Committee on the Medical Effects of Air Pollutants

Statement on quantifying mortality associated with long-term exposure to $PM_{2.5}$

Appendix B: Summary of COMEAP views on the studies in populations with low-level exposures and the shape of the concentration-response curve

This appendix includes the summary of COMEAP views on the studies in populations with low-level exposures and the shape of the concentration-response curve.

Summary

1. This summary reports COMEAP's views on the findings so far from studies of associations of mortality with long-term exposure to fine particulate air pollution ($PM_{2.5}$) in populations with low-level exposures. This includes a discussion of the shape of the concentration-response function (CRF). CRFs represent the relationship between a pollutant and an adverse effect on health and are used to quantify the health effects of air pollution and to predict the health benefits of reductions in air pollutant concentrations.

2. The newer studies provide evidence of effects at low concentrations, and no evidence of a lower exposure threshold for the adverse health effects of $PM_{2.5}$. Therefore, continuing efforts to reduce concentrations of $PM_{2.5}$, even where exposures are already low, would be expected to have a benefit to public health. This is a particularly important point for policy and decision making, as it suggests that reducing population exposure is an important public health goal, even when concentration-based air quality standards or targets are met.

3. Some studies have suggested that the CRF might be supra-linear: that is, that there might be more adverse effect per unit change in concentration (for example per 1 $\mu g/m^3$) at lower levels than at higher exposures. However, it is not clear to what extent these results may be due to the methods used or characteristics of the populations studied. Therefore, we do not consider the evidence sufficient, at this time, to recommend any change from the current assumption of a linear[1] CRF when quantifying the effects associated with long-term exposure to $PM_{2.5}$.

[1] Or log-linear, see footnote 4 below

COMEAP's views

4. Levels of ambient air pollutants have declined significantly over the last few decades in Europe, North America, and other developed regions. Nonetheless, recent epidemiological studies continue to demonstrate associations between exposure to ambient air pollution and adverse health effects. Notably, 3 large cohort studies funded by the Health Effects Institute (HEI) examining long-term exposures at low levels of $PM_{2.5}$ have reported associations with mortality.[2] Recent reviews and meta-analyses of the available evidence (for example, Papadogeorgou et al, 2019; Chen and Hoek, 2020) also suggest effects at low concentrations, including those below the then WHO air quality guideline of 10 μg/m^3 [3], with little evidence for a lower threshold for the adverse health effects of $PM_{2.5}$.

5. Some studies have suggested that the CRF might be supra-linear (that is, that the effect, per unit change in concentration, at lower levels is greater than for higher exposures). Examples of epidemiological studies which have reported supra-linear associations include some (for instance Pappin et al, 2019), though not all (for example Di et al, 2017) of the preliminary results from the HEI-funded studies mentioned above. Supra-linearity has also been suggested by some analyses combining results from multiple studies, such as the systematic review and meta-regression of associations between long-term exposure to $PM_{2.5}$ and mortality by Vodonos et al (2018). In addition to these studies on mortality, an examination of the relationship between long-term exposure to air pollutants with hospital admissions for cardiovascular and respiratory outcomes among the Medicare population of the United States by Yazdi et al (2021) has also reported supra-linearity. However, it is not clear whether the shapes of the curves reported may be due to (i) differences in populations (or sub-sections of populations) experiencing low exposures compared to those experiencing higher exposures; (ii) differential confounding in those exposed to lower and higher concentrations; (iii) the statistical methods that are used to fit the curves, particularly any constraints on the shape of the curve and methods for obtaining uncertainty estimates, that may influence the shape of the CRFs observed in some studies; (iv) the effects of variation in measurement error at different concentrations. In summary, the shape of the CRF, particularly at lower levels, may be due to variations in populations and/or the statistical models and other aspects of the methods used.

6. A supra-linear CRF could have important implications for quantification. If used to estimate the mortality burden associated with exposure to a population exposed to relatively low levels of air pollution, it would likely result in higher estimates than an assumption of a linear relationship extending to low concentrations.[4] For example, in Vohra et al (2021), each 1 μg/m^3 increase in $PM_{2.5}$

[2] Assessing Health Effects of Long-term Exposure to Low Levels of Ambient Air Pollution

[3] WHO published an updated Air Quality Guideline for $PM_{2.5}$ of 5 μg/m^3 in September 2021 WHO global air quality guidelines: particulate matter ($PM_{2.5}$ and PM_{10}), ozone, nitrogen dioxide, sulfur dioxide and carbon monoxide.

