COMMITTEE ON THE MEDICAL EFFECTS OF AIR POLLUTANTS

STATEMENT ON THE EVIDENCE FOR DIFFERENTIAL HEALTH EFFECTS OF PARTICULATE MATTER ACCORDING TO SOURCE OR COMPONENTS

Summary

1. Particulate air pollution is a complex mixture of many chemical components. Although it might be expected that some components are more harmful to health than others, the evidence available from population-based studies does not give a consistent view of their relative toxicity. Both particles emitted directly from a range of pollution sources, such as traffic and solid fuel combustion, and those formed by chemical reactions in the atmosphere are associated with adverse effects on health and the current consensus is that these associations are, at least in part, causal. Hence, reductions in concentrations of both types of particles are likely to benefit public health.

Background

2. In our report *Long-Term Exposure to Air Pollution: Effect on Mortality* (COMEAP, 2009), we recommended $PM_{2.5}$ as the most satisfactory metric for quantitative assessments of the mortality effects of long-term exposure to air pollution. Whilst acknowledging that there may be variations in toxicity between the various components of $PM_{2.5}$, we did not consider the available evidence sufficient to recommend quantification of the effects of different components of $PM_{2.5}$ separately.

3. The issue of whether some components of particulate matter are particularly detrimental to health continues to be an important one. It was included in questions addressed by the “Review of evidence on health aspects of air pollution” (REVIHAAP) project led by the World Health Organization at the request of the European Commission (WHO, 2013).

4. New evidence relevant to this question has also emerged from epidemiological and toxicological studies funded by the Health Effects Institute (HEI) under its National Particle Components Toxicity (NPACT) Initiative (HEI NPACT Review Panel, 2013; Lippmann et al, 2013; Vedal et al, 2013) and toxicological studies by the National Environmental Respiratory Center (NERC) in the US (e.g. Mauderly, 2014).

Evidence considered

5. We have considered evidence published in a number of authoritative reviews relevant to the health effects of: sulphates and coal combustion; nitrates; elemental/black carbon and traffic; and other sources or components of particulate matter. This evidence, along with the information available (at the time of its writing) on the results of the NPACT studies, is summarised in discussion paper COMEAP/2013/04.

6. We reviewed epidemiological studies that have investigated associations of health effects in the UK with sulphates or nitrates in more detail. We also examined epidemiological studies investigating associations of health effects with long-term exposure to multiple components of particulate matter. Summaries of these studies, along with information on the toxicity of sulphates and nitrates, are included in discussion paper COMEAP/2013/12.

7. We discussed these papers at meetings in June and November 2013. We discussed a draft statement in June 2014, in the light of results from the European Study of Cohorts for Air Pollution Effects (ESCAPE)[1] presented in discussion paper COMEAP/2014/01. There was also some discussion of this topic during our meeting in November 2014. We agreed a revised version by correspondence in March 2015 also taking into account recently published systematic reviews and meta-analyses of time-series studies on $PM_{2.5}$ (Atkinson et al, 2014a) and particle components (Atkinson et al, 2014b) funded by the Department of Health, and the results of a programme of toxicological studies by the National Environmental Respiratory Center (NERC) in the US (summarised in Mauderly, 2014). Points raised during our discussions can be found in the minutes of our meetings: COMEAP/2013/MIN1, COMEAP/2013/MIN2, COMEAP/2014/MIN2 and COMEAP/2014/MIN3. Some aspects of our joint discussion with the Air Quality Expert Group (AQEG) at a meeting in March 2013 are also relevant to this topic, and are captured in the note of that meeting COMEAP/AQEG/2013/Meeting Report.

8. Our evaluation focussed on assessing the strength of evidence that some components of particulate matter, or particulate matter from some sources, are more hazardous to health than others. In particular, we considered whether the evidence supports suggestions that primary particles, notably those emitted from combustion sources, are more detrimental to health than secondary particles. Studies investigating effects of components of both PM_{10} and $PM_{2.5}$ fractions are available. Where comparisons between effects associated with components are mentioned in this statement, it should be assumed that these are for particles within the same size range.

