COMMITTEE ON THE MEDICAL EFFECTS OF AIR POLLUTANTS

Committee on the Medical Effects of Air Pollutants

Statement on quantifying mortality associated with long-term average concentrations of fine particulate matter ($PM_{2.5}$)

Summary

1. We have previously provided advice on how the mortality effects of particulate air pollution can be quantified. Our recommendation was based on the link between levels of fine particulate air pollution ($PM_{2.5}$) and deaths found in a large population study undertaken in the US. Since that time, a number of other studies have been undertaken. Some of these were in the UK or elsewhere in Europe. We think that a summary estimate of the results from available studies, published in the peer-reviewed scientific literature in 2013, is suitable to update our recommendation.

2. There is good evidence that $PM_{2.5}$ plays a causal role in shortening life. Nonetheless, sources of pollutants (such as traffic) tend to emit a range of different pollutants. This makes it difficult, in population studies, to disentangle the effects of individual pollutants from each other. Therefore, it is likely that the coefficient linking $PM_{2.5}$ concentrations with an increased risk of death reflects the effect of both $PM_{2.5}$ and also, to some extent, of other pollutants such as other size fractions of PM, nitrogen dioxide (NO_2) and other components of the air pollution mixture.

3. The updated concentration-response function coefficient linking concentrations of $PM_{2.5}$ with mortality is the same as our previous recommendation: a relative risk of mortality of 1.06 per 10 μg/m^3 increase in $PM_{2.5}$. However, the new summary coefficient has less statistical uncertainty associated with it (95% confidence interval 1.04 - 1.08) than our previous recommendation. This greater precision reflects the larger number of people included when the results of several studies are combined. However, the confidence interval does not reflect other uncertainties in interpreting the available evidence.

Introduction

4. The Committee previously recommended an approach for quantifying mortality associated with long-term exposure to particulate air pollution in its report *Long-term Exposure to Air Pollution: Effect on Mortality* (COMEAP, 2009). The concentration-response function recommended was taken from a large and well-conducted study (Pope et al, 2002) which examined the association between mortality risk and concentrations of fine particulate matter ($PM_{2.5}$). Since then, the increased evidence base for the relationship between $PM_{2.5}$ concentrations and all-cause mortality has been subjected to systematic review and a meta-analytical

summary estimate published (Hoek et al, 2013). We were asked to consider whether we wished to adopt the summary effect estimate reported by Hoek et al as an updated recommendation for quantifying mortality.

Background

5. In its report *Long-term Exposure to Air Pollution: Effect on Mortality* (COMEAP, 2009) the Committee recommended the use of a relative risk of 1.06 (95% confidence interval 1.02 - 1.11) per 10 μg/m^3 increase in $PM_{2.5}$ for all-cause mortality. This coefficient was taken from the US American Cancer Society (ACS) study, the largest cohort study of long-term exposure to air pollution and mortality available at the time (Pope et al, 2002). Coefficients for mortality from cardiopulmonary diseases and lung cancer were also recommended, but have been less used.

6. Using an expert elicitation, COMEAP (2009) derived a plausibility distribution to take account of other aspects of uncertainty, such as the strength of evidence for causality and confidence in transferability of the coefficient from the USA where the underlying study was carried out. This plausibility distribution gave rise to a number of intervals which could be used for quantification; COMEAP proposed the interval of 1.01 – 1.12 for quantification purposes, based approximately on the 12.5th and 87.5th percentiles of the overall range of COMEAP Members' consolidated views of the probability. It was suggested that a wider interval of 1.00 – 1.15 should also be used.

7. Since COMEAP made these recommendations, the increased evidence base for PM has been subjected to systematic review and meta-analysis. Hoek et al (2013) reviewed cohort studies of PM metrics and mortality (all-cause and cause-specific) published up to January 2013. This review reaffirmed the association of a 6% increase in the risk of all-cause mortality per 10 μg/m^3 increase in $PM_{2.5}$. However, because of the increased statistical power afforded by the combination of several studies in a meta-analysis, the summary estimate reported by Hoek et al has tighter confidence intervals (95% CI: 1.04 - 1.08) than those reported from the ACS study. The meta-analysis includes coefficients from 11 studies. The weight of the ACS study by Pope et al (2002) in the combined effect estimate is 12%, with other studies contributing from <1% to 24%.

Discussion

8. At the COMEAP meeting held on 7th June 2017, we discussed whether updating the Committee's recommendations for quantification to reflect the reduced statistical uncertainty provided by the Hoek et al (2013) meta-analysis was preferable to retaining COMEAP's current (COMEAP, 2009) recommendations: COMEAP/2017/MIN/2. The main points of our discussion are summarised below.

9. The plausibility interval that had been derived by expert elicitation (COMEAP, 2009) was the focus of much of our discussion. This sort of approach allows uncertainties that are not reflected in the statistical confidence interval around a

coefficient to be taken into account in sensitivity analyses. Such uncertainties could arise from the exposure assessment or statistical methods used in epidemiological studies, or relate to consideration of the strength and consistency of evidence or of the transferability of results to the UK situation. Although we think an opportunity to reflect these wider uncertainties is helpful, we think that a similar exercise, if undertaken now, would be unlikely to produce the same distribution of views of the plausibility of coefficients as the evaluation reported in COMEAP (2009). The number of cohort studies available now is much larger than when the Committee made its previous recommendation and a number of these studies have been undertaken in Europe including the UK (e.g. Carey et al, 2013; Beelen et al, 2014), reducing the potential concern about transferability of results.

