COMMITTEE ON THE MEDICAL EFFECTS OF AIR POLLUTANTS

Committee on the Medical Effects of Air Pollutants

Advice on health evidence relevant to setting $PM_{2.5}$ targets

Introduction

This advice note provides responses to questions which Defra asked COMEAP (Committee on the Medical Effects of Air Pollutants) to address, relevant to consideration of the development of targets for ambient concentrations of $PM_{2.5}$ under the Environment Bill. These were prioritised in discussions between Defra, COMEAP Secretariat and COMEAP and QUARK (COMEAP's quantification Sub-group) Chairs.

The responses were developed to reflect discussion at the COMEAP meeting held on 24 November 2020 and Members' comments received by correspondence during December 2020 and January and February 2021. The agreed responses were provided to Members prior to the COMEAP meeting held on 8 March 2021, and Members' attention drawn to the changes made during the meeting.

(A) Cost Benefit Analysis

Quantifying health effects associated with $PM_{2.5}$ concentrations and interventions to reduce $PM_{2.5}$ concentrations

In setting the target we will be undertaking an impact assessment to consider the balance of costs and benefits of concentration-reductions arising from potential policies. The costs will be derived from the application of the range of measures envisaged to meet the targets and the health benefits will be derived from levels of pollution achieved through the application of those measures.

Relevant health-based science questions for COMEAP to address:

A1 Do recent systematic reviews provide a suitable basis for updating COMEAP's recommendations for assessing mortality associated with long-term average concentrations of $PM_{2.5}$ (for example, coefficient, cut-offs for quantification etc)?

Whether recent systematic reviews provide a suitable basis for updating COMEAP's recommendations for assessing mortality associated with long-term average concentrations of $PM_{2.5}$ was discussed at the COMEAP meeting held on 11 November 2020. A working group was set up, and brought revised

recommendations for discussion at the COMEAP meeting held on 8 March 2021. These recommendations were agreed and will be provided to Defra and published as a COMEAP statement.

A2 Do recent systematic reviews provide a suitable basis for updating COMEAP's recommendations for coefficients (and cut-offs) for outcomes associated with other pollutants that might be affected by interventions for use in cost-benefit analyses of proposed policies – that is, single-pollutant coefficients for mortality and hospital admissions associated with short-term exposure to PM, NO_2 and O_3 and single-pollutant coefficients for mortality associated with long-term exposure to NO_2 and O_3?

Whether recent systematic reviews provide a suitable basis for updating COMEAP's recommendations for outcomes associated with other pollutants that might be affected by interventions was discussed at the COMEAP meeting held on 11 November 2020. It was decided that, for mortality associated with long-term exposure to NO_2 and O_3, COMEAP will retain its current recommendations (2018 for NO_2,[1] 2015 for O_3[2]).

Members thought that, for mortality associated with short-term exposure to NO_2 and PM, the World Health Organization (WHO)-commissioned review by Orellano et al (2020)[3] may provide a suitable basis for updating COMEAP's recommendations. COMEAP's current recommendations are dated (1998) and would benefit from being updated. However, these pollutant-outcome pairs are not part of the IGCB Cost-Benefit Assessment methods[4], so are a lower priority to address.

For mortality associated with short-term exposure to O_3, the WHO-commissioned review by Orellano et al (2020) does not provide a suitable basis for updating COMEAP's recommendation for quantification, as Relative Risks (RRs) for two different averaging times have been combined in the meta-analysis. It might be possible to update COMEAP's recommendations by undertaking separate meta-analyses of the studies reviewed by Orellano et al (perhaps in collaboration with the authors) but this could not be undertaken in a timescale to contribute to the cost-benefit analysis for the $PM_{2.5}$ targets. COMEAP's 2015 recommendation is considered sufficient.

The recent WHO-commissioned systematic reviews did not include hospital admissions, other than for asthma. Therefore, COMEAP has adopted an approach which uses other reviews, available in the published literature, in order to propose updated recommendations for quantification in the required timescales. These will be provided to Defra and published as a COMEAP statement.

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[1] Nitrogen dioxide: effects on mortality

[2] COMEAP: quantification of mortality and hospital admissions associated with ground-level ozone

[3] Orellano P et al (2020) Short-term exposure to particulate matter (PM_{10} and $PM_{2.5}$), nitrogen dioxide (NO_2), and ozone (O_3) and all-cause and cause-specific mortality: Systematic review and meta-analysis Environment International Page 105876 Environment International | Update of the WHO Global Air Quality Guidelines: Systematic Reviews | ScienceDirect.com by Elsevier

[4] Mortality associated with long-term average concentrations of NO_2 and PM are included in the IGCB methods

A3. What location types are used within the epidemiological evidence base to estimate exposure? What does this suggest about which locations or scale of modelling might be most appropriate as the basis for application of these CRFs for quantification?

A range of geographical scales have been used in the exposure assessments in the cohort studies (long-term exposure). This makes it difficult to specify which scale of modelling is most appropriate for use in quantification. Nonetheless, very broad spatial scales (for example, 10 km by 10 km and above), are unlikely to pick up variations from locally emitted sources, which will likely have been reflected in the exposure metrics used for many, but not all, epidemiological studies.

A4. What might be the pros and cons of using baseline mortality or morbidity data at various different scales?

Work for a European Commission funded project has shown that calculations of mortality burden using ward level average population-weighted concentrations for NO_2[5] and mortality rates for England underestimate the mortality burden calculated using the same exposures and ward level mortality rates by 5 to 10% and by more when using a cut-off concentration (Mahieu et al, 2017)[6]. This is probably because areas with higher concentrations may tend to have higher mortality rates, for instance due to deprivation. It is more expensive and time-consuming to take this more detailed and granular approach and the degree to which it matters may depend on the exact scenarios, concentration-response functions and cut-offs considered. However, if mortality rates from a wider area are used for the main analysis, it might be sensible to perform checks using ward-scale mortality rates, at least as a sensitivity analysis.

(B) Additional Questions for COMEAP

B1. Effects of short-term vs long-term exposure

A firm conclusion of technical workshop 1 (Group 1, Question 1) was that targets should be focused on reduction of concentrations to which people are exposed for prolonged periods long-term (for example, annual average concentrations), rather than on elevated peaks of pollution which are short-lived (for example, daily or hourly average concentrations) because the evidence indicates that the effects of long-term exposure to $PM_{2.5}$ have a greater impact on public health than effects of short-term exposure. In addition, only in very specific circumstances would short-term action be effective in controlling elevated levels of $PM_{2.5}$, as episodic conditions are largely driven by specific meteorological conditions. Therefore, we plan to focus both $PM_{2.5}$ targets on delivering long term exposure reduction. Nonetheless, the current Limit Value for short-term (daily) average concentrations of PM_{10} will remain in place.

[5] the modelling scale prior to averaging by ward was 10km in rural areas, 2km in urban areas and 20m in 10 major UK cities

[6] Maiheu, B., Lefebvre, W., Walton, H. A., Dajnak, D., Janssen, S., Williams, M. L., Blyth, L. & Beevers, S. D. (2017) Improved Methodologies for NO_2 Exposure Assessment in the EU European Commission. 125p.

B1 (i) Does COMEAP agree that the health evidence suggests that reducing long-term exposure to $PM_{2.5}$, rather than a primary focus on short-term average concentrations, should be the priority aim of targets?

Summary:
A focus on reducing long-term average concentrations of $PM_{2.5}$ is appropriate. Nonetheless, an assessment of the expected impact on short-term (for example, daily) average concentrations should also be made. Health benefits of reducing concentrations of other pollutants (for example, NO_2, O_3) should not be overlooked.