[1] European Study of Cohorts for Air Pollution Effects (ESCAPE): http://www.escapeproject.eu/

Summary of the evidence and Members' views

Sulphates and nitrates

9. The epidemiological literature is fairly consistent in reporting associations of adverse health effects with concentrations of ambient particulate sulphate. There is evidence for effects which occur within a few days of short-term exposures, including from time-series studies conducted within the UK, and for effects associated with long-term exposure. The results of the NPACT studies, which suggest sulphates originating from coal combustion as being closely linked to cardiovascular effects associated with long-term exposure to $PM_{2.5}$, strengthen the evidence for this association.

10. Fewer epidemiological studies have examined associations with ambient nitrate. Nonetheless, associations with health effects have been reported in studies of both short- and long-term exposures.

11. There is little published evidence that "pure" sulphates and nitrates are toxic. However, some cardiovascular effects in hyperlipidaemic $ApoE^{-/-}$ mice were reported from the NPACT studies, particularly when the compounds were administered together with the gaseous components of motor vehicle exhaust.

12. Given the limited evidence for the direct toxicity of sulphates, possible alternative explanations for the observed associations of adverse health effects with ambient sulphate concentrations have been suggested. It is possible that ambient sulphate is physically or chemically associated with other, more toxic, substances or is a marker for a mixture of pollutants influenced by the combustion of sulphur-containing coal, for example in power generation. It could also facilitate the toxicity of other components of particulate matter. Nitrates could play similar roles although, being less acidic than sulphates, they are less likely to modulate the toxicity of particles.

Black/Elemental carbon

13. Various metrics (Black Smoke (BS), Black Carbon (BC), Elemental Carbon (EC)) have been used to measure carbonaceous ("sooty") particles emitted from combustion sources. There is ample epidemiological evidence linking such metrics with adverse health outcomes. Much of this evidence is for effects which occur within a few days of short-term exposures, but associations have also been reported in studies of long-term exposure. The elemental carbon component of particles is unlikely to be toxic itself: it is more likely that it acts as a carrier for a range of toxic components or as a marker for a closely correlated pollutant(s) from the same source.

14. There are different sources of such particles. Nonetheless, in much of Europe and the US, Black Carbon is a good marker of traffic emissions. Epidemiological studies have also shown adverse health effects to be associated with proximity to traffic, or exposure to traffic-derived pollutants. Overall, the evidence is suggestive of causal relationships of a number of health end-points with traffic-related air pollution, of which Black Carbon can be considered to be an indicator, even if it is not actually

causal. The REVIHAAP review (WHO, 2013) includes a proposal that consideration could be given to developing an Air Quality Guideline for traffic emissions, to capture health effects that are additional to those represented by the reported associations with $PM_{2.5}$. It was suggested that this guideline could build on work previously undertaken on Black Carbon (WHO, 2012).

15. In studies of both short- and long-term exposures, effect estimates tend to be higher when reported per unit of mass (e.g. $\mu g/m^3$) of Black Carbon Particles (BCP) than per unit of the total mass of particulate matter. However, when estimates are based on the ambient range (e.g. the interquartile range) the effect estimates are similar. This is because BCP comprise a small fraction of the total particle mass.[2,3]

16. We note that the results of the ESCAPE project do not provide convincing evidence of a relatively greater role of BCP (measured as $PM_{2.5}$ absorbance) in exerting the adverse health effects of air pollution than measures of total particulate mass concentration. In particular, associations found with particle mass concentration ($PM_{2.5}$ and/or PM_{10}) were more convincing than associations with BCP for many, though not all, of the health endpoints studied.

Other sources/components

17. Evidence exists for associations of health effects with emissions of particulate matter from a number of sources in addition to coal combustion and traffic. These include wood or biomass burning, shipping and the metals industry as well as particulate matter from crustal or road dust sources.

18. A role for metals in exerting the health effects of particulate matter is mechanistically plausible as they can increase the oxidative toxicity of particles including those from non-exhaust sources such as brakes and tyres, which have been found to have high oxidative potential.

