, we have changed the text accordingly. The paper no longer calls for the exemption of uncontrollable components. These revisions can be best identified by the blue font in the text.

We have also added new material to Section 5.1 "Legacy and emerging anthropogenic PM emissions" to have a balanced focus on both anthropogenic and biogenic emissions. This includes completing the list of important anthropogenic emissions, as suggested by reviewer 2 and the addition of the new table 2 on the gaps related to anthropogenic emissions. The revised text in section 5.1 reads as follows:

Anthropogenic emissions remain a predominant source of primary and secondary PM, posing a critical scientific and policy challenge in identifying the most harmful components to human health. Existing reviews have compiled epidemiological and toxicological evidence linking specific emissions to health endpoints (Wyzga and Rohr, 2015; Adams et al., 2015; Rohr and Wyzga, 2012; Yang et al., 2019). While ample literature covers short-term effects, especially through measurements at few stations, longitudinal epidemiological studies investigating the effect of PM chemical composition on chronic health outcomes are relatively scarce. Despite inconsistencies across studies, elemental carbon, organic aerosols, sulfate and metals have been consistently associated with increasing risks of cardiovascular and respiratory mortality and hospitalization (Chen et al., 2018a; Yang et al., 2019; Masselot et al., 2022; Wang et al., 2022; Wyzga and Rohr, 2015; Adams et al., 2015; Rohr and Wyzga, 2012; Badaloni et al., 2017; Wang et al., 2017).

We believe that a major limitation in establishing robust epidemiological associations with specific PM components has been the correlation between these components and with other pollutants (e.g. $O_3$ and $NO_X$). Therefore, we call for improved high-resolution large scale chemically detailed exposure models that will offer the necessary variability for overcoming limitations related to correlations. Moreover, we advocate for the continual development of epidemiological multi-component methods that estimates the joint health impacts of PM components, instead of isolating the effect of individual ones. In this section, we will focus on major anthropogenic emissions, including fossil fuel emissions, non-exhaust on-road emissions, volatile chemical products (VCPs), and residential biomass burning (Table 2).

Fossil fuel combustion is an important source of sulfate, nitrate, and elemental carbon. Numerous accounts reported the higher differential toxicity of primary elemental carbon emissions, especially leading to cardiovascular morbidity and mortality (Chen et al., 2020a). Consequently, in 2021, the WHO has listed the elemental (or black) carbon (EC or BC) as one of the pollutants of emerging concern, calling for more evidence on their chronic health effects that can be used for future guidelines and regulations. For this, it is vital to provide high resolution, national and continental BC maps suited for large scale epidemiological studies (Section 3), ideally distinguishing between biomass and fossil fuel burning BC emissions (Table 2).

Sulfate and nitrate are not toxic in isolation, and their high fraction in PM and extended spatial variation complicates the determination of their health effects. Yet, the toxicity of these secondary components is perhaps indirect, through a complex multiphase interplay with other components. Sulfate, from energy production emissions of $SO_2$, provides an acidic medium for organic reactions, and may increase the solubility and hence the bioavailability of metal particles, potentially increasing their toxicity. Mobile emissions of $NO_X$ have profound effects on atmospheric oxidation (Section 5.2), but also lead to enhanced partitioning (Lv et al., 2023) and subsequent multiphase reactions of soluble organic molecules, through nitrate formation. Traditionally, nitrate was considered the chemical end point of the reactive nitrogen life cycle in the atmosphere prior to wet or dry deposition. However, there has been growing evidence for particulate nitrate photochemical renoxification in the presence of light and organic molecules (Jiang et al., 2023; Bao et

al., 2020). While this process is mainly examined for its potential to produce oxidant precursors ($NO_X$ and HONO), how it alters the composition of the organic fraction is currently not understood. The mechanistic understanding of these multiphase processes involving the interactions of secondary inorganic particles with organic and metal components is indispensable for constraining their impact on PM chemical composition and differential toxicity (Table 2). There is a need for fundamental mechanistic investigations of these processes in the laboratory and the field, especially in polluted areas, like China, where multiphase chemistry plays a key role for haze formation (Section 4.2).

