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Ultrafine Particulate Matter in the San Francisco Bay Area

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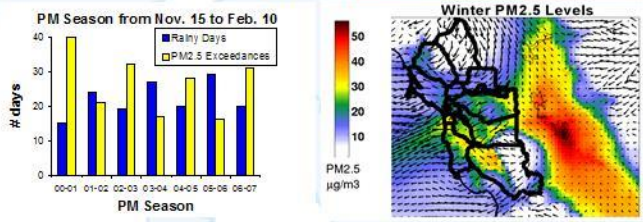

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Preface

This report consists of two parts. Part I was prepared by staff of the Bay Area Air Quality Management District (BAAQMD) and Part II was prepared by staff of the California EPA's Office of Environmental Health Hazard Assessment (OEHHA). The goal of the report is to provide estimates of the health impacts of ultrafine particulate matter (UFPM) in the San Francisco Bay Area based on currently available information. This is the first attempt to quantify public health burdens and associated monetary costs of UFPM at a regional scale.

The BAAQMD began studying UFPM in 2012. The study consists of continuous monitoring of UFPM at five air monitoring stations, emissions inventory preparation, modeling and analysis of health impacts. Because each of the UFPM study components is relatively new, uncertainty is expected in the estimated public health burdens and associated monetary costs; however, information obtained from the analysis is extremely important for the preliminary assessment of UFPM's ranking among other harmful pollutants. This ranking can be effectively used by BAAQMD as well as other air quality management agencies to allocate appropriate resources to reduce UFPM emissions, ambient levels and health impacts.

The on-going study is expected to continue providing information on UFPM and will expand to new areas of investigation such as speciated UFPM measurements and the use of associated markers in source apportionment and trend analyses. When significant progress or refinements are made, this report will be updated with new or refined information.

Ultrafine Particulate Matter in the San Francisco Bay Area
Part I: Health Impact Analysis

1. Introduction

Ultrafine particulate matter (UFPM) refers to particles with diameters less than 0.1 µm (also referred to as UFP and PM0.1). Though it is currently an unregulated pollutant, it has harmful effects on human health. Because of its potentially significant adverse health impacts, the Bay Area Air Quality Management District (BAAQMD) has been studying UFPM with the goal of reducing its emissions, ambient levels and health impacts in the Bay Area. The key components of this study, described in a BAAQMD document (BAAQMD, 2010), include ambient monitoring, data analysis, emissions inventory development, air quality simulation, and estimation of exposure and health impacts. Significant progress has been achieved in all of these areas. In the current report, we document the preliminary estimation of the public health burden and associated monetary costs of UFPM for the San Francisco Bay Area.

2. Background

The US Environmental Protection Agency (EPA) developed a methodology to assess the benefits of air quality improvements with respect to public health based on epidemiologic studies. This methodology was applied to quantify the benefits of lowering the National Ambient Air Quality Standards (NAAQS) for ozone and fine particulate matter (PM2.5) and was implemented in the Environmental Benefits Mapping and Analysis Program (BenMAP) software (US EPA, 2012).

BenMAP combines assessments of changes in air quality (expressed as a difference in ambient concentrations of a selected pollutant) with health impact functions. It then applies the results to detailed population and demographics data to estimate the change in the number of occurrences of air quality-related health endpoints. It further computes the monetary value of these changes using preset economic valuation functions. While BenMAP is designed to allow analysis of any pollutant, the current publicly released version is only set up for analysis of ozone and PM2.5.

California EPA's Office of Environmental Health Hazard Assessment (OEHHA) compiled worst-case scenario UFPM concentration-response functions from published epidemiologic literature. The BAAQMD then used the concentration-response functions to derive health impact functions for UFPM and incorporated these into BenMAP to analyze the health impacts of UFPM.

In the following sections, we describe how health impact functions were derived from the scientific literature, the process of estimating UFPM concentrations over the Bay Area, and the preparation of population and demographic data. Results from this analysis are then presented and discussed in light of those for PM2.5. Finally, the status of BAAQMD's ongoing and future work is summarized.

3. Derivation of UFPM Health Impact Functions

At the core of the BenMAP computer program are health impact functions, which quantitatively relate a given change in air quality to the resultant change in health outcome. These health impact functions in turn are based upon concentration-response functions reported in epidemiologic studies on the impacts of air pollution. For this work, OEHHA extensively searched published peer-reviewed articles on UFPM and its health impacts, and identified dozens of related articles suitable for developing health impact functions.