Rationale:
The designs of the available epidemiological studies make it difficult to draw clear conclusions about the health effects of long and short-term exposure to air pollutants. Most epidemiological studies on air pollutants investigate associations of health effects with either spatial variations in long-term average concentrations of pollutants (such as cohort studies) or temporal variations in short-term average concentrations (such as time-series studies). Associations in time-series studies provide information on how effects (usually measured by routine health statistics such as mortality or hospital admissions) vary with day-to-day variations in air pollution concentrations. These associations are often interpreted as representing an increased risk of additional events (deaths or hospital admissions) which would not have occurred without the elevated pollutant concentrations. However, it is not clear to what extent the associations may represent the bringing forward of events that would have occurred in the following weeks or months, even if the peaks in pollution had not occurred.

The associations between air pollutants and health effects reported in cohort studies are usually regarded as representing the effects of long-term exposure. However, this is an over-simplification: associations with long-term average concentrations likely represent the effects of both long-term exposure to pollutants (for instance effects resulting from disease initiation and progression) and short-term exposure to elevated concentrations (for instance arising from exacerbation of pre-existing medical conditions). This means that it is possible that associations found in cohort studies might be more related to spatial differences in short-term elevations in concentrations (and associated health effects) than representing effects of long-term exposure to pollution. For equivalent annual average exposures, it is possible that exposure to intermittent high peaks might be more damaging to health than constant exposure to lower concentrations. However, from the available evidence, it is not clear whether this is the case or to what extent these peaks of exposure contribute to the effects found to be associated with long-term average concentrations.

It is likely that associations with mortality reported in cohort studies represent the sum of most, or possibly all, of the effects of both short- and long-term

exposures. Some recent studies[7] have explored the combined use of information on both spatial and temporal variations in air pollution concentrations in order to assess the independence and relative importance of long- and short-term exposures on mortality effects. These have demonstrated some independence of the effects of short- and long-term exposure.

Despite these difficulties in interpretation, it is clear from epidemiological studies that both long-term and short-term average concentrations of $PM_{2.5}$ are associated with health effects, and that associations with long-term average concentrations represent a bigger effect on public health. Nonetheless, short-term exposure also needs to be considered because panel and volunteer studies have demonstrated that it affects health. However, this does not necessarily indicate a need for a separate short-term target or standard. This is because frequency distributions of daily average concentrations of $PM_{2.5}$ are fairly stable, suggesting that policies to reduce long-term average concentrations would also be effective in reducing peaks of short-term average concentrations. Indeed, the WHO's current short-term (24-hour mean) air quality guideline for $PM_{2.5}$ reflects the relationship between 24-hour and annual average concentrations, rather than health effects associated with short-term average concentrations, and WHO suggests that the annual average should take precedence (WHO, 2006)[8]. Nonetheless, the relationship between long-term (annual) and short-term (daily) average concentrations will likely be dependent on the air pollution climate and the policies being pursued at the time; changes in the pollution climate and policies can presumably change this relationship. Therefore, there is a need to evaluate the relationship between long-term and short-term average concentrations, and the extent to which policies to reduce long-term average concentrations would also be expected to reduce short-term (such as 24-hour) average concentrations.

The current evidence base supports a focus on reducing particulate air pollution, especially fine particles ($PM_{2.5}$). Nonetheless, there is ample evidence linking other air pollutants with adverse effects on health, and COMEAP would remind Defra to bear in mind the health benefits of reducing exposure to these when developing policies and interventions to improve air quality. These should be included in the cost-benefit analyses undertaken to support policy development.

B1 (ii) What does the health evidence indicate about the relative health impacts of long-term exposure to $PM_{2.5}$ vs short term exposure (for example, relative risks per 10 µg/m^3)?

Summary

It is not possible to quantitatively compare effects of long and short-term exposures due to methodological differences in the available studies.

[7] For example, Shi et al (2016) Low-Concentration PM2.5 and Mortality: Estimating Acute and Chronic Effects in a Population-Based Study | Environmental Health Perspectives | Vol. 124, No. 1; Kloog et al (2013) Long- and Short-Term Exposure to PM2.5 and Mortality

[8] WHO/Europe | Housing and health - Air quality guidelines. Global update 2005. Particulate matter, ozone, nitrogen dioxide and sulfur dioxide

Nonetheless, the epidemiological evidence indicates that, when compared per 10 µg/m^3 $PM_{2.5}$, larger associations are reported from cohort studies (which examine spatial variation in long-term average concentrations) than from time-series or case-crossover studies (which examine day-to-day variations in concentrations). However, the relative importance of long- and short-term exposures likely varies depending upon the health end-point under consideration.

Rationale
It is not possible to suggest a quantitative comparison of the effects of long and short-term exposures, as interpreting the results of cohort and time-series or case-crossover studies as representing exclusively (and completely) the effects of long- and short-term exposures, respectively, is an over-simplification (see discussion in the answer to part (i) above).

Mortality: long-term average concentrations (for example, in cohort studies) are larger than effects reported from time-series or case-crossover studies (when compared per 10 µg/m^3 $PM_{2.5}$).[9] However, we do not consider a direct comparison to be appropriate: these coefficients arise from types of studies with different designs and represent associations with different types of variation in air pollutant concentrations (spatial or temporal, respectively); therefore, the associations do not represent the same things.

An illustration from the APHEIS health impact assessment project (below) applied coefficients from time-series studies (lag 0 or 1 day; and distributed lags) and cohort studies in order to compare the corresponding estimated mortality benefits of achieving long-term average PM_{10} concentrations of 20 µg/m^3 in different European cities. These calculations suggest that most benefit is achieved by reducing the mortality effects seen in cohort studies (often interpreted as being effects of long-term exposure), with smaller mortality benefits predicted on the basis of results of time-series studies.

[9] COMEAP currently recognises a RR of 1.06 per 10 µg/m^3 $PM_{2.5}$ for the association between long-term average concentrations and mortality (Hoek et al 2013; COMEAP 2018), and recent meta-analyses have suggested RRs of 1.08 per 10 µg/m^3 (Chen and Hoek, 2020; Pope et al, 2020). A recent meta-analysis of associations with short-term variations in concentrations (Orellano et al, 2020) found a RR of 1.0065 per 10 µg/m^3.

