Questions for Non-Member Consultants on the PM PA from Dr. Sabine Lange

Ambient PM2.5 Concentrations in Locations of Epidemiology Studies

In section 3.2.3.2 the EPA summarizes the mean ambient PM concentrations measured in various key epidemiology studies (section 3.2.3.2.1); and then for a subset of these studies, the EPA considers whether the paper's study areas would have been in attainment for the current PM standards by deriving pseudo-design values for those study areas (section 3.2.3.2.2). When summarizing mean ambient PM concentrations measured in key epidemiology studies, the EPA includes studies that are investigating effects of both short-term exposure (on the scale of daily to weekly) and long-term exposure (on the scale of one to multiple years). The total mean concentrations of PM2.5 from both study types are then considered in the context of the current annual standard (section 3.2.3.3).

I looked at measured PM2.5 concentrations from one of the monitors in the Houston area (ID # 48211035) for a better general understanding of short-term and long-term PM2.5 concentrations. Included here is a figure that shows the daily and annual average PM2.5 concentrations from 2010 (Figure 1). This information helps to inform some of the questions that I ask below.

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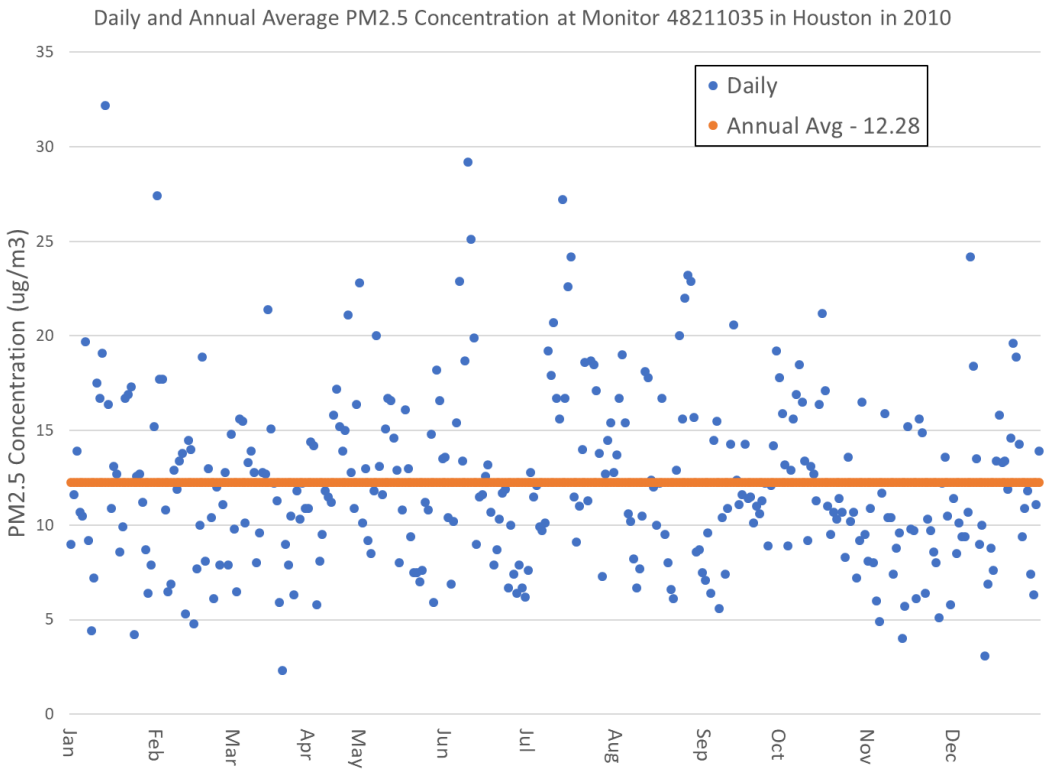

Figure 1. Daily and annual average PM2.5 concentrations measured at monitor 48211035 in Houston, Texas in 2010.

While it seems appropriate to compare the study mean PM2.5 concentration from a long-term exposure to the annual design value (both are on similar time scales), my question is:

1) **Is it appropriate to compare daily PM2.5 concentrations to the annual average?** Typically, this kind of comparison would not be done when deriving a toxicity factor, with short-term exposures being used to derive short-term toxicity factors, and long-term exposures for long-term toxicity factors. The concentration-response functions in the short-term epidemiology studies are derived using day-to-day changes in PM2.5, which doesn't seem like it would be captured in an overall average concentration (as in Figure 1).

In section 3.2.3.2.2 the EPA asks the question: are positive associations between PM2.5 and health effects occurring in areas that meet the current or potential alternative PM2.5 NAAQS standards? To answer this question, they calculate pseudo-design values for each of the study areas in the key papers that have monitoring data available for the DV calculation. With this information the EPA then summarizes the pseudo-design values associated with a proportion of the population in each study. The EPA does this for both the annual and 24-hour standard, and for both short-term and long-term studies. My questions are:

2) **Is it informative to derive annual average pseudo-design values for study areas in short-term studies (that look at effects of day-to-day PM2.5 concentration changes), in order to determine whether these study areas attained the current annual standard?** Although the EPA can technically determine if daily changes in PM2.5 concentration increased health effects in an area meeting the annual standard, **does this really inform the health protectiveness of the annual standard?** It seems that whether an area showed a positive effect or not could be completely independent of the annual standard and instead dependent on how much the PM2.5 concentrations changed from day-to-day.
3) In contrast to short-term studies that investigate the effects of day-to-day changes in PM2.5 concentrations within a certain geographic area, long-term cohort studies often look at the association between annual average PM2.5 concentrations and time-to-event data (such as the time from cohort entry to death) over long periods of time. For these studies, it is not uncommon for all study subjects in a single geographic area to have the same (or very similar) exposure assignments (e.g. Jerrett et al., 2017; Thurston et al., 2016), in which case the study is assessing the effects of PM2.5 between geographic areas, instead of within geographic areas. **In this case, is the pseudo-design value in a single geographic area particularly informative, when the association between PM2.5 and the health effect is driven by the differences between study areas?**

<u>Results of Risk Analysis</u>

In section 3.3.2.4 the EPA presents information about the variability and uncertainty in their risk estimates. They capture some quantitative estimates of uncertainty and variability, such as using concentration-response (C-R) functions from different studies, and deriving estimates using the 95% confidence intervals of the C-R functions. However, many more uncertainties are assessed only qualitatively, and several of those uncertainties are considered to have medium to high impacts on the risk estimates, including: simulating air quality to just meet current and alternative standards, representing population-level exposure in 12x12-km grid cells, and the shape of the C-R relationship at low PM concentrations. In addition to these considerations, there are multiple other aspects of the risk assessment that confer uncertainty on the risk estimate. Table 1 below shows very generally some example magnitudes of the potential uncertainties.

Table 1. An incomplete list of possible uncertainties in deriving risk estimates from reductions in PM2.5 concentrations.

Source of Uncertainty	Example Magnitude	Example Reference
Generating the Concentration-Response (C-R) Function in Epidemiology Studies		
Exposure Measurement Error	31-85%	Spatial error + population error (Dionisio et al., 2016)
Model Misspecification Error	50%	Generalized linear vs generalized additive models for PM10 (Sheppard, 2003)
Alternative C-R Functions within One Study	200%	Range of HRs generated using different exposure models (Jerrett et al., 2017)
Causal Relationship	0.35-1	US EPA Expert Elicitation of PM2.5 causality – provided is the range of probabilities that PM2.5 is causing mortality (Mansfield et al., 2009)
Air Quality Monitoring/Modeling		
Air Monitoring	± 10%	Allowable variation in 24-hour PM2.5 monitored concentrations
Air Modeling	± 30%	10-90% range for prediction of change in PM2.5 concentrations (Mansfield et al., 2009)
Applying the Concentration-Response Function		
Choice of C-R Function	400%	Variability in PM2.5 long-term all-cause mortality estimates presented in Table 3-7 using C-R functions from different studies (PM PA 2019)
Baseline Incidence Rates	± 5%	Influence Analysis 10-90% range for prediction of base mortality rates (Mansfield et al., 2009)
Population Forecasts	± 10%	Influence Analysis 10-90% range for census 2020 population forecasts (Mansfield et al., 2009)
Use of National Estimates	± 1000%	Range of C-R estimates across 77 study cities, compared to the national estimate (Baxter et al., 2017)
Threshold in C-R	6-90%	Change in premature mortality from CPP repeal cutpoint analysis (LML cutpoint on low end of scale; NAAQS on high end of scale) (USEPA, 2017)

The EPA notes that they lack the information to conduct a full probabilistic uncertainty analysis, which is the type of analysis recommended by the World Health Organization (WHO) for this level of complexity of a risk assessment. However, this does not remove the need for a more quantitative assessment of the many sources of uncertainty in the risk estimates.

4) **Is there a quantitative uncertainty analysis method that the EPA could use for this risk assessment that captures more of the uncertainty and variability of the risk estimates (such as those described in Table 1), in order to better inform CASAC and the EPA Administrator about the impact of these uncertainties**?

Potential Alternative Standards

In section 3.4.2.1 the EPA discusses whether the available data warrant a different indicator for the PM2.5 standard. This determination is primarily based on whether particular PM2.5 species show more consistent associations with health effects than total PM2.5. This kind of determination seems like it would fall prey to a specific problem that can be caused by exposure measurement error: namely, that having different levels of error associated with different explanatory variables in a regression can cause misleading results such that, for example, the variable measured with the least error is identified as the primary "culprit" for the health effect regardless of whether it is causally associated with the health effect (Carrothers and Evans, 2000; Fewell et al., 2007; Lipfert and Wyzga, 1996; USEPA, 2018). Because of monitoring technology and precision, as well as spatial variability in total PM2.5 compared to speciated PM2.5, total PM2.5 could be measured with less error than its constituents. My questions are:

5) **Could different magnitudes of error amongst different variables in regression analyses be masking the effect of a speciated constituent of PM2.5**?
6) **What happens when multiple potential explanatory factors are included in a single variable in an already-complex multiple regression system?** Presumably each PM2.5 component has a different C-R relationship with the health effect (even if that relationship is zero), and each is a somewhat better or worse surrogate for the relationship between actual exposure vs measured exposure. **What kind of an impact would this inclusion of multiple potential explanatory factors into one variable have on the final C-R function, and how accurate would that C-R function be?**

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