The concentration-response functions from studies that addressed the same health outcome were then combined via meta-analysis to arrive at estimates of the impacts of UFPM on four health endpoints: mortality, cardiovascular hospital admission, respiratory hospital admission, and respiratory emergency room visits. The details of this search and compilation process are discussed in Part II. Here, we note two important assumptions regarding the use of the published information. First, OEHHA assumed that the effects reported were attributable to UFPM although some studies showed the presence of other correlated co-pollutants, such as PM2.5. (Even so, about half the studies used have correlations less than 0.5 between UFPM and PM2.5, so we have some confidence that those studies are able to measure independent effects of the two particle sizes.) Second, most studies relied upon ambient measurements at a single monitor (and exposure was assumed to be at the levels recorded by that monitor) although UFPM concentrations tail off considerably 300-500 meters away from a source. Both of these assumptions introduce large uncertainties into the association between the assumed exposure and the observed health outcomes.

Table 1 summarizes the results of our findings. The table lists the percent change in the incidence of each health outcome given a 10,000 particles/cm^3 increase in ambient UFPM levels. Numbers in parentheses represent the range of impact within a 95% confidence interval (CI). Studies contributing to the values shown in Table 1 assumed a log-linear form for the concentration-response functions.

The information in Table 1 was used to derive the parameters specifying the health impact functions, which were then incorporated into BenMAP as the mean of the beta parameter and its standard error (designated "sigma"). These were computed using

guidance given in the BenMAP model documentation (US EPA, 2012). The results are shown in Table 2.

Table 1. Estimated excess risk associated with a 10,000 particles/cm^3 increase in ultrafine particles in the Bay Area.

Outcome	Age Group	Estimate (95% CI)
All-cardiovascular hospitalizations	All	1.4% (-0.5, 3.3)
All-respiratory hospitalizations	All	19.5% (7.2, 34.4)
All-respiratory emergency room visits	<15 yrs	1.6% (-0.2, 3.5)
	≥65 yrs	1.3% (-0.1, 2.7)
	All*	1.4% (0.3, 2.5)
All-cardiovascular mortality	All	2.3% (1.0, 3.7)
All-respiratory mortality	All	2.3% (-0.1, 4.7)
All-cause mortality	All#	1.6% (0.7, 2.5)

*An "all-ages" estimate can be used in place of the age-specific results.
#An "all-cause" estimate can be used in place of the respiratory plus cardiovascular estimates.

Table 2. UFPM health impact function parameters derived from information in Table 1.

Outcome	Age Group	Mean Beta	Sigma Beta
All-cardiovascular hospitalizations	All	1.39e-06	9.56e-07
All-respiratory hospitalizations	All	1.78e-05	5.77e-06
All-respiratory emergency room visits	<15 yrs	1.59e-06	9.29e-07
	≥65 yrs	1.29e-06	7.05e-07
	All	1.39e-06	5.53e-07
All-cardiovascular mortality	All	2.27e-06	6.73e-07
All-respiratory mortality	All	2.27e-06	1.20e-06
All-cause mortality	All	1.59e-06	4.52e-07

These parameters are compatible with UFPM input concentrations expressed in units of particles/cm^3.

4. Estimation of UFPM Concentration Fields

BenMAP estimates the impacts of changes in air quality; therefore, it requires two spatially resolved concentration fields: a baseline field and a control field. (The latter typically represents concentrations expected after implementation of control strategies.)

Additional requirements are that the periodicity and units of the concentration data match those implicit in the health impact functions.

With respect to periodicity, all of the epidemiologic studies for which results were chosen for this analysis relied on 24-hour average UFPM concentration data. Furthermore, all studies used concentration data in units of particles/cm^3 (i.e., number concentration).

BenMAP supports two options for inputting air quality fields – point-based observations, which BenMAP uses to populate the air quality grid via interpolation, or a grid-based field such as those obtained from air quality models. We explored both options for this work.