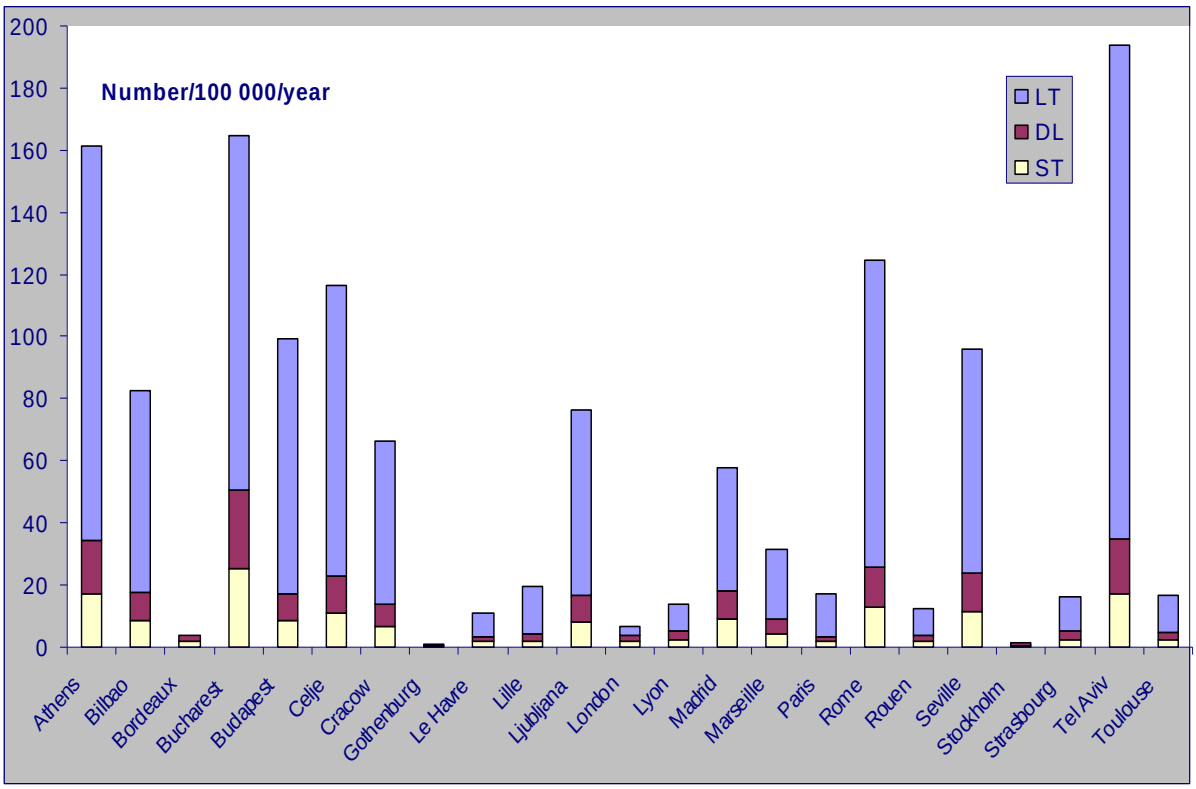


Figure from the APHEIS project (published in 2005): PM_{10}: Short term (ST: time-series); cumulative short-term (Distributed lag, DL: from time-series studies), long term (LT: from cohort studies) health impact on all cause mortality (ICD 9 < 800). Reductions to 20 µg/m^3. Number of deaths per 100 000 inhabitants per year. [10]

Morbidity: As well as effects on mortality, long-term exposure is also likely to contribute to morbidity, by both increasing incidence of disease and worsening the prognosis of those with pre-existing conditions. For example, a recent systematic review and meta-analysis and subsequent consideration by COMEAP[11] found the following, for ischaemic heart disease (IHD) and cerebrovascular disease (CBD):

- Viewed in the context of mechanistic evidence, the epidemiological evidence suggests that there is likely to be a relationship between long-term average concentrations of fine particulate matter ($PM_{2.5}$) and new cases of IHD and CBD (that is, disease incidence). We found summary effects estimates of:
  - 1.07 (95% CI 0.99, 1.16) per 10 µg.m^{-3} increase in $PM_{2.5}$ for IHD incidence
  - 1.11 (95% CI 0.99, 1.25) per 10 µg.m^{-3} increase in $PM_{2.5}$ for CBD incidence

[10] Medina S, Boldo E, Krzyzanowski M, Niciu EM, Mueke HG, Atkinson R, Zorilla B, Cambra K, Saklad M, Le Tertre A, Franke F, Cassadou S, Pascal L, Maulpoix A, and the contribution members of the APHEIS group . APHEIS health impact assessment of air pollution in 26 European cities. Third-year report. Saint-Maurice: Institut de Veille Sanitaire; 2005.

[11] COMEAP report on Quantification of the effects of long-term exposure to ambient air pollution on cardiovascular morbidity, in preparation

- The comparatively high estimate of the relative risk for mortality in those with IHD exposed to $PM_{2.5}$ (1.21 (95% CI 1.09, 1.34) per 10 $\mu g.m^{-3}$ increase in $PM_{2.5}$) compared with the relative risk for disease incidence may suggest that long-term exposure to $PM_{2.5}$ has an even greater effect on progression of the disease to death than on its initiation. However, we must treat this observation with caution because we identified only three studies on which to base the estimate for case fatality, and all three were of heart attack survivors who may have a different level of risk from the wider population with IHD
- Mechanistic evidence suggests that the reported effect of $PM_{2.5}$ on the initiation and/or progression of IHD and CBD is likely to be causal

Effects of short-term exposure: The relative importance of long- and short-term exposures likely varies depending upon the health end-point under consideration. There are relatively few health end-points which have been investigated using both cohort and time-series or case-crossover study designs, to allow a comparison to be made, and not all health effects have obvious short and long-term exposure equivalents. Therefore, we instead note here some aspects of the health effects evidence from daily variations in $PM_{2.5}$ concentrations.

The COMEAP (2011) Review of the UK Air Quality Index[12] notes that "The acute effects of particle exposure include increases in hospital admissions and premature death of the old and sick due to diseases of the respiratory and cardiovascular systems. The evidence is that both $PM_{2.5}$ and PM_{10} cause additional hospital admissions and deaths on high pollution days. There are also less severe effects of short-term particle exposure during pollution episodes, such as worsening of asthma symptoms and even a general feeling of being unwell leading to a lower level of activity (termed reduced activity days)".

A systematic review and meta-analysis of time-series studies of hospital admissions commissioned by the Department of Health (Atkinson et al, 2014)[13] found the following summary effects estimates for cardiovascular and respiratory hospital admissions per 10 $\mu g/m^3$ $PM_{2.5}$:

[12] COMEAP: review of the UK air quality index

[13] Atkinson et al, 2014 Epidemiological time series studies of $PM_{2.5}$ and daily hospital admissions: a systematic review and meta-analysis Thorax 69:660-665

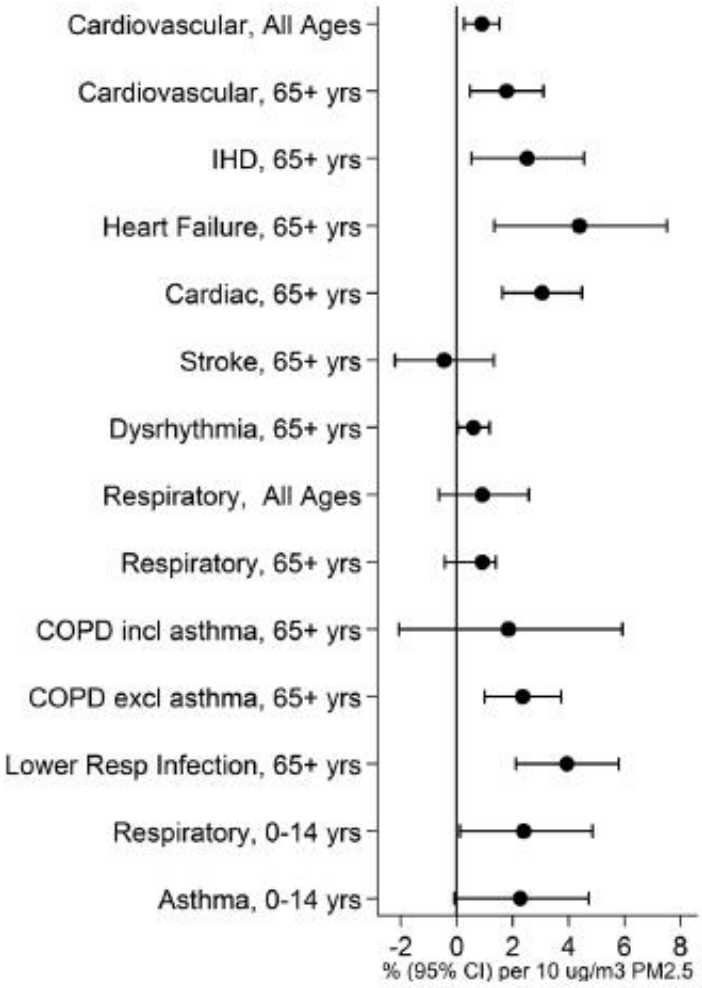


Figure 2 Summary estimates (95% confidence intervals) for cardiovascular and respiratory hospital admissions.

Figure reproduced with permission from: Atkinson et al, 2014 Epidemiological time series studies of $PM_{2.5}$ and daily hospital admissions: a systematic review and meta-analysis Thorax 69:660-665 [13]

B1 (iii) Are there other aspects of the health evidence which Defra should be aware of when considering the importance and effects of long and short-term exposure? For example:

- Are the same or different people affected?
- Are there effects of short-term exposure to elevated concentrations (for example, mortality or hospital admissions) that would likely have not occurred if that peak of exposure had not been experienced

Summary:
Both long-term and short-term exposures affect health but likely in different ways. People with pre-existing disease are likely to be most sensitive to effects of short-term exposure, including effects that might not have occurred without peaks of elevated concentrations. Long-term exposure likely has the potential to affect everyone, by contributing to the initiation and/or progression of disease.