19. Along with black/elemental carbon and secondary inorganic aerosol (SIA), organic carbon (OC) is a major component of ambient particulate matter. OC has been less frequently evaluated in epidemiological studies, but there is growing evidence that it may have adverse health effects. OC is a complex mixture of primary and secondary organic aerosols and may contain specific compounds of health relevance.[4]

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[2] Because BCP contributes only a proportion of the total mass of particulate matter, a small change in mass concentration (e.g. $\mu g/m^3$) of BCP can be accompanied by a relatively large change in mass concentration ($\mu g/m^3$) of total particulate matter. When such changes are associated with adverse health outcomes, it therefore follows that risk estimates for the change in concentration of BCP (as $\mu g/m^3$), are higher than those for change in the total mass concentration of particulate matter (as $\mu g/m^3$). We do not consider that the higher effect estimate of BCP when reported per $\mu g/m^3$ should be interpreted as indicating that it is a particularly toxic component of particulate matter.

[3] There are, in addition, difficulties in comparing associations observed with a fraction (BCP) and associations reported with the total (PM mass concentration) of which it is a part, as the two are not independent.

[4] Examples include polycyclic aromatic hydrocarbons and quinones

Studies of associations with exposure to multiple constituents

20. Most studies examining the health effects associated with multiple components of particulate matter provide information about short-term exposures. These have reported associations of health effects with a wide range of different constituents. A recent systematic review and meta-analysis of time-series studies (Atkinson et al, 2014b) funded by the Department of Health found that concentrations of sulphate, nitrate, EC and OC were all associated with increased daily mortality.

21. Whilst such effects are important, long-term exposure to air pollutants has a much bigger effect on public health. The few studies which have examined the associations of adverse health effects with long-term exposure to multiple components of particulate matter have been undertaken in the US. These have provided conflicting results as to the relative importance of different constituents: associations with sulphate, nitrate, OC and EC have been variously highlighted. Associations of health effects with secondary sulphate were a consistent finding in the NPACT epidemiological studies. Traffic sources were implicated to a lesser extent and the findings regarding the importance of EC and OC varied.

22. The results of the programme of toxicological studies on diesel and gasoline engine exhausts, hardwood smoke and simulated downwind coal emissions undertaken by the National Environmental Respiratory Center (NERC) in the US (Mauderly, 2014) confirm that different pollution mixtures elicit a different range of toxicological responses. However, we note that the results of these studies did not allow an overall ranking of relative toxicity of these mixtures. The ranking was different depending on which toxicological responses were considered: each mixture could be deemed to be the most or least toxic, depending on the toxicological model, response indicator and exposure metric used for comparison.

Discussion

23. Epidemiological studies have reported associations of health effects with a wide range of components and sources of particulate matter. No clear picture has emerged as to which are most likely to be particularly relevant to health. The interpretation of associations between various particle metrics and adverse health effects must consider several possibilities including: (a) that the specific metric (e.g. sulphate, nitrate, black carbon etc) is causal; (b) that some other toxic component which is physically or chemically associated with the particle metric is causal or (c) that the metric is a marker for exposure to a pollution mixture characteristic of a specific source (sulphur-containing coal, diesel engine exhaust etc) and that the pollution mixture is causal. These possibilities are not mutually exclusive.

24. Toxicological studies, particularly of “pure” compounds, are of only limited help in understanding the reported associations, and in establishing mechanistic and biological plausibility. This is because components of particulate matter which may not be, in themselves, particularly toxic could contribute to the health effects of the ambient aerosol in a number of ways, for example by modifying the toxicity of other components of particulate matter, or acting as a carrier and delivery mechanism for other components of the air pollution mixture.

25. We have previously (COMEAP, 2009) suggested that sulphate could facilitate the toxicity of ambient particulate matter, for example by mobilising metal components, or decreasing the pH of the lung-lining fluid. We commented that, since nitrates are only weakly acidic, they are less likely than sulphates to mobilise metals or induce alterations in the pH of lung lining fluid. Nonetheless, we could not rule out the possibility that they play a role. We note that the REVIHAAP review has similarly concluded that, based on current evidence, it is possible that these secondary inorganic components have an influence on the bioavailability of other components, such as metals (WHO, 2013). Nonetheless, it remains the case that effects linked with ambient particulate nitrate have been less studied, and that there is less direct evidence for effects of nitrate than for some other major components of particulate matter.

