Dear Reviewer 2,

We thank you for your constructive feedbacks, which 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 reviewers' 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.

Comment: *This long manuscript proposed opinions about how are advances in aerosol science informing understanding of the health impacts of outdoor particulate matter pollution. It's a very detailed review paper systematically introduced the development of aerosol pollution and corresponding control demands, summarized the globally monitoring or modelling and discussed the roles of PM components on human health. Some improving comments are suggested for considering as follows:*

Response: We thank the reviewer for their comments, which we address below.

General Comments:

Key objective of this article was to introduce the concept of using specific PM components as metrics for health assessments in addition to total PM mass, and for reevaluation of air quality guidelines. However, the health effects of PM constituents had been widely cognized and investigated either by toxicology or epidemiology studies, so the known and unknown of this issue might be key contents and suggested in this review. There is still road for connecting specific PM components independently with health effects by reliable epidemiological evidences and toxicological mechanisms clearly, qualitatively and quantitatively.

Response: The reviewer is correct that previous epidemiological studies have considered the effect of PM composition on PM health effect. However, these studies mainly focus on PM acute effects combining daily mortality and morbidity data, typically on a city scale, with measured or modelled PM composition typically at a background site. However, most of PM induced mortality is caused by chronic exposure, the quantification of which requires PM chemical composition data ideally at address level. Such data have been until very recently rarely available, especially for large scales. Hence, connections between chronic exposures and PM chemical composition have rarely been established. In the corrected version of the manuscript, we have added an explanation in this regards, which reads as follows:

3. Modelling exposures to individual PM components

The investigation of acute health effects requires the time-series analysis of daily exposures to specific components, typically obtained at an urban background site through long-term measurements (> 3 years) or modelling outputs. By contrast, longitudinal epidemiological studies of chronic diseases require long-term exposures determined at high spatial resolution – ideally at address level. Because high resolution PM composition data are scarce, existing epidemiological analyses considering PM chemical composition have mainly focused on acute effects, while health effects resulting from chronic exposure to individual PM components have rarely been assessed. In this section, we define the state-of-the-art in modelling PM exposure and discuss how recent advances in modelling PM chemical composition can help informing our understanding of PM differential toxicity.

Comment: *Moreover, PMs are chemical and biological mixture, their combined health effects result in the total PM mass exposure effects, surely not only additive by individual components.*

Response: The reviewer is correct. We have added this information in Section 5.1, as follows:

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.

And Section 6.2, as follows:

Working together will advance understanding of the involvement of specific PM components or combination of components in disease development and the detection of early changes resulting from exposure.

Comment: *Furthermore, the aerosol pollution varied spatially and temporally, the moving personal exposure also varied spatial-temporally, how could the PM monitoring serve the health risk assessments more helpful?*

Response: We consider outdoor concentrations at residence place to be a reasonable proxy of exposure to outdoor pollution. To determine the exposure at residence place, PM composition data from multiple fixed sites can be a suitable strategy – this is what is used for PM. However, we consider it is also important to integrate personal mobility data to refine exposure estimations. In section 2.2, we provide our opinion how information about human mobility can be considered when estimating human exposures. The section reads as follows:

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.

In section 4.3, we also mention how urban mapping can help refining exposure estimation, including the effect of mobility. The section reads as follows:

Street-level PM composition data can enhance, challenge, or confirm various air quality datasets used to retrieve PM differential toxicity, such as CTM outputs, land-use regression predictions, and remotely sensed observations. This refinement can also aid addressing the effect of human mobility in epidemiological studies (Zeger et al., 2000).

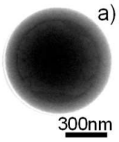
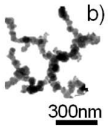
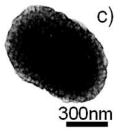
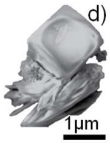
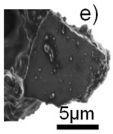
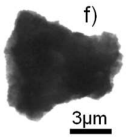
Comment: *Since there are both primary and secondary aerosols from both natural and anthropogenic sources, not all components are known and could be monitored in the complicated atmospheric PMs. All these facts should be considered in current discussion.*

Response: We believe that the eight components we have suggested are directly measurable or traceable. Their inclusion into epidemiological assessments could be a first step towards considering the PM differential toxicity in regulations. These eight fractions include: organic aerosol, elemental carbon, sulfate, nitrate, ammonium, sea-salt, brake-wear copper, and dust. All components have a dominant and known source except for the organic fraction, which can originate from primary and secondary, natural and anthropogenic sources. While these organic aerosol classes cannot be directly measured, they might be retrieved through receptor modelling based on spectrometric measurements or chemical transport modelling. This is discussed in section 2.1.