The BAAQMD has been collecting UFPM data continuously at four air monitoring stations (Santa Rosa, San Pablo, Redwood City, and Livermore) since 2012. (A fifth station was added in 2014, so its data were unavailable for this study.) The extrapolation of UFPM concentrations from these stations to a domain covering the entire Bay Area, however, is not representative. For instance, important sources of UFPM such as freeways cannot be distinguished; therefore, we opted to proceed with the second option.

Typically, this option makes use of modeled concentrations of the pollutant of interest; however, the BAAQMD's UFPM modeling is still in its preliminary stage, and the model currently overestimates UFPM concentrations by a factor of 2-3 compared to available observations. We therefore decided to estimate UFPM fields using a combination of observations and modeled NO_2 concentrations rather than relying on direct outputs from UFPM simulations.

We studied the relationships between measured UFPM concentrations and other co-measured pollutants at the four stations listed above. The seasonal average UFPM concentrations correlated well with seasonal average NO_2 concentrations. Subsequently, we developed statistical regressions between these two pollutants. The details of the derivation of the regressions and the rationale for selecting NO_2 are given in Appendix A.

These regression formulas were then applied to simulated 2010 NO_2 concentrations from the BAAQMD's PM2.5 modeling work to obtain baseline seasonal average UFPM gridded concentration fields. (The BAAQMD models PM2.5 using the 4 km resolution grid domain from the Central California Ozone Study [CCOS] so the resulting UFPM concentration fields are of the same horizontal resolution.) To be consistent with the 24-hour average UFPM concentration periodicity used in estimating the health impacts functions, each day of a season is assumed to have concentrations the same as the average for that season.

The control UFPM field was assumed to be zero for all seasons because there is no existing information to suggest a threshold level below which UFPM constitutes no public

health risks. This also implies that the estimated health impacts are due to all sources, not just anthropogenic activity.

The average of seasonal concentrations (representing the annual average) is shown in Figure 1. The nine-county Bay Area annual average UFPM concentration was estimated to be around 7700 particles/cm^3. The resulting UFPM concentration field also shows that the Bay Area's core experiences the highest levels of UFPM. In particular, Berkeley, Oakland, and San Jose bear the largest burden in terms of high annual average UFPM concentrations – greater than 12,500 particles/cm^3, which is more than 1.5 times the regional average. For reference, the observed annual average UFPM level across the four measurement stations was around 9700 particles/cm^3 for 2012.

Though not shown, seasonality is also apparent, with winter having the highest region-wide UFPM levels (~8600 particles/cm^3), followed by summer (~7900). Spring and fall show similar UFPM levels, with ~7400 and 7100, respectively. Based solely on actual observed UFPM data (from the four stations), winter still shows the highest concentrations (~11,700 particles/cm^3) followed by spring (~10,800) and fall (~9000), with summer having the lowest levels (~8900). The differences in seasonal trends between observed and estimated data may be attributable to the regression equations used to estimate UFPM from NO_2 (see Section 1 in Appendix A).