The new Table 2 is as follows:

**Table 2:** Future changes in anthropogenic emissions, key observations needed for coupling with health data, high priority model developments for understanding the health effects of anthropogenic emissions and their future evolution.

| Source | Future changes | Key observations | Model developments |
|---|---|---|---|
| Fossil fuel combustion | Decrease by several % per year of $SO_2$, $NO_X$ and BC in the West and China. | Long-term, multi-site measurements of BC, ammonium sulfate and nitrate for model improvements.<br><br>Mobile measurements of BC in urban and rural locations.<br><br>Apportionment of BC between fossil and non-fossil emissions.<br><br>Fundamental studies and field observations of the multiphase interactions between ammonium sulfate and nitrate with the organic and metal components. | Fine resolution modelling of BC concentrations, ideally from different combustion sectors.<br><br>Implementing the effects of nitrate and sulfate on the organic and metal components and estimating future changes with decreasing fossil fuel emissions. |
| Non-exhaust emissions | Increase of the total burden by several % per year with the increase and electrification of the vehicular. | Long-term, multi-site measurements of elements, with a focus on copper.<br><br>Mobile measurements of trace elements in urban and rural locations. | Fine resolution modelling of PM elemental composition, with a focus on copper.<br><br>Utilization of long-term trends for separating between the effects of exhaust and non-exhaust emissions.<br><br>. |
| Volatile chemical products (VCPs) | Increase of the total burden by several % per year with the increase and westernization of the global population. | Identification and multi-site measurements of VCPs and VCP SOA markers.<br><br>Determination of SOA formation potential of individual and real-world mixtures of VCPs. | Modelling of SOA and ozone formation from VCPs on continental levels for exposure assessment. |
| Biomass burning for residential heating | Area dependent. | Long-term, multi-site measurements of biomass burning primary and aged emissions.<br><br>Mobile measurements of primary and aged biomass burning emissions in urban and rural areas.<br><br>Fundamental studies of biomass smoke aging. | Fine resolution modelling of biomass burning emissions.<br><br>Implementing biomass burning aging mechanisms in models.<br><br>. |

**Comment:** *As the paper illustrates in Figure 6, categorisation of sources of PM as controllable or not controllable is not straightforward. Land-use and human activities can influence the emissions of biogenic VOCs and the likelihood of wildfires, for example. And the WHO good practice statement on particles originating from sand and dust storms (SDS) (in the WHO 2021 AQG document) includes measures that can be implemented to mitigate exposure. This distinction between natural/uncontrollable and anthropogenic/controllable emissions could therefore be discussed in a more nuanced way in the paper.*

**Response:** We have modified the discussion about the distinction between natural/uncontrollable and anthropogenic/controllable emissions as follows:

In the introduction of Section 5:

Human activities have profoundly altered the earth's environment, impacting emissions, atmospheric composition, global temperatures, and land cover. In Figure 6, we categorize the complex anthropogenic effects on PM composition into four broad classes:

- **Direct emissions:** encompassing anthropogenic PM and PM precursors directly released into the atmosphere.
- **Land-use changes:** including changes in urban infrastructure, green initiatives, deforestation/forest management, and agricultural practices, affecting emissions and their accumulation patterns.
- **Direct effects of anthropogenic emissions on the chemistry of natural PM:** whereby pollutants from human activities react with biogenic emissions leading to PM formation.
- **Indirect perturbation of natural PM:** through anthropogenic emissions that impact natural ecosystems, such as global warming, increased $CO_2$ concentrations, shifts in vegetation patterns, or desertification.

This section addresses existing gaps in understanding anthropogenic emissions, their atmospheric transformation, and their direct and indirect influence on natural PM. It is crucial for the atmospheric science community to approach these gaps from a mechanistic standpoint and incorporate them into models to accurately quantify the anthropogenic impacts on PM composition and thereby health effects. In section 5.1, we discuss anthropogenic PM sources that hold relevance for public health, while in section 5.2, we examine the future trajectory of the natural PM background and its interactions with anthropogenic activities.

In the introduction of Section 5.2:

With the increasing regulations on anthropogenic emissions, the contribution of natural emissions, including biogenic volatile organic compounds (BVOCs), wildfires and desert dust, will gain prominence (Figure 4). While these emissions stem from natural ecosystems, they are also significantly perturbed by anthropogenic activities, as illustrated in Figure 6. The traditional picture that distinguishes biogenic and anthropogenic sources obscures human impacts on ostensibly natural systems. Anthropogenic effects on natural PM can be either direct, through the alteration of atmospheric reactivity, or indirect, through feedback mechanisms triggered by changes to the biosphere. We need to understand these effects quantitatively to devise best practices to mitigate their impacts. For example, WHO good practice statement on particles originating from sand and dust storms (SDS in the WHO 2021 air quality guideline document) includes measures that can be implemented to mitigate exposure. In this section, we discuss the human influence on natural PM concentrations, chemical composition, and future trends (Table 3).