Rationale:
Short-term exposures to elevated concentrations of pollutants can have immediate physiological effects. For example, WHO (2013)[14] noted "There is significant evidence from toxicological and clinical studies on effects of combustion-derived particles that peak exposures of short duration (ranging from less than an hour to a few hours) lead to immediate physiological changes; this is supported by epidemiological observations." Individuals can be at increased risk of effects of air pollution due to either experiencing high levels of exposure, or because they are more sensitive to the effects of pollutants – or both. Effects of short-term exposure to intermittent high concentrations might be different from those of long-term low exposures. For example, some groups might be particularly sensitive to short-term peaks, and experience symptoms that might not have been triggered by longer-term lower level exposures. These groups may include, for example: asthmatic children, those with underlying heart and lung conditions and older people. This makes it difficult to confidently identify geographic areas where populations might be at particular risk. We note that Asthma UK's 2019 annual survey [15] indicates that, while there might not be differences in asthma prevalence between different socioeconomic groups, the asthma of those in lower income groups tends to be less well controlled, with consequences for symptoms experienced and hospitalisation.

The methods used for cost-benefit analysis apply generic concentration-response functions to the overall health risks in the general population. As the concentration-response functions and underlying health data include vulnerable groups, this means that effects on vulnerable groups are captured in the analyses, even if the spatial distribution of where these people live is not clearly demonstrated in the analyses. Nonetheless, for concentration-based targets, the level of protection afforded to those most sensitive to effects should be considered.

Most spatial epidemiological studies consider residential exposure. Exposure at locations where vulnerable people spend large amounts of time, such as schools in the case of children, are also relevant.

B2. Using the health evidence to develop a concentration "limit value" type target for long-term exposure to $PM_{2.5}$:

Defra propose two "targets" to drive reductions in long-term average $PM_{2.5}$ concentrations. The current proposal is that one target will be a Population Exposure Reduction Target (PERT), and the other a concentration-based "Limit Value" type target which should not be exceeded. Previous evaluations of the health evidence have suggested little evidence for a threshold of effect at the population level, below which there is no health harm.

B2 (i) What does the evidence suggest about the shape of the exposure-response curve? Is there any evidence that it is non-linear, or that there is a threshold below which the risk (per unit concentration) decreases?

[14] (Source: REVIHAAP Project: Technical Report Page 12)
[15] Available from: https://www.asthma.org.uk/support-us/campaigns/publications/survey/

B2 (ii) Does the newer evidence continue to support the view that there is little evidence for a threshold of effect, below which there is no or minimal health harm? If there is no threshold below which there is no or minimal health harm, or below which the risk per unit concentration decreases, Defra proposes to use a cost-benefit approach to derive targets.

Summary:

The newer evidence indicates associations of adverse effects with lower concentrations than were previously studied. The studies have not indicated a threshold of effect below which there is no harm nor a threshold below which there are decreases in relative risk (for example, the risk per 10 µg/m^3 $PM_{2.5}$) associated with long-term average concentrations of $PM_{2.5}$. These findings suggest that continuing to reduce concentrations even below the WHO guideline value of 10 µg/m^3 would benefit public health. There is a suggestion from some recent studies that the relative risk might be greater at lower concentration ranges. However there is, as yet, no consensus on the shape of the concentration-response function 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 concentration-response function when quantifying the effects associated with long-term exposure to $PM_{2.5}$.

Rationale:

A recent review for WHO (Chen and Hoek, 2020)[16] included evaluation of the shape of the concentration-response function linking all-cause mortality with long-term average $PM_{2.5}$ concentrations. This concluded that the majority of studies which had analysed the concentration-response function had no evidence of a threshold and showed linear or supra-linear functions.

This finding is consistent with our view that current epidemiological studies have not provided evidence of a threshold concentration below which no effects of $PM_{2.5}$ are observed in the studied populations. Thus, the available evidence suggests that there are adverse effects associated with even low annual average concentrations of $PM_{2.5}$. A meta-analysis of cohort studies of all-cause mortality and $PM_{2.5}$ by Chen and Hoek (2020) included one study in which the 5th percentile of exposures was as low as 3.0 µg/m^3. However, the interpretation of the evidence is constrained by the range of $PM_{2.5}$ concentrations to which the studied cohorts have been exposed: few populations are exposed to very low levels of PM, so the lower end of the exposure-response curve is uncertain. It remains possible that future studies – with more participants exposed to low concentrations – might suggest the presence of a threshold. Also, the apparent lack of a threshold for effect at the population level should not be interpreted to mean that there is no threshold for effect 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.

[16] Chen J and Hoek G (2020) Long-term exposure to PM and all-cause and cause-specific mortality: A systematic review and meta-analysis Environment International Article No:105974. Environment International: Update of the WHO Global Air Quality Guidelines: Systematic Reviews

There is some suggestion from the current epidemiological evidence that the exposure-response function might be supra-linear at low levels (that is with a bigger effect, per unit change in concentration, at lower exposures than higher exposures). However, it is not clear to what extent these results may be due to differences in the populations studied and/or the methods used. For example, it is possible that there may be differences in populations (or sections of populations) with low exposures compared to those experiencing higher exposures, and/or that confounding may also be different in those exposed to lower concentrations. It is also possible that, in some studies, the constraints imposed by the statistical models may have influenced the shape of the exposure-response curves. There is, as yet, no consensus on the shape of the concentration-response function 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 concentration-response function when quantifying the effects associated with long-term exposure to $PM_{2.5}$.

We note that WHO (2006) has recommended an air quality guideline of 10 µg/m^3 $PM_{2.5}$ as an annual average. This was based on the evidence available at the time, which largely drew on the American Cancer Society (ACS) and Harvard Six Cities studies. The USEPA has implemented a primary standard for $PM_{2.5}$ of 12.0 µg/m^3 as an annual average, set in 2013 (USEPA, 2013)[17]. This was intended to provide increased protection against health effects associated with long- and short-term exposures (including premature mortality, increased hospital admissions and emergency department visits, and development of chronic respiratory disease).

The current evidence suggests that continuing to reduce concentrations of $PM_{2.5}$, even where exposures are already quite low, would be expected to have a benefit to public health. Assuming no threshold for effects within the currently studied range of $PM_{2.5}$ concentrations, the health evidence alone is not sufficient to define the concentration at which targets should be set. Targets could therefore be defined in terms of the costs and benefits of achieving them, if this can be undertaken in a rigorous fashion in time to inform the derivation of targets. This approach would help to ensure that the investment required to meet the air quality targets is proportionate to the benefit gained, and that it would not inappropriately consume resources that could achieve more public benefit if they were invested to address other problems.

B2 (iii) We are considering what approaches may be useful in target setting or for tracking progress towards targets. One option is to assess the reduction in the exposure of those exposed to levels higher than the specified concentration, that is, the concept of population weighted mean exceedance (PWME). Does COMEAP have views on such an approach and suggestions of alternative measures of progress from the perspective of delivering public health benefits?

[17] US Federal Register, 2013

Summary

We suggest that metrics such as PWME would be more appropriate to help assess the effects of legislation and interventions than for formal incorporation into a legislative targets framework. In addition, any such metric would require careful definition to avoid generating potentially misleading results.

Rationale

Metrics such as the number of people exposed over the limit value, or metrics combining this number with information on the exposure of these individuals, may be useful indicators. A metric such as “number of people over the limit value” does not capture the full population health gain of reductions in pollution levels, because people’s exposure may have reduced but still be above the limit value. Therefore, a metric such as population-weighted concentration above the limit value might appear attractive, as it could give a more complete picture of the public health effect of pollution or the benefit of interventions which have been implemented. This could be important in informing the public regarding expected health gains which may, in fact, be greater than suggested by a simple indicator of changes in the numbers of people exposed to concentrations above a limit value.