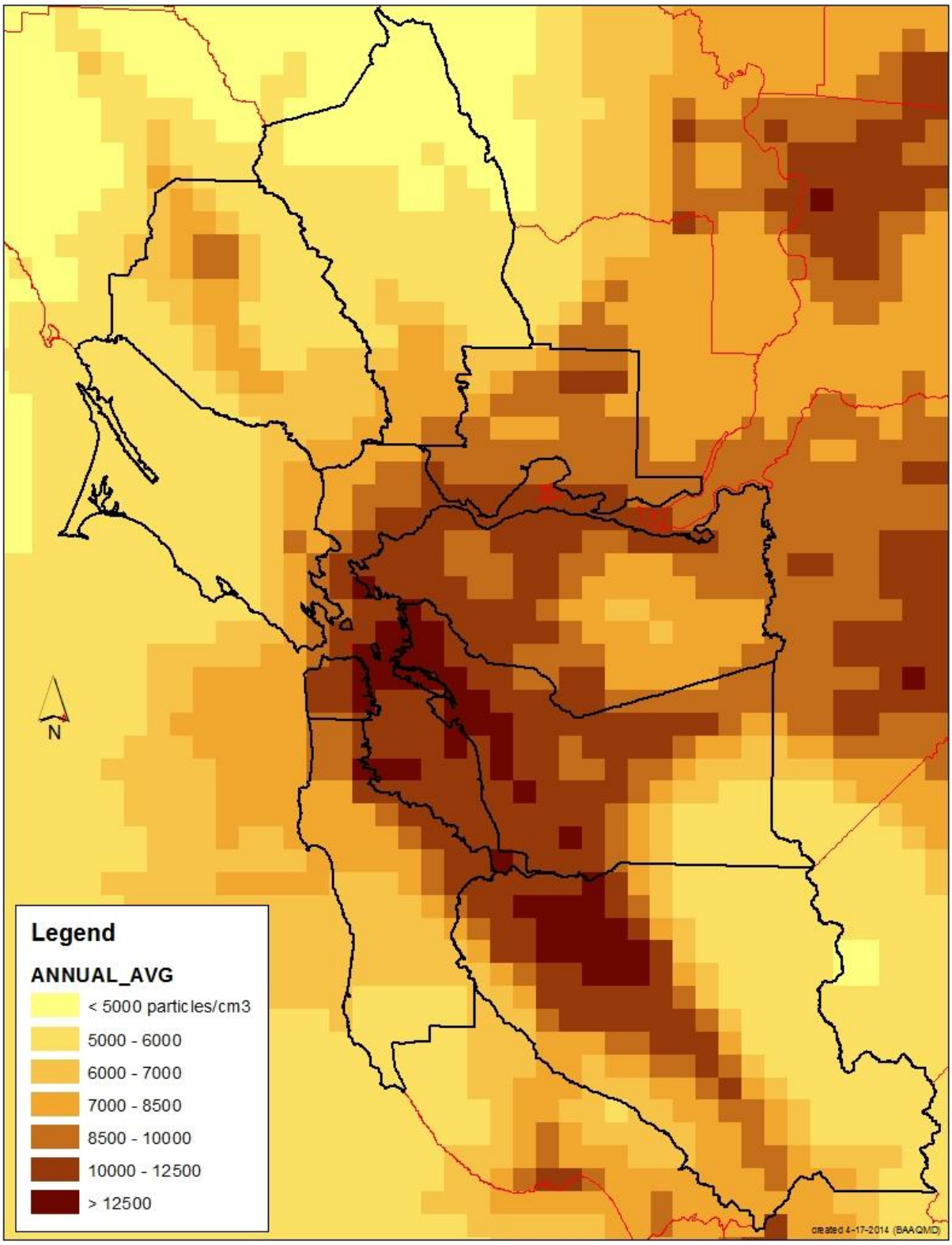

Figure 1. Annual average UFPM concentration derived from simulated 2010 NO_2.

5. Preparation of Population Data

Population and demographic data comprise the other major input to BenMAP. The model's main constraint with regard to these data is that they contain sufficient detail concerning age range, gender, and race/ethnicity categories to match the specific requirements of the health impact functions. Furthermore, while BenMAP is capable of estimating population within a grid cell[1] from population data at any resolution (using areal overlap), it is recommended that population inputs be prepared from the most highly resolved data source available. This is particularly important for pollutants with large spatial variability, such as UFPM.

For this work, we used the US EPA's PopGrid tool to process 2010 Census data for input to BenMAP. PopGrid generates spatially resolved population estimates for a prescribed grid domain, i.e., the CCOS 4 km modeling domain, based on detailed block-level US Census population data. The resulting demographic categories are those used by EPA in their NAAQS analyses. The results for two age groups are illustrated in Figures 2 and 3, which show the population of individuals under 20 years old and over 64 years old, respectively. These age groups are typically considered sensitive populations. (Note that while we only used all-age health impact functions in this current work, detailed demographic data are in place in anticipation of more robust, age-specific functions becoming available.)

The use of block-level data is essential to maintaining precision in exposure calculations, particularly in the most densely populated locations, because these tend to have geographically smaller census blocks. A comparison of Figures 2 and 3 to Figure 1 shows that these locations also tend to coincide with areas with high UFPM levels. About half of the Bay Area's population resides in areas where the annual average UFPM level is at least 1.5 times the regional average. These areas represent only 10 percent of the total geographical area of the Bay Area. More than 90 percent live in areas with UFPM levels above the regional average. These statistics indicate that these areas have the most influence upon exposure and cumulative health impacts.