In the conclusion of Section 5:

While anthropogenic emissions are destined to decrease, natural emissions will most likely increase. Part of this increase can be controllable through reducing anthropogenic emissions and managing land-use. The atmospheric science community is now ready to provide the field measurements, laboratory observations and model outputs needed to quantify the contribution of anthropogenic, and controllable natural emissions globally and predict their evolution with global

changes. This data will form the foundation for understanding the toxicity of anthropogenic PM sources and determining the natural PM background in different regions.

**Comment:** *Figure 4: The source of the data underpinning the illustration (in Figure 4) of the contribution of natural components to total PM, and how it varies with PM mass concentration, is not clear. The source of this data should be given, so that readers can access it. (Some locations / regions with high total PM also have high contributions of "natural" PM – arising from sources such as wind-blown desert dust, or wildfires – this doesn't seem to be reflected in the discussion, or in the figure.)*

**Response:** We have added the source of the data illustrated in the caption of Figure 4, as follows:

For illustration, we have chosen a natural background concentration of 5 μg m$^{-3}$, representing the level to which 50% of the global population would be exposed if all anthropogenic emissions were eliminated (Pai et al., 2022).

**Comment:** *Targeting interventions: based on toxicity or source contribution?: it is unclear whether the authors' overall focus is on identifying PM components that are most detrimental to health or identifying local sources that are major contributors to PM mass concentration and should therefore be targeted. Both are important, and both are discussed – but separately. A summary of the different ways in which atmospheric science, monitoring and modelling can inform policy-making and operational decisions would be useful to tie these different aspects together.*

**Response:** The overall focus of the paper is on PM differential toxicity and the identification and abatement of detrimental PM components. Indeed, some of these components are also major PM contributors and targeting them would result in a reduction in total PM mass concentration. The revised paper now presents more clearly the different ways in which atmospheric science, monitoring and modelling can inform policy-making and operational decisions. In addition, we have rewritten the first part of the conclusion, adding a summary of developments in atmospheric science needed to inform policy -making and operational decisions. The modified conclusion section reads as follows:

In the 21st century, we have witnessed a remarkable rise in life expectancy and shifts in global disease patterns, attributable to a combination of public health interventions and advancements in healthcare and healthcare accessibility. Yet, ten million deaths attributable to environmental exposures can still be preventable every year (Neira and Prüss-Ustün, 2016; Landrigan et al., 2018), highlighting the need for proactive measures. Relying solely on high-tech medical interventions for managing disease progression may exacerbate existing social inequalities within healthcare systems and yield diminishing returns. Therefore, we advocate to shift towards enhancing quality of life and promoting healthy aging through early prevention and the creation of healthy environments for all. Our vision for realizing this goal is a close collaboration between atmospheric scientists and epidemiologists, to integrate chemically detailed global air quality data with large-scale personalized medical information from citizen cohorts. The provision of global PM composition maps will require the atmospheric science community to (1) develop spatially and chemically detailed exposure models, (2) provide long-term time-series of PM chemical composition from monitoring networks, (3) map pollution hot-spots through mobile measurements, (4) understand emerging anthropogenic emissions and their chemical transformation, especially in heavily polluted areas like China and India, and (5) understand the future evolution of natural emissions with climate and land-use changes.

As an aggressive attempt to promote healthy environments, WHO has set new guidelines to limit PM concentrations to below 5 μg m$^{-3}$. Achieving these limits may be challenging for many

regions due to the contribution of natural emissions from wildfires, biogenic species, and desert dust. Concurrently, scientific consensus underscores the critical role of PM chemical composition in influencing associated health effects, necessitating a revaluation of how we should be mitigating PM pollution and the development of new generation of air quality metrics focusing on detrimental PM components. Focusing on the PM differential toxicity offers two key advantages. First, it allows for targeted measures aimed to limit specific health-relevant PM sources. Second, PM chemical composition is intertwined with other properties that may also drive PM's health effects, such as solubility, number size distribution and oxidative potential. Atmospheric science has reached a pivotal moment to provide detailed global air quality maps, at a sufficiently fine resolution, supporting epidemiological studies to determine the differential toxicity of PM components, crucial for integrating PM chemical composition into regulatory frameworks, informing targeted policy-making and operational decisions.