[4] Statistical methods used in cohort studies of mortality typically assume a log-linear relationship between exposure and risk. Some studies that have investigated the shape of the concentration-response relationship have demonstrated a linear or supra-linear relationship on the log scale (plotting log hazard ratio (log HR) against concentration), while others have not used a log scale (see Chen et al, 2020 Appendix 5 in supplementary material file 6). In practice, for a small HR (as found in most air pollution studies) and over a small concentration range (as typically found in a single-site

was associated with a 1.29% increase in all-cause mortality at a mean exposure of 10 μg/m^3 and the attributable fraction was about 12% at these concentration levels (compared with an attributable fraction of 7-8% estimated at 10 μg/m^3 based on the COMEAP updated coefficient for quantification of 1.08). The effect on population burden or health impact calculations may depend upon the proportion of the population exposed to different concentrations. A supra-linear relationship would also suggest that greater health benefit (per unit concentration) might be achieved by reducing levels of $PM_{2.5}$ for someone already exposed to low levels than by reducing exposures for someone experiencing higher levels of $PM_{2.5}$. This raises questions related to the best approach to perform cost-benefit assessments to support policy analysis in a way that avoids increasing inequalities in exposure.

7. Clearly, the shape of the CRF at low concentrations is a very important issue which requires careful consideration. Some primary studies, as well as reviews/meta-regressions, have suggested that the CRF might be supra-linear. Nonetheless, given the implications, our view is that it will be important to clarify some of the methodological issues which might influence the results obtained from recent studies investigating the shape of the CRF, some of which use novel approaches. We therefore recommend, at this stage, to continue to apply the current assumption of a linear[5] CRF for use in quantification. However, we will be following the literature on this topic closely, including reviewing the final results of the HEI-funded studies when they are available. We also intend to perform further investigation of the methods used in the available studies, and to discuss other recent developments, in our future work programme.

8. The current epidemiological studies have not provided evidence of a threshold concentration below which there are no adverse effects of $PM_{2.5}$ in the populations being studied. However, interpretation of the evidence should be considered in the context of the range of exposures within the individual cohort studies. The lowest value reported as a 5th percentile of population exposure from studies included in the Chen and Hoek meta-analysis was 3 μg/m^3, suggesting that there are associations between $PM_{2.5}$ concentrations and health effects at very low levels of particulate air pollution. It remains possible that future studies – with more participants exposed to low concentrations – might present evidence of a threshold. It should be noted that apparent lack of a threshold at the population level should not be interpreted as meaning there is no threshold for effects at an individual level. The level of exposure which can be tolerated without adverse effects (that is, at which physiological responses can be regarded as protective or adaptive, rather than as adverse or of potential clinical relevance) would be expected to vary between individuals. It would also likely vary across the life-course for any given individual, depending upon factors such as age and health status.

9. In summary, there is some evidence that the adverse health effects associated with increases of the same increment in $PM_{2.5}$ may be greater for low exposures than higher exposures but no evidence of a lower exposure threshold. Therefore, continuing to reduce concentrations of $PM_{2.5}$, even where exposures are already low, would be expected to have a benefit to public health. There is, as yet,

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study) there is little difference between a linear and log-linear relationship. This might not be the case when larger concentration differences are being considered.

[5] Linear on the log scale, that is log-linear

no consensus on the shape of the CRF at lower levels of $PM_{2.5}$ and we do not consider the evidence sufficient, at this time, to recommend any change from the current assumption of a linear CRF when quantifying the effects associated with long-term exposure to $PM_{2.5}$.

COMEAP
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References

Chen and Hoek (2020) ‘Long-term exposure to PM and all-cause and cause-specific mortality: A systematic review and meta-analysis’ Environment International Article No:105974.

Di et al (2017) ‘Air Pollution and Mortality in the Medicare Population’ N Engl J Med 29;376(26):2513-2522. doi: 10.1056/NEJMoa1702747.

Papadogeorgou et al (2019) ‘Low Levels of Air Pollution and Health: Effect Estimates, Methodological Challenges, and Future Directions’ Curr Environ Health Rep 6(3):105-115.

Pappin et al (2019) ‘Examining the shape of the association between low levels of fine particulate matter and mortality across 3 cycles of the Canadian Census Health and Environment Cohort’ Environ Health Perspect 127:10.

Vodonos et al (2018) ‘The concentration-response between long-term $PM_{2.5}$ exposure and mortality: a meta-regression approach’ Environmental Research 166:677-689.

Vohra et al (2021) ‘Global mortality from outdoor fine particle pollution generated by fossil fuel combustion: Results from GEOS-Chem’ Environmental Research 195:110754.

Yazdi et al (2021) ‘Long-term association of air pollution and hospital admissions among Medicare participants using a doubly robust additive model’ Circulation DOI: 10.1161/CIRCULATIONAHA.120.050252.

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