26. The limited toxicological data available suggests that, rather than being directly toxic itself, the elemental carbon core of particles measured as BC/EC might act as a carrier of a variety of chemical constituents of varying toxicity arising from combustion. Similarly, sulphate could act as a carrier of other constituents from the combustion of fossil fuels with which it is correlated, including metals and organic compounds. Particulate nitrate, which also arises from emissions from combustion processes, could also act as a carrier of toxic components.

27. Another interpretation of the associations seen in epidemiological studies is that they represent the effects of the complex pollutant mixture emitted from a particular source and then modified by atmospheric interactions. In much of Europe, for example, BC/EC can be viewed as an indicator of traffic-related pollution. In our previous consideration of the possible role of sulphates (COMEAP, 2009), we suggested they could act as markers of toxic products of complex chemical reactions of emissions from the burning of sulphur-containing fuel. We note that the REVIHAAP review (WHO, 2013) also suggests that sulphate could be considered to be an indicator of harmful constituents from oil and coal combustion. Further, it states that nitrate is another indicator of emissions from combustion sources, including traffic exhausts which are rich in oxides of nitrogen.

28. Because many pollutants are highly correlated (temporally and/or spatially) it has been difficult to distinguish between their effects in epidemiological studies. For example, some researchers have suggested that associations observed with either EC or nitrate could be explained by their correlation with OC. In addition, methodological issues such as likely differential exposure misclassification which could arise, for example, from differences in the spatial scales over which concentrations of different pollutants vary, or differences in their penetration into the indoor environment, make interpretation of comparisons of effects estimates for different components difficult. Therefore, we should be cautious when using associations with particular components of particulate matter observed in epidemiological studies to infer the likely health benefits of reductions in those components specifically, unless there are also commensurate reductions in other components.

29. The available evidence can be interpreted as either demonstrating that many toxic components contribute to a spectrum of effects, or as being insufficiently powerful to discern a small number of key causal components.

30. Differential toxicity is only one of several factors relevant to the consideration of which measures to tackle particulate air pollution would be most effective in reducing its health effects in the population. For example, measures which reduce $PM_{2.5}$ in large conurbations will be important in reducing population exposure, and in achieving the required reduction in the Average Exposure Indicator[5].

Conclusions

31. It is unlikely that all components of particulate matter have the same potency in causing health effects. There is heterogeneity in coefficients representing associations between particle mass concentrations and health effects in epidemiological studies, and there is evidence suggesting that particles of differing composition elicit different toxicological responses and interact differently with different cell types.

32. However we consider that, overall, the current evidence is mixed and remains insufficient to draw reliable conclusions about which are the most health-damaging components or sources of ambient particulate matter. Differences in pollutant sources, or variations in the constituents of pollutant mixtures, only partly explain variation in effects of particulates reported from epidemiological studies, and it is not clear which are the most important constituents. Our view is that there is insufficient evidence to assess, on the basis of relative toxicity, whether reduction of one component of particulate matter would improve health more than targeting other components. Nor are we able to recommend differential coefficients for quantification.

33. We note that this is similar to the view reached in the REVIHAAP review (WHO, 2013) that, despite the increased number of studies (especially epidemiological) now available, the general conclusion remains that "there are many components contributing to the health effects of $PM_{2.5}$, but not sufficient evidence to differentiate those constituents (or sources) that are more closely related to specific health outcomes." Similarly, the HEI Review Panel concluded that the NPACT studies "do not provide compelling evidence that any specific source, component or size class of particulate matter may be excluded as a possible contributor to particulate matter toxicity."

34. There is evidence to suggest that both primary and secondary (particularly sulphate) particulate matter are detrimental to health. Therefore, we think that reductions in both primary and secondary particulate matter are likely to be beneficial to health. A similar view was reached by the HEI Review Panel for the NPACT studies, whose view was that "better understanding of exposure and health effects is needed before it can be concluded that regulations targeting specific sources or components of $PM_{2.5}$ will protect public health more effectively than continuing to

[5] Average Exposure Indicator (AEI) as defined in EU Directive 2008/50/EC on Ambient Air Quality

follow the current practice of targeting $PM_{2.5}$ mass as a whole." These observations provide support for the approaches currently recommended for use in the UK to estimate the health effects attributable to particulate air pollution. These methods use a concentration-response coefficient for particulate matter mass, rather than using coefficients for specific components of the PM mixture.[6]

35. Differential toxicity is only one of the factors that need to be considered when evaluating the effectiveness of interventions which reduce particulate air pollution and influence health.