Nonetheless, careful definition of such a metric would be needed – particularly regarding how changes in exposure “across” the limit value are handled – in order to avoid perverse outcomes in what the metric appeared to be indicating. For example, a situation could be envisaged in which the population-weighted mean exceedance of those exposed above the limit value increased, due to reductions in exposure of those who had previously been just above the limit value so that their exposures were now below it. A metric defined as population-weighted mean exceedance expressed with respect to total population would avoid this problem and be suitable for tracking progress.

However, all such metrics would need care in definition and interpretation, as they would depend upon the size and location of the local population, as well as on pollutant concentrations. Additionally, the use of a metric(s) which includes population data in reporting the “limit value” target would make the system more complex, which could be a barrier to action. This is essentially a “hotspot” approach which offers less public health benefit than the PERT approach, and duplicates the function of the “limit value” type target which is required by the Environment Bill (and will be implemented alongside the PERT). For all these reasons, such metrics may perhaps be best used to assess how the legislation is working, or is projected to work, rather than as a formal part of the targets framework.

Additional question B2 (iv) What are the lowest concentrations at which there is evidence of an effect?

Chen and Hoek (2020) report that four studies in their systematic review assessed natural-cause mortality effects for participants’ exposure to long-term average $PM_{2.5}$ concentrations below certain exposure levels and that positive associations remained below 10 $\mu g/m^3$ or 5 $\mu g/m^3$ in the Medicare

and CanCHEC cohorts, respectively. In a CanCHEC study (Pinault et al, 2016) included in the Chen and Hoek meta-analysis, $PM_{2.5}$ concentrations (1 x 1 km resolution) were derived using a combination of satellite and surface monitor data together with modelling using GEOS-chem, and assigned to post codes. The mean $PM_{2.5}$ concentration in this study is reported as 6.3 µg/m^3 with a range (min-max) of 1.0 – 13.00 µg/m^3 and a 5th percentile of 3.0 µg/m^3.[18]

B3. Regional targets for exposure reduction

The existing National Exposure Reduction Target (NERT) is calculated as a national average of measurements made at representative urban background locations across the country. In developing a Population Exposure Reduction Target (PERT) approach we have been considering the opportunities to apply this approach in a more regional manner in order to link the target to positive action. Potentially, regionality would provide a means by which to drive cost-effective action beyond a concentration target. However, a conclusion of technical workshop 1 (Group 1, Question 4) was that regional targets were not appropriate because the cons outweigh any potential benefits of doing so. Therefore, we plan to focus on developing targets which are delivered at the national level.

B3 (i) When considering the pros and cons of regional assessments, what information on the health evidence (for example, about the risks to populations in different regions) should Defra be aware of?

Summary

Air pollution would be expected to have a bigger adverse effect on populations with poorer underlying health.

Rationale

The mortality effects of exposure to $PM_{2.5}$ are estimated by multiplying the underlying age-specific mortality risk in the population under consideration by the increase in risk due to exposure to air pollution. Age-specific mortality risk varies across the country, with populations living in deprived areas generally having poorer health – and a higher mortality risk – than those in more affluent areas. Therefore, there would be a bigger mortality effect of a given concentration of $PM_{2.5}$ in an area with higher mortality risk than one with a lower mortality risk (assuming a similar population age-distribution).

However, we note that the regions potentially under consideration by Defra for separate targets are quite large – likely too large for the granularity in socioeconomic and health status to be well reflected, in any case.

B4. Metrics for PM

Based on an extensive evidence base of adverse health effects, $PM_{2.5}$ (mass concentration) has been regarded as the most appropriate particle metric for use in defining air quality guidelines or health-based targets and assessing the progress and benefits of interventions. In its 2015 Statement on the evidence for differential

[18] (see supplementary material file to the paper "…mmc3")

health effects of particulate matter according to source or components, COMEAP came to similar conclusions, noting that there was evidence to suggest that both primary and secondary particulate matter were detrimental to health, and that the available evidence did not allow the recommendation of differential coefficients for quantification for different components or sources of PM. An updated view from COMEAP on this topic is requested.

B4 (i) To what extent does the available evidence support a focus on $PM_{2.5}$ mass concentration? For example:

a) Are the majority of health impacts captured through the metric of $PM_{2.5}$ mass?
b) How strong is the evidence for differential toxicity of particulate matter according to composition, source or fraction (for example, PM_{10}, $PM_{10\text{-}2.5}$, UFP, BC)?

Summary

It is almost certainly the case that some components or sources of particles are more detrimental to health than others. Nonetheless, at this stage, the health evidence continues to suggest that a focus on $PM_{2.5}$ mass remains appropriate.

Rationale

Our 2015 Statement on the evidence for differential health effects of particulate matter according to source or components (COMEAP, 2015[19]) presents the view that "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".

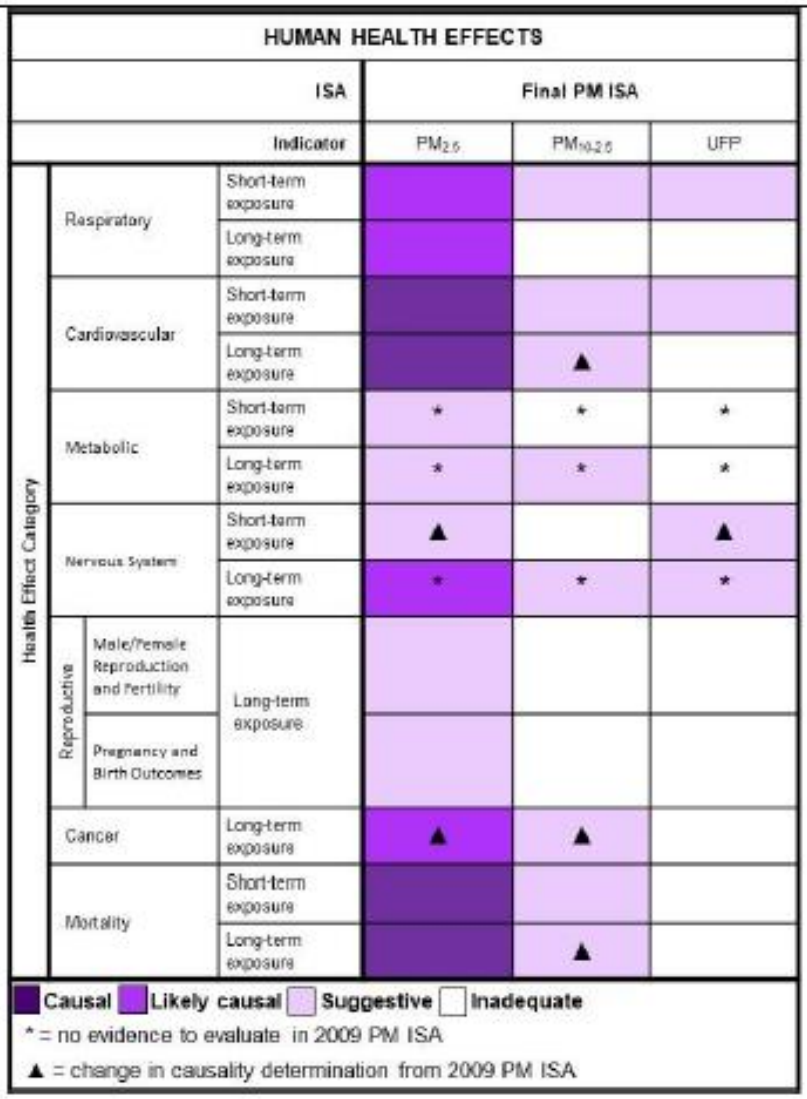
Two recent reviews (ANSES, 2019[20]; USEPA ISA for PM, 2019[21]) which we discussed at our meeting held on 11 November 2020 confirm and strengthen this view. The comprehensive review by ANSES found that the evidence linking a wide range of constituents and sources of ambient particulate matter had increased since the WHO REVIHAAP review (WHO, 2013). The USEPA's Integrated Science Assessment (ISA) for Particulate Matter (USEPA, 2019) reviews the evidence linking sources or components of particulate matter with adverse health outcomes. It concludes that "The assessment of PM sources and components confirms and continues to support the conclusion from the 2009 PM ISA: Many $PM_{2.5}$ components and sources are associated with many health effects, and the evidence does not indicate that any one source or component is more strongly related with health effects than $PM_{2.5}$ mass." It also reviews the

