Review Comments on "Spatiotemporal Analysis of Air Pollution and Mortality in California Based on the American Cancer Society Cohort: Final Report." Jerrett et al., June 2011

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Introduction and Purpose

As stated in the abstract, the purpose of this CARB project is to provide valid estimates of long-term effects of air pollution on all California residents. The project mandated that such estimates be based on the mortality experience of the American Cancer Society's Second Cancer Prevention Study (hereafter "ACS CPS II"). However, it becomes clear from Jerrett et al. (hereafter "the report") that the main target is actually fine particulate matter, as indicated by the available $PM_{2.5}$ measurements, rather than all pollutants, as implied by the title. Further, nothing in the report justifies the restriction of this inquiry to ACS CPS II; it is simply stated as a given, even though it is acknowledged that the demographic make-up of the ACS cohort does not match that of California and that other cohort studies are available. The abstract cites "a lack of other large cohort studies on long-term effects" as part of this justification; however, a simple search of Medline using PubMed finds 98 such published and available studies (without ACS CPS II papers), which were reduced to 48 after excluding Asian studies and non-mortality endpoints. Adding some studies from my own files increased the number to 61, as shown in Appendix A. Note that no single cohort can adequately represent a population as diverse as California's; the proper approach would thus be a meta-analysis of all of the available cohort and population studies.

Three groups of citations in Appendix A merit special attention:

1. Other California cohort studies: #7, 33, 48, 58-61. (six papers on 3 cohorts)
2. Studies involving appreciable numbers of non-white subjects: #10, 26, 41, 42, 49, 50, 54, 55.
3. Studies emphasizing vehicular traffic effects: #2, 5, 9, 10, 13,16, 17, 18, 20, 25, 43, 49, 52, 54, 55.

The relative importance of the first group of studies is obvious. The second group of papers could help respond to the actual makeup of the California population, which is only about 77% white. By contrast, the California component of ACS CPS II is 92% white, but the Washington University – EPRI Veterans Cohort is only 65% white (refs 10, 26, 41, 42, 50, 54, 55 above) and our studies with this group show substantial hazard differences by race. Note that since the report assigned exposures by home address, it is likely that predominantly non-white California neighborhoods were not included. The fundamental importance of vehicular traffic effects (15 citations above) is borne out by the report's conclusion that "combustion-source air pollution, especially from traffic is significantly associated with premature death", even though it did not directly consider specific traffic-related particles.

The report emphasizes its efforts in trying to define exposures based on the home addresses of cohort members and the need to cover the whole state. Problems with these requirements include:

1. non-residential exposures are neglected.
2. the hazard analysis will intrinsically be weighted towards the locations with the most members, so that members in remote locations will have little impact on the analysis in any event. (The report should include numbers of subjects assigned to each ambient monitor.)

It is perhaps ironic that the report devotes considerable effort to defining $PM_{2.5}$ exposures and effects (note Table 1 in the abstract) yet the bottom-line conclusions on p. 7 refer to traffic. For example, there are detailed discussions of previous analyses of long-term effects of $PM_{2.5}$ (p. 20) but not for traffic exposures. There are many sources of $PM_{2.5}$ other than traffic, and the report provides no correlations between traffic exposure and ambient air quality. Had the 15 prior studies of traffic effects been consulted at the beginning of the project, for example on exposures, better results would have been likely.

Specific Comments

Table 21 provides mean air quality levels based on individual home addresses, but other sources of exposure are not considered. While the effort expended in using home addresses may be admirable, use of averages over county or sub-county areas may actually be more realistic, taking into account commuting and occupational exposures. Several studies have shown that long-term air pollution risks tend to be higher for younger adults (see [Villeneuve et al., 2002 for example), so that residential and employment mobilities may pose real issues. Ostro et al. (2010, erratum) found major differences in hazards within 8 km of monitors and within 30 km.

The correlations in Tables 24 and 25 should be subject-weighted. The values shown are so high as to preclude any real hope of defining separate hazards associated with any of them.