Recommendations for further research

36. We note that reductions in UK and European emissions of sulphur dioxide (SO_2) have occurred in recent years, and that further reductions are expected. Studies investigating the health effects of these reductions might be informative, not only about the health effects of SO_2 (e.g. Le Tertre et al, 2014), but also the health relevance of sulphate particulate matter.

37. Examining the reasons for the heterogeneity in reported coefficients for associations of health effects with particulate matter and its constituents might provide insight into the relative toxicity of components.

38. Application of advanced aerosol characterisation techniques (e.g. single particle aerosol mass spectrometry) could give information on both bulk composition and the make-up of individual particles and would help improve attribution of sources and characterisation of effects.

39. Monitoring specific components of particulate matter to identify those that are indicative of a particular source would enable signatures of sources to be developed. This might facilitate the identification of pollutant sources associated with adverse health effects, which can then be targeted for action.

40. Experimental source apportionment studies based upon aerosol composition would allow associations between health effects and various source types, chemical components and/or particle size fractions to be explored further.

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[6] This statement does not address whether other PM metrics (e.g. particle number concentration) might now, or in the future, additionally be useful.

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Glossary of Terms and Abbreviations

Ambient air	Outdoor air
Association	A statistical relationship between two measured quantities. In the context of this statement, an association is a statistical relationship between measured concentrations of an air pollutant and a health endpoint.
BC, Black Carbon	A metric used to measure carbonaceous (“sooty”) particles.
BCP	Black Carbon Particles
Black Smoke	A metric used to measure carbonaceous (“sooty”) particles. Black Smoke measurements have largely been superseded by metrics such as Black Carbon or Elemental Carbon
Concentration-response coefficient	A quantitative relationship between the concentration of a pollutant and an increased risk of an effect on health, based on effects estimates reported from epidemiological studies
EC, Elemental Carbon	A metric used to measure carbonaceous (“sooty”) particles.
Epidemiological studies	Studies of the causes of diseases in populations
ESCAPE	European Study of Cohorts for Air Pollution Effects
Hyperlipidaemic $ApoE^{-/-}$ mice	Mice genetically engineered to be predisposed to develop atherosclerosis, a condition where arteries become clogged with fatty substances. This can cause heart attacks and strokes.
Interquartile range, IQR	A measure of the spread/dispersion of values. The IQR is the difference between the upper and lower quartiles of the range of values (i.e. the 75^{th} – the 25^{th} percentile).
OC	Organic Carbon
Oxidative potential	A measure of the capacity to induce oxidative stress, a likely mechanism by which air pollutants exert their adverse health effects
$PM_{2.5}$:	$PM_{2.5}$ is defined as the mass per cubic metre of particles passing through the inlet of a size selective sampler with a transmission efficiency of 50% at an aerodynamic diameter of 2.5 micrometres (µm). In practice, $PM_{2.5}$ represents the mass concentration of all particles of generally less than 2.5 micrometres in diameter. Often referred to as fine

	particles. **This fraction can penetrate deep into the lungs**.
PM_{10}	PM_{10} is the mass concentration of particles of generally less than 10 µm aerodynamic diameter. **This fraction can enter the lungs.** PM_{10} includes $PM_{2.5}$.
Primary particles	Particles emitted directly to the air. Examples include particles emitted during combustion, brake and tyre wear, and crustal materials such as road dust resuspended by vehicles.
Secondary particles	Particles formed from precursors by atmospheric processes. Examples include nitrates and sulphates, which are major components of the secondary inorganic aerosol (SIA). The ambient aerosol is the suspension in outdoor air of small solid particles or liquid droplets. Precursors of secondary particulate matter include nitrogen dioxide, sulphur dioxide, ammonia and volatile organic compounds.