[19] Particulate air pollution: health effects of exposure

[20] ANSES (2019) Particulate matter in ambient air: Health effects according to components, sources and particle size; Impact on air pollution of the technologies and composition of the motor vehicle fleet operating in France. ANSES Opinion Amended summary report and recommandations from the collective expert appraisal. August 2019 – Scientific Edition

[21] USEPA (2019) Integrated Science Assessment (ISA) for Particulate Matter EPA/600/R-19/188 United States Environmental Protection Agency

evidence for the coarse fraction ($PM_{10-2.5}$) and ultrafine particles UFP, and finds less evidence for causality than for $PM_{2.5:}$ (see below)



PM = particulate matter; $PM_{2.5}$ = particulate matter with a nominal mean aerodynamic diameter less than or equal to 2.5 µm; $PM_{10-2.5}$ = particulate matter with a nominal mean aerodynamic diameter greater than 2.5 µm and less than or equal to 10 µm; UFP = ultrafine particles.

Note: Those health effect categories for specific exposure durations and size fractions where an asterisk is present indicate the first time studies were available to evaluate evidence and assess the causal nature of relationships between PM exposure and the health effect category of interest. Table P-2 provides a description of each of the five causality determinations and the types of scientific evidence that is considered for each category.

Figure 1-1 Summary of causality determinations for health effect categories for the PM ISA.

Figure taken from USEPA's Integrated Science Assessment (ISA) for Particulate Matter (USEPA, 2019)[21]

COMEAP has previously reviewed the evidence on some specific types and sources of particulate matter. It found that there was insufficient evidence to provide a quantitative comment on the risk of non-exhaust emissions of particles from road transport (COMEAP, 2020)[22] or on the London

[22] COMEAP Statement on the evidence for health effects associated with exposure to non-exhaust particulate matter from road transport (COMEAP Statement non-exhaust PM health effects

Underground (COMEAP, 2019).[23] Its review of evidence relevant to understanding whether air pollution causes new cases of asthma (COMEAP, 2010)[24] indicated that it was possible that air pollution plays a part in the induction of asthma in some individuals who live near busy roads, particularly roads carrying high numbers of heavy goods vehicles. A potential role for particulate pollutants acting as adjuvants to enhance allergic sensitisation was suggested.

The question of relative toxicity of different components of PM remains important, and it is almost certainly the case that some components or sources of particles are more detrimental to health than others. Additionally, it is likely that the size of particles could also influence their health effects, although there is limited epidemiological evidence to address this issue adequately at present. More work is needed on this important topic, and the issue needs to be kept under review as new evidence emerges. Nonetheless, at this stage, the evidence continues to suggest that a focus on $PM_{2.5}$ remains appropriate.

There may be reasons, other than differential toxicity, why Defra might want to consider focusing interventions on reducing particular types or sources of PM. For example, in its report on Mitigation of United Kingdom $PM_{2.5}$ Concentrations (AQEG, 2013[25]), AQEG noted that reducing primary $PM_{2.5}$ emissions was likely to be an effective strategy to reduce the impacts of $PM_{2.5}$ on public health, as this would deliver reductions in $PM_{2.5}$ mass predominantly in areas of higher population density. This strategy should, therefore, be a natural consequence of the application of an ambitious PERT designed to reduce integrated population exposure across the country. However, we note that consideration of cost or feasibility might mean that this approach is not adopted if the PERT is derived using cost-benefit analysis, or the pathway to achievement is based upon cost-benefit analysis. Reductions in primary emissions might also be a suitable target if the intention was to reduce inequalities in exposure (see discussion of inequalities in the response to Question 5 (iii) below).

B5. Groups at risk from the health effects of air pollution

We know that certain groups of the population are more at risk of the effects of air pollution – either due to personal characteristics (susceptibility), or due to their level of exposure. We propose that the aim of national targets is to deliver at least a ‘minimum’ standard of air quality across the country, incentivise actions that deliver the greatest public health benefits, and drive continuous improvement. However, we are interested in whether there is evidence that can help us build on this vision and develop an additional focus that would enable us to address health inequalities further. The response in our first technical workshop (Group 2, Question 3) suggested that metrics to address susceptibility to air pollution should not be developed. COMEAP’s views on the following would be welcomed

[23] COMEAP TfL statement
[24] Does outdoor air pollution cause asthma?
[25] Air Quality Expert Group: Mitigation of United Kingdom PM2.5 Concentrations

B5(i) From the perspective of delivering the greatest public health benefit, does the health evidence support a national target being focused on delivering improvements for the whole population rather than focusing on highly exposed or susceptible groups?

Summary

Reducing exposure of the whole population would be expected to achieve the greatest overall public health benefit and would also reduce the exposure of those most at risk.

Rationale:

Some individuals or groups are more at risk from the effects of air pollution than others – either because they are more highly exposed, or because they are more sensitive to the effects of pollutants.

Concentration-response functions for susceptible groups are not as well established as those for the general population (which do include the susceptible groups, as well as individuals without underlying health conditions). It is also difficult to envisage reduction strategies that would specifically deliver greater reductions for susceptible groups, as they are very dispersed geographically.

B5 (ii) What groups within the population are more susceptible to the health effects of air pollutants?

Summary

Older people, and people with heart and lung conditions are known to be susceptible to the effects of short-term exposures. Some risk factors may be less obvious; for example genetics, lifestyle choices or co-exposures to other pollutants may mean that some individuals have lower antioxidant capacity to combat adverse effects of exposure. Other vulnerable life stages likely include pregnancy and early childhood, when the body is developing.

Rationale

Older people, and people with heart and lung conditions are susceptible to the effects of short-term exposures (COMEAP 2011, Review of the UK Air Quality Index). WHO's REVIHAAP project (2013)[26] noted that "Susceptible population groups and effect mechanism differ for short-term and long-term exposures …. Even apparently healthy people are susceptible to the effects of long-term exposure to PM, because exposure can potentially accelerate progression of a disease, or perhaps even initiate it, until it is clinically diagnosed. Most susceptible to the effects of short-term exposures are those with an unstable disease. Progression of a disease due to particle exposure may be associated, for example, with acceleration of inflammatory processes, whereas other mechanisms may also play a role in triggering acute exacerbation of diseases, such as changes in autonomic nervous control of the heart in the case of cardiovascular diseases …."

[26] REVIHAAP Final technical report final version (Page 31)

In addition, the RCP/RCPCH report Every breath we take[27] has noted that "Pregnancy, infancy and early childhood are critical times when all the body's systems are formed, and start maturing……Therefore, it is clearly a vulnerable phase of life."

Although some people with increased susceptibility may be identifiable (for instance those with underlying respiratory or heart conditions) others may not be so obviously identifiable. For example, poor antioxidant balance may make an individual more susceptible to the adverse effects of air pollutants. This could arise due to genetics, lifestyle choices or as a result of other exposures. Minelli et al (2011)[28] have reviewed possible interactions between air pollutants and polymorphisms in genes coding for enzymes which produce the body's antioxidant defences.

The USEPA ISA for PM (2019) included an evaluation of whether specific populations and life stages are at increased risk from health effects of PM. Evidence of particular risks to children was found: although the available evidence did not indicate a difference in PM-related health effects between children and adults, it was noted that studies indicated effects that were specific to growing children, for example, impaired lung growth, decrements in lung function and the development of asthma. Adequate evidence for differential effects according to race was noted. Non-white populations in the US were also found to be more likely to be highly exposed. There was also evidence suggesting an increased risk in those with pre-existing cardiovascular or respiratory disease, those who are overweight or obese, those of low socioeconomic status, those who were current or former smokers and those with particular genetic variants in the glutathione antioxidant pathway.

