Comments on the ISA from Dr. Michael Jerrett (updated 08-05-15)

ISA – Summary Chapter

The document is much improved and more tractable. I had no major concerns, except with the characterization that most studies have not dealt with co-pollutants and this is only partly correct. Many studies have dealt with one or two co-pollutants, but not all; so this should be softened to haven't dealt adequately.

On types of evidence, there needs to be some mention of the scripted exposures such as the McCreanor et al. (2007) study. This is a hybrid between controlled exposures and epidemiology and could inform the determinations as well because the exposures are often more realistic than in chambers because they are in real world conditions.

Noise should be mentioned more prominently as a potential confounder.

The idea that we don't understand "double jeopardy" that well should be revised; there are specific studies on stress for example Shankardass et al. (2009) that do elucidate this area.

On exposures, could you delineate truck vs vehicle dominated roadways – this has important implications for understanding the impact of control measures given the high direct emissions of diesel?

There needs to be some caution in comparing to England because there is a larger proportion of diesel vehicles and therefore more primary NO_2. I wasn't sure why EPA didn't compare to the Canadian data. Health Canada has prepared all of this because they too are revising the NO_2 guidelines. Check with Barry Jessiman, Health Canada.

The discussion of roadway gradients could be refined by including mention of the types of roadways and volumes of traffic. In general much of the document talks about distance to roadways as though all roads are the same, whether they have 40,000 or 400,000 vpd. This needs to be addressed directly because it could explain why some cities observe higher NO_2 levels away from roadways.

Conceptual Model still Incomplete

- doesn't take physical activity into account
- fuzzy on what was meant at an indoor environment – in vehicle – how do we deal with that – not clear from the current presentation.
- The entire document is silent on intake fraction – this is a problem because so much of the NO_2 exposure probably occurs close to or at the source so the intake will likely be much greater

3.3 – Missed several studies on natural interventions – several physical activity studies (Andersen et al., 2015; Kubesch et al., 2015), road closures due to construction (Levy et al., 2004)

There is a literature on scripted exposure studies – the McCreanor study - increasingly important hybrid type models

3.3.1.1 – hard to compare between categories of distance to road with so many different impact zones cited

Could EPA conduct some systematic GIS analysis to show populations affected by near road exposures to make all the comparisons complete?

The review of LUR models is uneven and incomplete – many studies were missed (e.g. Jerrett et al. 2007 – and many more) – not sure why some were included and others not – needs to be clear; they did not deal at all with the issue of monitor siting and how this might affect the results; also there was no discussion of over-fitting and potential biases this introduces (see Beckerman et al. 2013a, 2013b - Beckerman et al. (2013b) only deals with PM2.5, but the point is that many of the current efforts in the literature on land use regression have over fit the data to the sample and probably are overestimating their predictive capacity. Beckerman et al. (2013a) does include NO2 also makes this point.) The comment that city-specific factors would differentiate the variable selected is partly correct, but how much would there be commonality – virtually all the models or the vast majority would have used some indicator of roadway proximity or traffic density. So there are some variables to go across many cities and locales.

Concerned about the spatiotemporal modeling discussion – not very sophisticated or subtle. See comments from Dr. Sheppard.

If you are going to mention other types of models that have not been used in Epi you should mention microsensors. I would recommend cutting those model types that have not been used so far.

On cancer, I found it odd that there wasn't any reference to IARC's recent pronouncements on traffic pollution being classified as a group 1 carcinogen; I also thought that the authors could improve the document by comparing, where possible, their conclusions to those of WHO or other national (e.g., Canada) or state level assessments (e.g. California).

Comments on Chapter 7

Please comment on the effectiveness of the integrated analysis and the extent to which the strengths and limitations of the evidence and the extent to which the strengths and limitations of the evidence are explicitly and consistently described in communicating the rationale for the conclusions about at-risk populations.

The chapter is an improvement over the previous version. Overall, the conclusions are the chapter are sound and well-justified.