**Comment:** *Indoor air: There is inconsistency in different sections of the paper in the way that indoor pollutants are addressed. Early in the paper, the authors suggest that indoor air pollution "should be treated as a separate risk factor distinct from outdoor air pollution, akin to contaminated water". The reasoning which led the authors to this view is not clear: is it because different policies are needed to address emissions from indoor and outdoor sources, for example? Conversely, later in the paper, considerable emphasis is put on volatile chemical products (VCPs - including cleaning agents and personal care products, which are used indoors) as sources of outdoor organic aerosol. This inconsistency should be addressed.*

**Response:** Our reasoning on treating indoor and outdoor sources separately is because (1) different regulatory frameworks are needed to address emissions from indoor and outdoor sources, (2) these sources are often distinct, and (3) they require different control measures. Indeed, some indoor sources are also important sources of outdoor pollution such as VCPs.

We had revised Section 2 to better reflect our view on the distinction between indoor and outdoor sources:

In epidemiological analyses, outdoor PM concentrations at residences are commonly used as proxies for exposure. While there is evidence supporting this approach, its applicability across different settings requires further investigation (Wei et al., 2023). As we spend most of our time indoors and new buildings are increasingly airtight for energy saving, outdoor concentrations may not reflect indoor levels (Schweizer et al., 2007). While indoor emissions, primarily from cooking (Klein et al., 2019) and smoking (Hyland et al., 2008), may influence health, they represent a separate risk factor distinct from outdoor air pollution, akin to contaminated water. This is because (1) different regulatory frameworks are needed to address emissions from indoor and outdoor sources, (2) these sources are often distinct, and (3) they require different control measures. Unlike outdoor air pollution, which often requires collective and regulatory abatement strategies to control emissions, indoor air pollution can be more effectively managed at the individual or household level, by improving ventilation and eliminating or reducing indoor sources. In the absence of indoor emissions, indoor concentrations are 30 to 70% lower than outdoors (Chen and Zhao, 2011) due to variability in infiltration rates. Moreover, exposures can also be influenced by outdoor pollution in other settings, such as workplaces and during commuting, where we spend a large fraction of our time. Health data from citizen cohorts often include questionnaires that offer valuable insights into indoor infiltration rates, workplace conditions and individual's mobility. While we consider outdoor concentrations at residence to be a reasonable proxy of exposure to outdoor pollution, integrating such information can

help refining exposure estimations. First, however, the issue of downscaling air quality models to finer resolutions must be tackled.

We had also revised Section 5.1 mentioning that a large fraction of VCPs may come from indoor sources:

With the drastic reduction of on-road transportation emissions, VCPs, which are partly from indoor emissions, have emerged as one of the largest sources of outdoor urban organic emissions in US and European cities, modulating urban chemistry (Coggon et al., 2021; Gkatzelis et al., 2021; Mcdonald et al., 2018).

**Comment:** *Differential toxicity: Section 5.1 "Health effects of anthropogenic PM emissions" includes "Our review reveals mixed results regarding the differential health effects associated with different anthropogenic PM components". How was this review undertaken? What search terms and literature sources were used? Were recent reports which have reviewed the evidence related to the differential toxicity of ambient PM consulted? [Examples include (USEPA PM ISA, 2019; ANSES, 2019; COMEAP, 2022) and the HEI NPACT initiative.]*

**Response:** The paper is not meant as a systematic review of the toxicological and epidemiological evidence on PM differential toxicity, as previous reports, which are the basis for WHO regulations, have already offered a much more thorough overview. Therefore, we changed the title of Section 5.1 to "Legacy and emerging anthropogenic PM sources". Furthermore, we have omitted from Table 2 and Table 3 the last column: level of scientific understanding, which deserves a dedicate review. Following the reviewer comment we have cited the recent reports which have reviewed the evidence related to the differential toxicity of ambient PM. This section reads as follows:

Anthropogenic emissions remain a predominant source of primary and secondary PM, posing a critical scientific and policy challenge in identifying the most harmful components to human health. Existing reviews have compiled epidemiological and toxicological evidence linking specific emissions to health endpoints (Wyzga and Rohr, 2015; Adams et al., 2015; Rohr and Wyzga, 2012; Yang et al., 2019)(Morton Lippmann Lung, 2023 #3276). While ample literature covers short-term effects, especially through measurements at few stations, longitudinal epidemiological studies investigating the effect of PM chemical composition on chronic health outcomes are relatively scarce. Despite inconsistencies across studies, elemental carbon, organic aerosols, sulfate and metals have been consistently associated with increasing risks of cardiovascular and respiratory mortality and hospitalization (Chen et al., 2018a; Yang et al., 2019; Masselot et al., 2022; Wang et al., 2022; Wyzga and Rohr, 2015; Adams et al., 2015; Rohr and Wyzga, 2012; Badaloni et al., 2017; Wang et al., 2017).