B5 (iii) What groups within the population are more exposed to air pollution?

Summary

Some people who spend considerable amounts of their working life at roadsides, and those living close to busy roads, can be highly exposed. There is evidence to suggest that there are inequalities in exposure to pollution, with ethnic minorities and lower socioeconomic groups more highly exposed to particles and nitrogen dioxide.

Rationale

There are people who spend considerable amounts of their working life at roadsides – and some who live there. Some of these residents, or people in vehicles, may be those who are particularly vulnerable to the effects of air pollution, for example children or elderly people with underlying health conditions. Certain occupations have higher exposures, for example, professional drivers and others whose job requires them to spend long periods near roadsides, such as telephone engineers and shop assistants on roads with high levels of pollution. The exposure of those travelling on roads and pavements will depend upon their mode of travel.

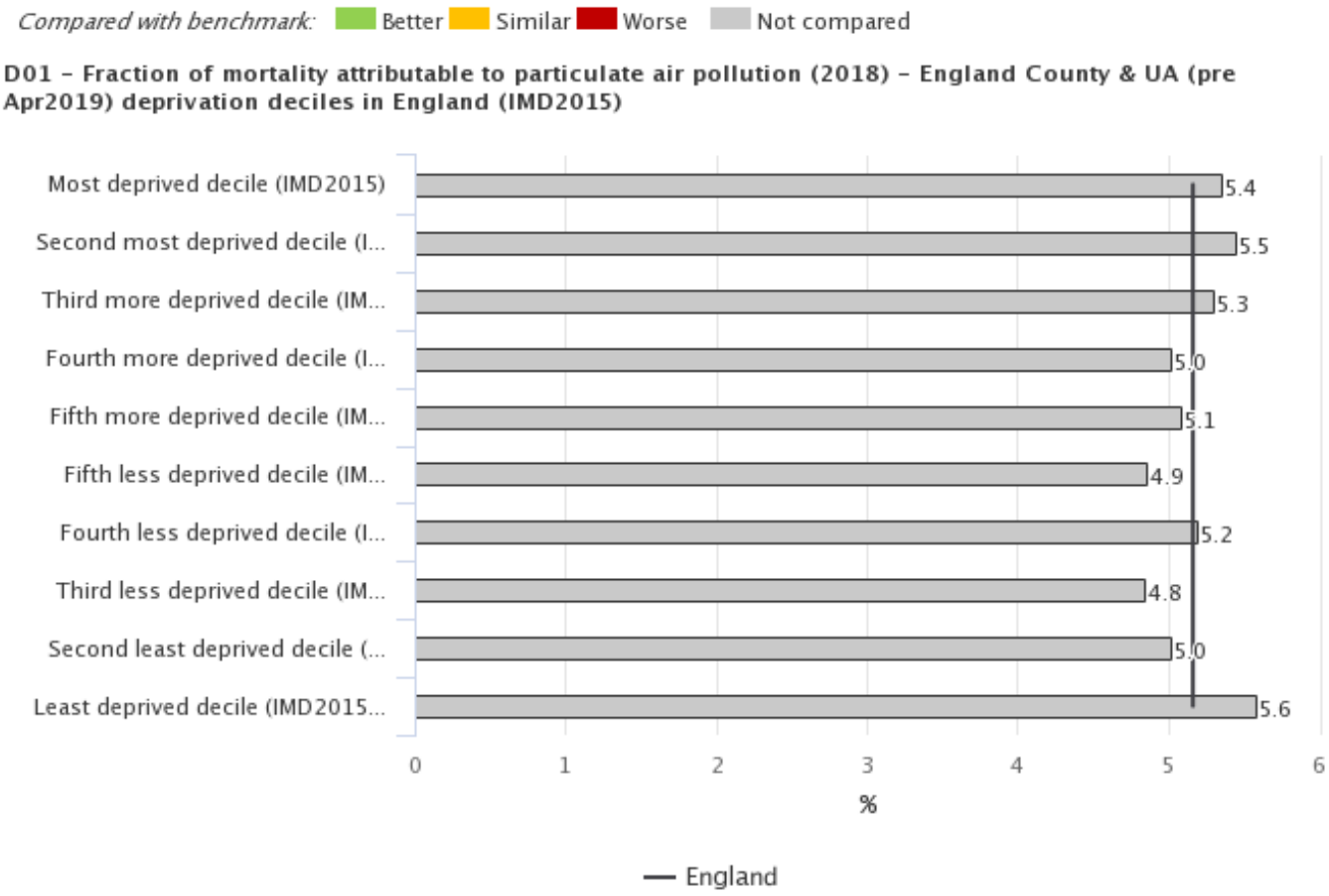
[27] Every breath we take: the lifelong impact of air pollution

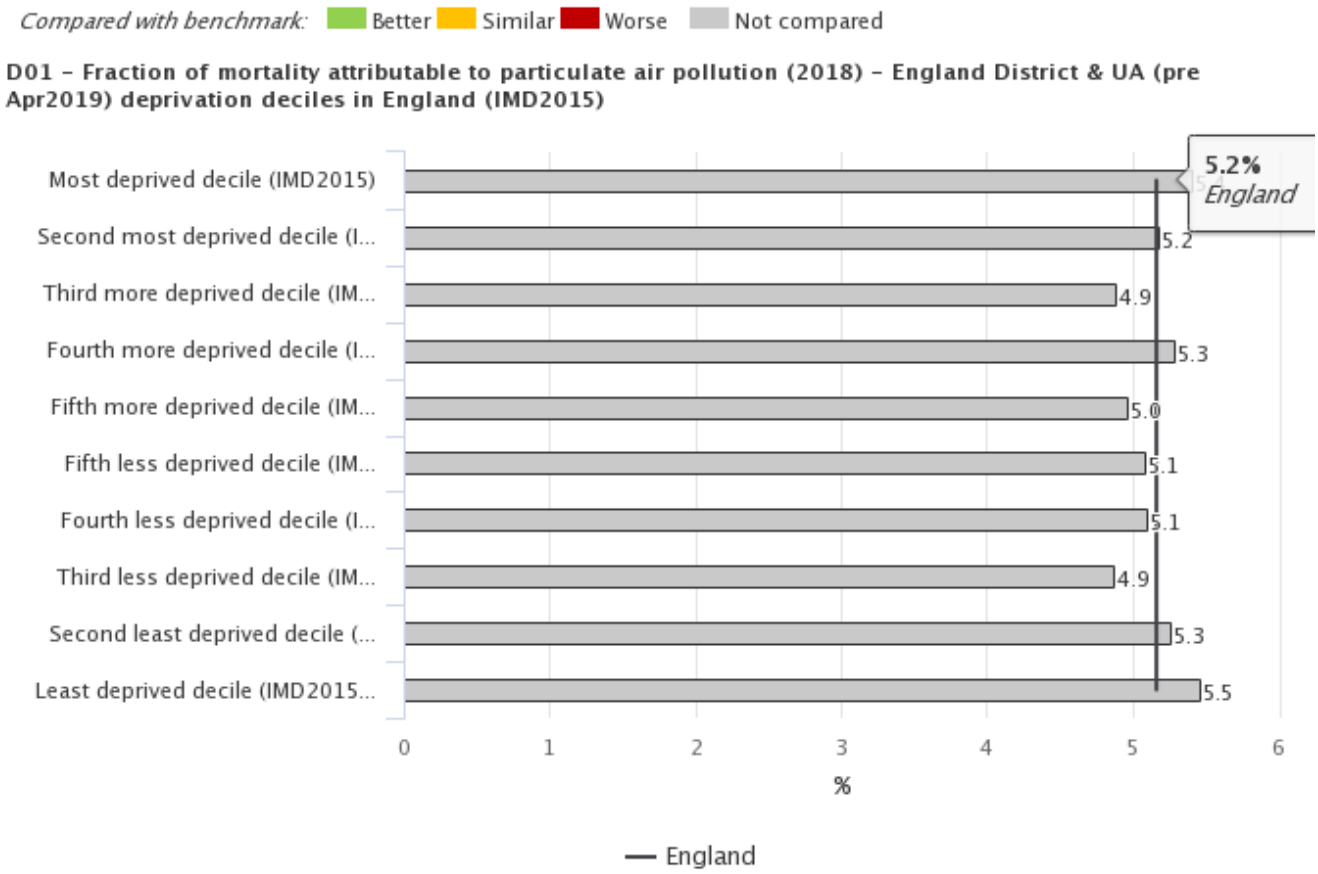
[28] Interactive Effects of Antioxidant Genes and Air Pollution on Respiratory Function and Airway Disease: A HuGE Review

The evidence regarding inequalities in exposure to pollution depends upon both the pollutant and the scale at which an assessment is undertaken.