10. The original intention of providing a plausibility distribution had been for it to be used in Monte-Carlo analyses which would reflect the probability density function generated by the expert elicitation. We note that, in practice, only the upper and lower extremes of the 75% plausibility interval tend to be used in sensitivity analyses in routine use, giving an unrealistic impression of the uncertainty around the central estimates.

11. We also recognise that the Hoek et al (2013) meta-analysis draws on a larger and more up to date evidence base than was available to the Committee when it made its previous recommendations. We acknowledge that the review by Hoek et al does not reflect all of the latest evidence, including some studies in Europe and the UK eg Carey et al (2013) or results of the ESCAPE project (Beelen et al, 2014). The same is true of other existing reviews eg the 2009 Integrated Science Assessment on PM and the 2012 provisional assessment by the US EPA (US EPA 2009; 2012) and WHO's REVIHAAP review (WHO, 2013a). Nonetheless, the review by Hoek et al is the most up to date systematic review and meta-analysis currently available.

12. For these reasons, we have decided to update our recommendation for quantifying mortality to reflect the summary effect estimate reported by Hoek et al (2013). We note that the authors of the World Health Organization (WHO) project "Health risks of air pollution in Europe" (HRAPIE) also adopted the summary estimate from this meta-analysis as their recommendation for assessing the mortality benefits of reductions in $PM_{2.5}$ (WHO, 2013).

13. We are aware that the WHO is expected to commission systematic reviews of the epidemiological evidence linking long-term average $PM_{2.5}$ concentrations with mortality risk, in preparation for reconsidering its Air Quality Guidelines. This will likely provide an authoritative and updated re-evaluation of the available evidence in due course, which we will wish to examine when it becomes available.

14. When we used our previous recommendation in order to quantify mortality associated with air pollution in the UK (COMEAP, 2010) we suggested this might represent the effect of particulate air pollution, as represented by $PM_{2.5}$. Our view of the available evidence was that the associations reported in the literature linking long-term average concentrations of particulate air pollution, represented by $PM_{2.5}$, and effects on mortality almost certainly represented causal relationships in respect of the air pollution mixture of which $PM_{2.5}$ forms a part, and were highly likely to be causal in terms of particulate air pollution specifically (COMEAP, 2009). Our recent

discussions regarding the evidence linking mortality with long-term average concentrations of air pollutants indicate that caution is needed in interpreting coefficients linking individual air pollutants with health effects. This is particularly the case for coefficients, such as those considered in this statement, from single-pollutant models - ie analyses in which no attempt is made to adjust for effects associated with other pollutants. Annual average concentrations of pollutants are often highly correlated spatially, making it difficult to disentangle effects caused by individual pollutants. Therefore, it is likely that the coefficient reflects the effect of $PM_{2.5}$ and also, to some extent, other pollutants with which annual average $PM_{2.5}$ is correlated in the epidemiological studies. These include other fractions of PM, NO_2 and other components of the air pollution mixture. Nonetheless, there is good mechanistic evidence to indicate an important causal role for $PM_{2.5}$.

15. Statistical techniques (two- or multi-pollutant models) have been developed to try to address this issue, and to allow the derivation of associations with individual pollutants which are independent of associations with other pollutants. However, there can be difficulties in interpreting the results of two- or multi-pollutant analyses when pollutants are highly correlated, or when there is exposure misclassification. These issues were highlighted while considering recommendations for quantification of mortality on the basis of nitrogen dioxide (NO_2) concentrations, and are discussed in some detail in our report *Associations of long-term average concentrations of nitrogen dioxide with mortality* (COMEAP, 2018).

16. There is likely to be an overlap in the effects reported as being associated with correlated pollutants (eg $PM_{2.5}$ and NO_2) in single-pollutant models. We have previously concluded (COMEAP, 2015) that "….the combined effect of NO_2 and $PM_{2.5}$ estimated using coefficients where each is adjusted for the effects of the other, is either similar to or only a little higher than what would be estimated for either $PM_{2.5}$ or NO_2 alone, using unadjusted single-pollutant coefficients". This led us to observe that "....using a single pollutant coefficient for NO_2 and a single-pollutant coefficient for $PM_{2.5}$ and adding the results, would give an overestimate of the combined effects of the two pollutants." Similarly, adding effects estimated using a single-pollutant coefficient for $PM_{2.5}$ and an adjusted NO_2 coefficient would also produce an overestimate.

Key points

17. We therefore conclude that, until such time as an updated systematic review becomes available, the review and meta-analysis by Hoek et al (2013) is a suitable source from which to adopt a summary coefficient to update our recommendations for quantification of mortality attributable to long-term exposure to particulate air pollution.