**Comment:** *As the paper notes, epidemiology using chemical speciation data will be key to investigating which components of PM might be most health-relevant. However, there will be limitations to how far epidemiology, alone, can address this question. If differential toxicity is to be a main focus of the paper (as suggested by the abstract) it would benefit from more discussion of these limitations. The authors note that confounding might occur because of the strong correlation between various PM components. Confounding by other co-emitted or co-located pollutants (eg NO₂, VOCs, SO₂) is likely an equally important issue, which should be mentioned. Such limitations suggest a need*

*for experimental toxicological data (in vitro and/or in vivo) to inform considerations of differential toxicity.*

**Response:** We agree with the reviewer that the strong correlation between various PM components and with other pollutants is a major limitation of epidemiology. However, we contend that long-term, large scale and high-resolution data would help overcoming the problem of correlation. We have clarified our viewpoint in section 5.1 as follows:

We believe that the principal challenge in establishing robust epidemiological associations with specific PM components lies in their correlation with other pollutants, such as other PM components, $O_3$ and $NO_X$. Therefore, we call for improved high-resolution large scale chemically detailed exposure models that will offer the necessary variability for overcoming limitations related to correlations. Moreover, we advocate for the continual development of epidemiological multi-component methods that estimates the joint health impacts of PM components, instead of isolating the effect of individual ones. In this section, we will focus on major anthropogenic emissions, including fossil fuel emissions, non-exhaust on-road emissions, volatile chemical products (VCPs), and residential biomass burning (Table 2).

**Comment:** *Attributable mortality: I would recommend making it clearer that all air pollution mortality burden figures are estimates, and are dependent upon the underpinning assumptions and data used (estimated pollution concentrations, exposure-response functions, counterfactuals etc). The approaches may differ between the different estimates quoted. I would also suggest use of a term such as "attributable deaths" or "an effect equivalent to x deaths" or similar, rather than "premature" deaths: in public health, "premature deaths" is often used refer to deaths in those aged less than 75 years old.*

**Response:** Based on the reviewer comment, we have replaced the term premature deaths by attributable deaths or estimated deaths. These modifications are best seen by the blue font in the updated version of the manuscript.

*Dosimetry of PM within the lung, translocation and causation of health effects:* discussion of these aspects could be more nuanced (for example, only a very small proportion of even nano-sized particles are understood to enter the blood stream). But I don't think that this is a main focus of the paper, so an alternative might be to scale these sections back.

**Response:** Based on the reviewer comment, we have significantly scaled section 6 back. The focus of this section is on the collaboration between atmospheric scientists and epidemiologists. The revised version can be seen in the main text.

**Technical corrections**

**Comment:** *Line 32: "about 400 before our era" is unclear. "400 BCE" is more commonly used*

**Response:** modified to 400 BCE.

**Comment:** *Line 154: "To quantify the health impacts of PM, we currently rely on dose-response relationships that link* **cause-specific** *mortality" : many authoritative organisations use all-cause/natural cause mortality as the basis of estimates, rather than cause-specific mortality.*

**Response:** We removed cause-specific in the updated version of the manuscript.

**Comment:** *Line 183 "insoluble particles, such as asbestos or elemental carbon, can* **bioaccumulate** *and lead to chronic inflammation". The more correct term is "biopersistence" or*

*similar (bioaccumulation is more usually used for accumulation of chemicals within food chains, for example bioaccumulation of dioxins in fish species such as salmon).*

**Response:** We have modified the sentence as follows:

'whereas insoluble particles like asbestos or elemental carbon are biopersistent in the body, leading to chronic inflammation.'

**Comment:** *Line 869 "WHO has set new guidelines to limit* **PM** *concentrations to below 5 µg m$^{-3}$." This should specify PM$_{2.5}$*

**Response:** We have specified that this is for PM$_{2.5}$.

**Comment:** *Footnote 1: For this audience, I think the formal definition of PM$_{10}$ and PM$_{2.5}$ should also be included.*

**Response:** We have already defined PM$_{10}$ and PM$_{2.5}$ in the footnote as: Particulate matter with a size lower than 2.5 and 10 µm, respectively.

**Comment:** *Some of the referencing needs to be checked. For example:*

- *Line 102 "WHO, has recently updated its air quality guidelines to propose a much more stringent limit value of 5 µg m$^{-3}$ (Who)" – this reference is not listed*
- *Line 246 (Pope* ***Iii*** *et al., 2002)*

**Response:** We have checked and adjusted the references.