Comment: *In the key section of PM components, the list of known PM components to be monitored could be showed. In the section of PM sources, not all sources were covered and suggested to complete.*

Response: In section 2.1, we included Table 1 to represent PM components that we suggest monitoring. The new table 1 is shown below.

Table 1: PM chemical components suggested to be monitored and modelled for integration into epidemiological assessments and determination of PM differential toxicity. Components' physical properties that are important determinant of health effects are shown, including size, morphology, and solubility. Components major sources are also shown. a), b), and c) Transmission electron microscopic images of organic aerosol, elemental carbon aggregates and sulfate adapted from (Li et al., 2011). d) Scanning electron microscopic image of a fresh sea-salt particle adapted from (Li et al., 2016b). e) Scanning electron microscopic image of a coarse brake ware particle adapted from (Kukutschová and Filip, 2018). f) Transmission electron microscopic image of a mineral dust particle adapted from (Xu et al., 2021).

Component	Size	Morphology	Solubility	Source
Organic aerosol	Fine		Moderately soluble for POA Soluble for SOA	Natural and anthropogenic, primary and secondary
Elemental carbon	Fine		Insoluble	Biomass and fossil fuel combustion
Sulfate	Fine		Soluble	Aqueous (65%) and gas phase OH (35%) oxidation of SO_2 from natural marine emissions (15%) and anthropogenic emissions from electricity generation and industries (85%) (John H. Seinfeld, 2016)
Nitrate	Fine		Soluble	Oxidation of NO_X emissions mainly from traffic exhaust
Ammonium	Fine		Soluble	Condensation of gas-phase ammonia mainly from agriculture emissions producing ammonium sulfate and nitrate
Sea salt	Coarse		Soluble	Natural marine emissions through bursting bubbles at the air-sea interface
Brake wear (Cu)	Coarse		Depending on the element	Brake pads
Mineral dust (Al, Si, Ti, Fe)	Coarse		Depending on the element and atmospheric age	Mainly natural wind-blown dust

In section 5.1, we have discussed a more exhaustive list of sources and have include Table 2 to represent the gaps. This is shown below:

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).

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).

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).

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. Mobile measurements of BC in urban and rural locations. Apportionment of BC between fossil and non-fossil emissions. 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. 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. Mobile measurements of trace elements in urban and rural locations.	Fine resolution modelling of PM elemental composition, with a focus on copper. Utilization of long-term trends for separating between the effects of exhaust and non-exhaust emissions. .
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. 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. Mobile measurements of primary and aged biomass burning emissions in urban and rural areas. Fundamental studies of biomass smoke aging.	Fine resolution modelling of biomass burning emissions. Implementing biomass burning aging mechanisms in models. .

Comment: *Particle size is a very important parameter influencing PM health risks, which is also related to components and sources, but was not considered much in this paper.*

Response: In Table 1 (please see previous comment), we have now listed PM size of different chemical fractions as an important determinant of health effects. We have also specified the fraction of PM in WHO regulations.

Comment: *Finally, a question is suggested for consideration: How to control the specific harmful components in the particles selectively?*

Response: There exist strong correlations between PM chemical composition and sources (Table 1), for example sulfate with electricity generation or nitrate with traffic exhaust. We have added the following sentence in Section 2.1

The classification of aerosols based on their chemical composition will also establish a direct link to aerosol sources (Table 1), offering policy makers effective and operational strategies for selectively mitigating the most important PM sources for health.

Minor comments:

Comment: *Line 102: Who should be WHO. Check overall similar typos.*

Response: Done in the updated version of the manuscript.

Comment: *More figures than words are suggested to show the opinions.*

Response: We have added 2 new tables to better illustrate our opinions (Table 1 and Table 2, shown above).