18. There is good mechanistic evidence for a causal role of $PM_{2.5}$ in shortening life. Nonetheless, because of the close correlations between pollutants, it is likely that the recommended coefficient reflects the effect of $PM_{2.5}$ and also, to some extent, of other pollutants such as other fractions of PM, NO_2 and other components of the air pollution mixture.

19. Our previous comparison of coefficients for PM and NO_2 from single- and two-pollutant models indicates that, if mortality effects estimated using this single-pollutant coefficient for $PM_{2.5}$ are added to estimates of mortality associated with other pollutants, this will likely give an overestimate of the effects of the pollution mixture.

Recommendations and observations

i. We recommend the use of the summary effect estimate reported by Hoek et al (2013) of 1.06 (95% CI: 1.04 - 1.08) per 10 µg/m^3 for quantification of all-cause mortality on the basis of $PM_{2.5}$ concentrations.

ii. This coefficient is not adjusted for effects of other pollutants. This means that:

a. Mortality estimates will likely include effects caused by other correlated pollutants[1] (eg NO_2) to some extent
b. If mortality effects estimated using this coefficient are added to estimates of mortality effects associated with other pollutants, this will likely give an overestimate of the effects of the pollution mix

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References

Beelen R, Raaschou-Nielsen O, Stafoggia M, Andersen ZJ, Weinmayr G, Hoffmann B (2014) Effects of long-term exposure to air pollution on natural-cause mortality: an analysis of 22 European cohorts within the multicentre ESCAPE project. *Lancet*. **383**(9919):785-95

Carey IM, Atkinson RW, Kent AJ, van Staa T, Cook DG, Anderson HR. (2013) Mortality associations with long-term exposure to outdoor air pollution in a national English cohort. *Am J Respir Crit Care Med.* **187**(11): 1226-33.

COMEAP (2009) Committee on the Medical Effects of Air Pollutants Long-term Exposure to Air Pollution: Effect on Mortality https://www.gov.uk/government/publications/comeap-long-term-exposure-to-air-pollution-effect-on-mortality

COMEAP (2010). The Mortality Effects of Long-Term Exposure to Particulate Air Pollution in the United Kingdom, Committee on the Medical Effects of Air Pollutants. https://www.gov.uk/government/publications/comeap-mortality-effects-of-long-term-exposure-to-particulate-air-pollution-in-the-uk

[1] ie pollutants correlated with $PM_{2.5}$ in the epidemiological studies from which the coefficient is derived

COMEAP (2015). Interim statement on quantifying the association of long-term average concentratons of nitrogen dioxide and mortality. Committee on the Medical Effects of Air Pollutants. https://www.gov.uk/government/publications/nitrogen-dioxide-interim-view-on-long-term-average-concentrations-and-mortality

COMEAP (2018) Associations of long-term average concentrations of nitrogen dioxide with mortality. Committee on the Medical Effects of Air Pollutants *https://www.gov.uk/government/collections/comeap-reports*

COMEAP/2017/MIN/2 Minutes of the COMEAP meeting held on Wednesday 7 June 2017 https://www.gov.uk/government/groups/committee-on-the-medical-effects-of-air-pollutants-comeap#minutes

Hoek G, Krishnan RM, Beelen R, Peters A, Ostro B, Brunekreef B, Kaufman J. (2013) Long-term air pollution exposure and cardio-respiratory mortality: a review. Environ Health **12**: 43.

Pope CA III, Burnett RT, Thun MJ, Calle EE, Krewski D, Ito K, and Thurston GD. (2002) Lung cancer, cardiopulmonary mortality, and long-term exposure to fine particulate air pollution. JAMA. **287**: 1132–1141

U.S. EPA. (2009) Final Report: Integrated Science Assessment for Particulate Matter. U.S. Environmental Protection Agency, Washington, DC, EPA/600/R-08/139F. https://cfpub.epa.gov/ncea/isa/recordisplay.cfm?deid=216546

U.S. EPA. (2012) Provisional Assessment of Recent Studies on Health Effects of Particulate Matter Exposure. U.S. Environmental Protection Agency, Washington, DC, EPA/600/R-12/056 https://cfpub.epa.gov/ncea/isa/recordisplay.cfm?deid=247132

(WHO) (2013a) Review of Evidence on Health Aspects of Air Pollution – REVIHAAP Project: Final technical Report. World Health Organization Regional Office for Europe, Copenhagen, Denmark http://www.euro.who.int/en/health-topics/environment-and-health/air-quality/publications/2013/review-of-evidence-on-health-aspects-of-air-pollution-revihaap-project-final-technical-report

WHO (2013b). Health risks of air pollution in Europe – HRAPIE project. Recommendations for concentration–response functions for cost–benefit analysis of particulate matter, ozone and nitrogen dioxide. World Health Organization Regional Office for Europe, Copenhagen, Denmark http://www.euro.who.int/en/health-topics/environment-and-health/air-quality/publications/2013/health-risks-of-air-pollution-in-europe-hrapie-project.-recommendations-for-concentrationresponse-functions-for-costbenefit-analysis-of-particulate-matter,-ozone-and-nitrogen-dioxide