There are several areas that could be improved:

1) The overall framework and discussion of types of evidence is useful. It was not clear, however, why a causal framework similar to earlier chapters was not derived.
2) Most of the studies would not have had effect modification as the primary hypothesis as effect modification. The authors at EPA should acknowledge this limitation. It would be useful to identify which, if any, of the studies was undertaken with the effect modification as the primary hypothesis. The reason for concern is whether most of the studies would have been under-powered to detect effects.
3) I would like to see for each section some discussion of whether there are exposure differences vs differences in the health effects. My concern here is that if we do find that NO_2 has causal associations with certain health outcomes, then higher exposures would, likely, in a well-designed study, lead to higher effects. There is substantial evidence the groups in poverty or who are non-white experience higher exposures to NO_2, but the epidemiological evidence is still lacking. But it is important to clearly show how the exposure differences follow SES or racial gradients, since for those that are considered causal or likely to be causal, there is high potential for larger health effects even if the epidemiological evidence of a direct effect modification is lacking.
4) In some cases, such as older adults, there is contradictory evidence base between epidemiology and controlled human studies. It is not as clear how the evidence is being weighted.
5) There were some instances of conflation between individual and group level SES. It is important to distinguish between these levels because they might have very different potential to modify the effects of NO_2 and could operate along difference biological pathways.

Also Arain et al. (2009) discusses temporal and land use controls over NO2 concentrations from Canadian data, which has more directly relevant traffic and industry impacted sites than in the U.S. - this might be helpful, since it more thoroughly combines meteorology data with land use influences on NO_2.

References

Andersen, Z. J. J., de Nazelle, A., Mendez, M. A. A., Garcia-Aymerich, J., Hertel, O., Tjønneland, A., Overvad, K., Raaschou-Nielsen, O., and Nieuwenhuijsen, M. J. (2015). A study of the combined effects of physical activity and air pollution on mortality in elderly urban residents: the danish diet, cancer, and health cohort. *Environmental health perspectives*, 123(6):557-563.

Arain, M. A., Blair, R., Finkelstein, N., Brook, J., and Jerrett, M. (2009). Meteorological influences on the spatial and temporal variability of NO2 in toronto and hamilton. *The Canadian Geographer / Le Géographe canadien*, 53(2):165-190.

Beckerman, B. S., Jerrett, M., Martin, R. V., van Donkelaar, A., Ross, Z., and Burnett, R. T. (2013a). Application of the deletion/substitution/addition algorithm to selecting land use regression models for interpolating air pollution measurements in California. *Atmospheric Environment*, 77:172-177.

Beckerman, B. S., Jerrett, M., Serre, M., Martin, R. V., Lee, S.-J., van Donkelaar, A., Ross, Z., Su, J., and Burnett, R. T. (2013b). A hybrid approach to estimating national scale spatiotemporal variability of PM2.5 in the contiguous united states. *Environ. Sci. Technol.*, 47(13):7233-7241.

Jerrett, M., Arain, M. A., Kanaroglou, P., Beckerman, B., Crouse, D., Gilbert, N. L., Brook, J. R., Finkelstein, N., and Finkelstein, M. M. (2007). Modeling the intraurban variability of ambient traffic pollution in toronto, canada. *Journal of Toxicology and Environmental Health, Part A*, 70(3-4):200-212.

Kubesch, N. J., de Nazelle, A., Westerdahl, D., Martinez, D., Carrasco-Turigas, G., Bouso, L., Guerra, S., and Nieuwenhuijsen, M. J. (2015). Respiratory and inflammatory responses to short-term exposure to traffic-related air pollution with and without moderate physical activity. *Occupational and Environmental Medicine*, 72(4):284-293.

Levy, J. I., Baxter, L. K., and Clougherty, J. E. (2006). The air quality impacts of road closures associated with the 2004 Democratic National Convention in Boston. *Environmental Health*, 5(1):16+.

McCreanor, J., Cullinan, P., Nieuwenhuijsen, M. J., Stewart-Evans, J., Malliarou, E., Jarup, L., Harrington, R., Svartengren, M., Han, I.-K., Ohman-Strickland, P., Chung, K. F., and Zhang, J. (2007). Respiratory effects of exposure to diesel traffic in persons with asthma. *N Engl J Med*, 357(23):2348-2358.