Modelled population-weighted $PM_{2.5}$ concentrations at a county or district level in England do not show a clear pattern according to deprivation deciles (see below, from the PHOF data tool). In interpreting this, the following points should be borne in mind:

- There is a North-West (low) to South-East (high) gradient in $PM_{2.5}$ concentrations in the UK, reflecting the influence of long-range transport of pollutants from continental Europe on the pollution climate of the UK. There is a similar socioeconomic gradient in the UK.
- $PM_{2.5}$ and socio-economic data at county or district level may not be sufficiently granular to capture spatial variations and correlations that occur within districts, regions and cities
- There is less spatial variation in concentrations of $PM_{2.5}$, even at a fine scale, than for some other pollutants, particularly primary pollutants such as Black Carbon (BC), ultrafine particles (UFP), NO_2



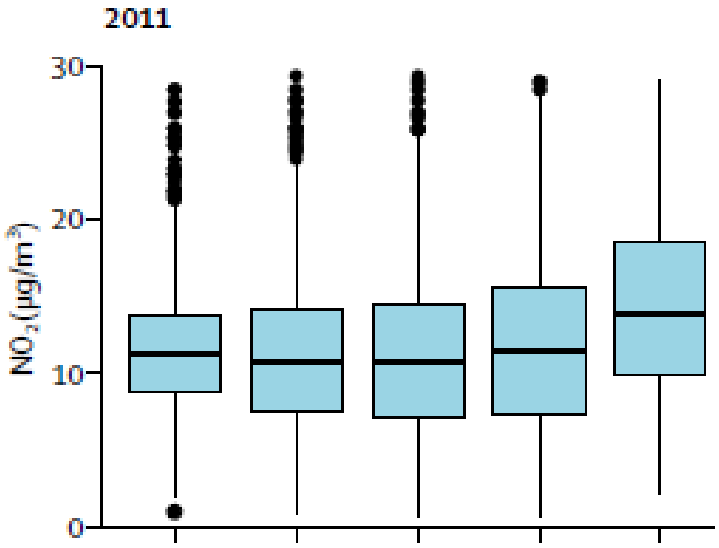


Source: Public Health Outcomes Framework (PHOF) datatool[29] Contains public sector information licensed under the Open Government Licence v3.0

A recent study by the ONS,[30] in the context of air pollution and coronavirus (COVID-19), found that ethnicity was strongly correlated with both NO_2 and $PM_{2.5}$ exposure, with ethnic minorities more likely to live in polluted areas. Other studies have also suggested higher exposures in deprived communities and areas with higher proportions of ethnic minority residents (for example, Fecht et al, 2015 Associations between air pollution and socioeconomic characteristics, ethnicity and age profile of neighbourhoods in England and the Netherlands,[31] and Fairburn et al 2019, Social Inequalities in Exposure to Ambient Air Pollution: A Systematic Review in the WHO European Region[32]). Williams et al (2018 The Lancet Countdown on health benefits from the UK Climate Change Act: a modelling study for Great Britain[33]) found a correlation between NO_2 concentrations and socioeconomic status (Carstairs index) at ward level

[29] Public Health Outcomes Framework (PHOF)
[30] Does exposure to air pollution increase the risk of dying from the coronavirus (COVID-19)?
[31] Associations between air pollution and socioeconomic characteristics, ethnicity and age profile of neighbourhoods in England and the Netherlands
[32] Social Inequalities in Exposure to Ambient Air Pollution: A Systematic Review in the WHO European Region
[33] Williams ML, Lott MC, Kitwiroon N, Dajnak D, Walton H, Holland M, et al (2018) The Lancet Countdown on health benefits from the UK Climate Change Act: a modelling study for Great Britain The Lancet Planetary Health **2:** e202-e213

(Pearson's coefficient 0.309). $PM_{2.5}$ concentrations were also correlated with socioeconomic status, but the correlation was less strong (Pearson's coefficient 0.139).



Distribution of ward level 2011 NO_2 concentrations in Great Britain, plotted by Carstairs 2011 deprivation quintiles (least deprived to most deprived). Reproduced under the Creative Commons CC-BY licence from Williams et al 2018: The Lancet Countdown on health benefits from the UK Climate Change Act: a modelling study for Great Britain [33]

Although Defra might want to consider whether or how it might develop an exposure reduction target which also addresses inequalities in exposure, or health inequalities, this might prove to be complex. Alternatively, consideration could be given as to whether the concentration-based "limit value" type target, or a separate policy, could play a role in addressing inequalities in exposure. Rather than incorporation within the formal targets framework, a possible approach might be to use nested modelling and sensitivity or supplemental analyses to assess whether interventions (proposed or implemented) reduce inequalities in exposure or have undesirable consequences for inequalities.

B6. Assessment of the target

In setting a target we need to consider how the target will be assessed and where the target will apply.

COMEAP's views on relevant health-based science questions are requested:

B6 (i) What location types are used within the epidemiological evidence base to estimate exposure?

Exposure assessments based on a range of locations (for example, monitors at background sites, modelling at residence) have been used in the exposure assessments in cohort studies, which are relevant to long-term exposure (see, for example, Chen and Hoek, 2020).

B6 (ii) What is the relationship of concentrations at different location types with the exposure metrics used in epidemiological studies?

This relationship will depend upon the method of exposure assessment used in the epidemiological studies. Sites near emission sources (for example, traffic-orientated monitoring sites) will likely experience higher concentrations than exposure metrics in epidemiological studies based on monitoring or modelling of concentrations at background locations. However, cohort studies using methods such as land-use regression modelling may well include concentrations at residences that are beside roads, roughly similar to roadside though not kerbside sites. A range of types of sites and geographical scales have been used in the exposure assessments in the cohort studies (long-term exposure) (for example, Chen and Hoek, 2020).

B6 (iii) What contribution does exposure at different location types make to overall individual or population exposure?

Roadside exposure might be unlikely to make a significant contribution to $PM_{2.5}$ exposure at a population level, both in terms of the proportion of population whose residence would be designated as roadside, or time spent on average by the population in a roadside location during a year. However, work undertaken in London[34] suggests that a large proportion (approximately 30%) of the population lives within 50m of a major road. This might not be representative of the situation in other parts of the UK, and the definition of a road as "major" or otherwise might not necessarily reflect traffic flow and, hence, pollutant exposure. Nonetheless, there are people who spend considerable amounts of their working life at roadsides – and some who live there. Although roadsides represent small areas within any specific local authority area, this equates to a large area across the country as a whole.

We note that a recent study (Castro et al, 2020)[35] found that, if 99% of all residential sites were to comply with the WHO guideline value of 10 µg/m^3 $PM_{2.5}$, the population-weighted mean concentration would be 17% below the guideline value (that is, 8.3 µg/m^3).

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March 2021

[34] Williams et al, 2019: Personalised-health-impacts-Summary for Decision Makers
[35] Castro, A., Götschi, T., Achermann, B. et al. Comparing the lung cancer burden of ambient particulate matter using scenarios of air quality standards versus acceptable risk levels. Int J Public Health 65, 139–148 (2020).