The analysis does not include carbon monoxide or any other non-sulfate constituents of PM, like elemental carbon or nitrate. Ostro et al. (2010) used such data; which are available at 8 California monitors. They found 44,000 female subjects living with in 30 km of a monitor. This approach should have been considered with ACS CPS II.

The analyses of Ostro et al. (2010) merit specific attention, especially the more recent erratum. For example. They estimated 216 all-cause deaths associated with $PM_{2.5}$ within 8 km of a monitor, but only 75 after expanding the catchment area to a 30 km radius. This implies that 141 lives were “regained” by this change in definition, whereas one would have though that additional lives would have been lost because of the regional nature of $PM_{2.5}$. The ACS report should have included such an analysis.

Similarly, when one computes the difference between all-cause deaths associated with $PM_{2.5}$ in Ostro et al., and deaths associated with specific causes, one concludes that “other” deaths (causes not mentioned) must be strongly negatively associated with

$PM_{2.5}$. This is the reason that only all-cause deaths are important for public health policies.

The conclusions relative to traffic cite "combustion-source air pollution." However, no attempts were made to consider traffic noise, CO, road dust, or traffic-related air toxics like benzene of formaldehyde. Thus, there is no basis for assuming that "combustion products" *per se* are responsible for all of the observed traffic-related effects.

The report considers subjects by age but not risks by age, which have been shown to decrease in other studies. Brunekreef (1997) and Englert (1999) have shown that such distributions are crucial when estimating the changes in life expectancy within a closed cohort, which differ from those in an open population (ecological) study. It is important to recognize that early deaths within a closed cohort leave a remainder of hardy survivors for whom environmental risks are less likely. This is seen in Engstrom's analysis of the California ACS CPS-I cohort (Ref. 10 in the report). Englert (1999) carried out life expectancy calculations that show this "cohort depletion" effect and concluded: "Applying the relative risk derived from cohort studies directly as a multiplier on daily or annual mortality leads to a considerable overestimation of effects."

The tables of results (hazard ratios) (Tables 27-42) are bewildering and would appear to allow the reader to choose any value that meets his/her prior expectation, from major risk to major benefit. No measures of overall model fit are presented and there is thus no basis for selecting one model over another. Perhaps most telling are the frequent occurrences of apparently beneficial effects with respect to "other" causes of mortality (often significant). Unfortunately, we cannot limit air pollution exposures to persons having specified diseases, and thus it is only risks of all-cause mortality that matter. (The report does not specify whether trauma deaths are included; they should not be.)

It would have been useful to test whether using individual home exposures rather than area averages actually improves overall model performance.

There several alternative measures of traffic proximity besides residential proximity to highways, for example traffic density (VMT per unit area). People in the work force are exposed to many situations other than those at home. Given the final conclusions about the importance of traffic, more attention should have been placed on traffic exposures.

This report is entitled "spatiotemporal" analyses, yet the temporal portion is quite minor, was unsuccessful, and did not consider either traffic or PM. Villeneuve et al. (2002) considered temporal variations within the Six Cities Study and commented:

1. "Mortality risks associated with $PM_{2.5}$ did not depend on when exposure occurred in relation to death…."
2. "The inclusion of the number of years of residence did not change appreciably the risk of mortality due to $PM_{2.5}$."

Similar information should have been obtained for ACS CPS II; it bears directly on the crucial public health question, whether intervention by pollution abatement would actually have any effects. Until the effects of prior pollution abatement have been demonstrated, it seems problematic to call for further abatement.

As a result, this report provides no evidence about the extent to which improved public health that might result from further abatement of air pollution or traffic. "Abatement" is not even mentioned in the report, yet it is a main task of CARB..

Conclusions

It is clear that a large amount of effort went into this report. However, when viewed as a whole, it is also clear that selecting and emphasizing a particular hypothesis to be supported *a priori* (mortality risks associated with $PM_{2.5}$) is fraught with peril. The beginning of the report is laced with $PM_{2.5}$ issues; traffic risks are emphasized at the end. Had the investigators approached the topic (public health) with a more open mind at the outset, a better result might well have been achieved.

I recommend that this report be rejected in its present state until the above deficiencies have been addressed.

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Appendix A Long-term cohort and ecological mortality studies, as of 6/24/2011

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