To take full advantage of the more highly resolved population data, it is necessary to have air quality (concentration) data at a similar resolution. In this respect, the current 4 km horizontal grid resolution defining the UFPM concentrations is not optimal. We expect that if the resolution were finer, the statistics presented in the paragraph above would point toward an even narrower geographical area of concern.

[1] A grid can be any polygonal domain including regular rectangular cells or county boundaries.

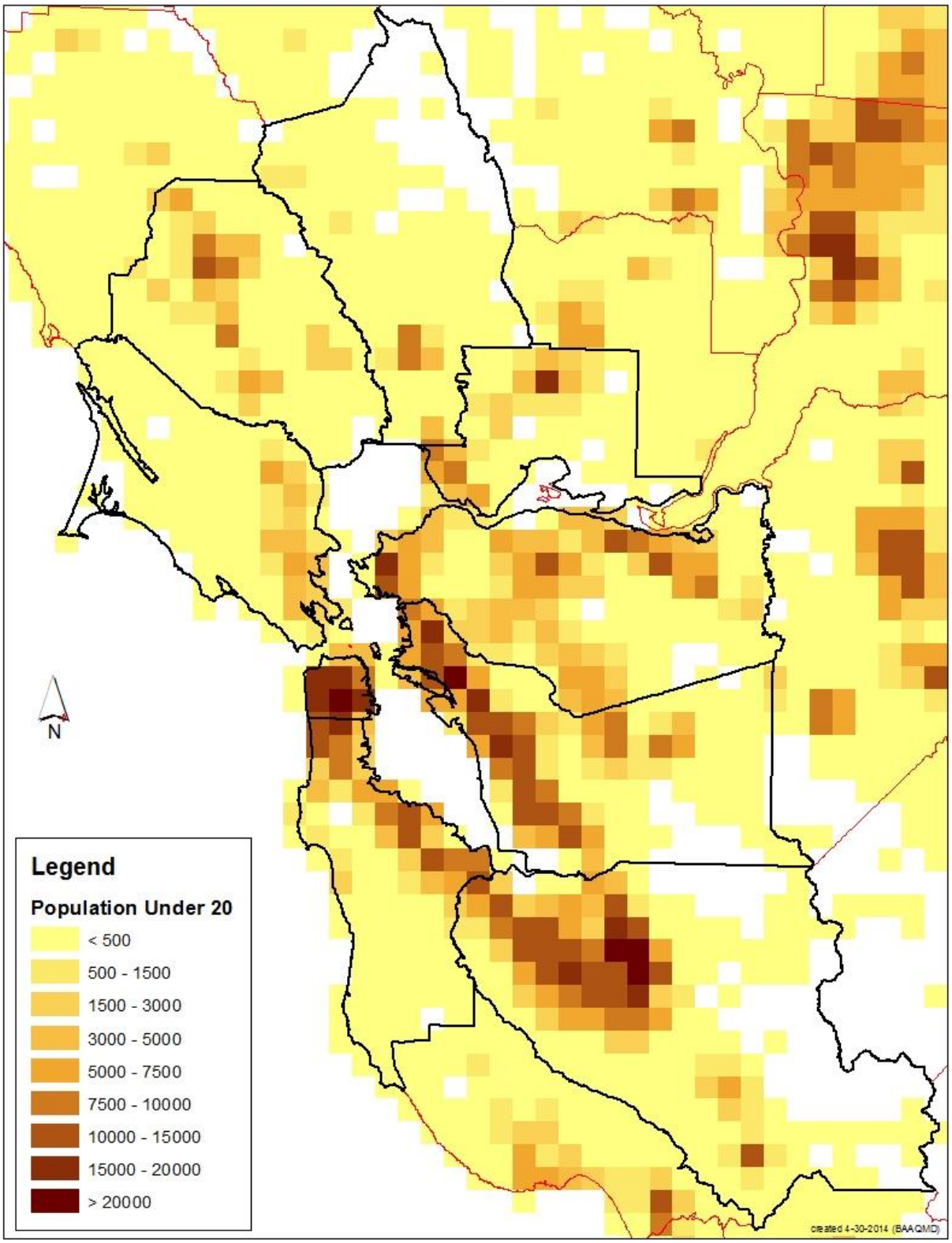

Figure 2. Gridded population of those under age 20 derived from 2010 Census block-level data.

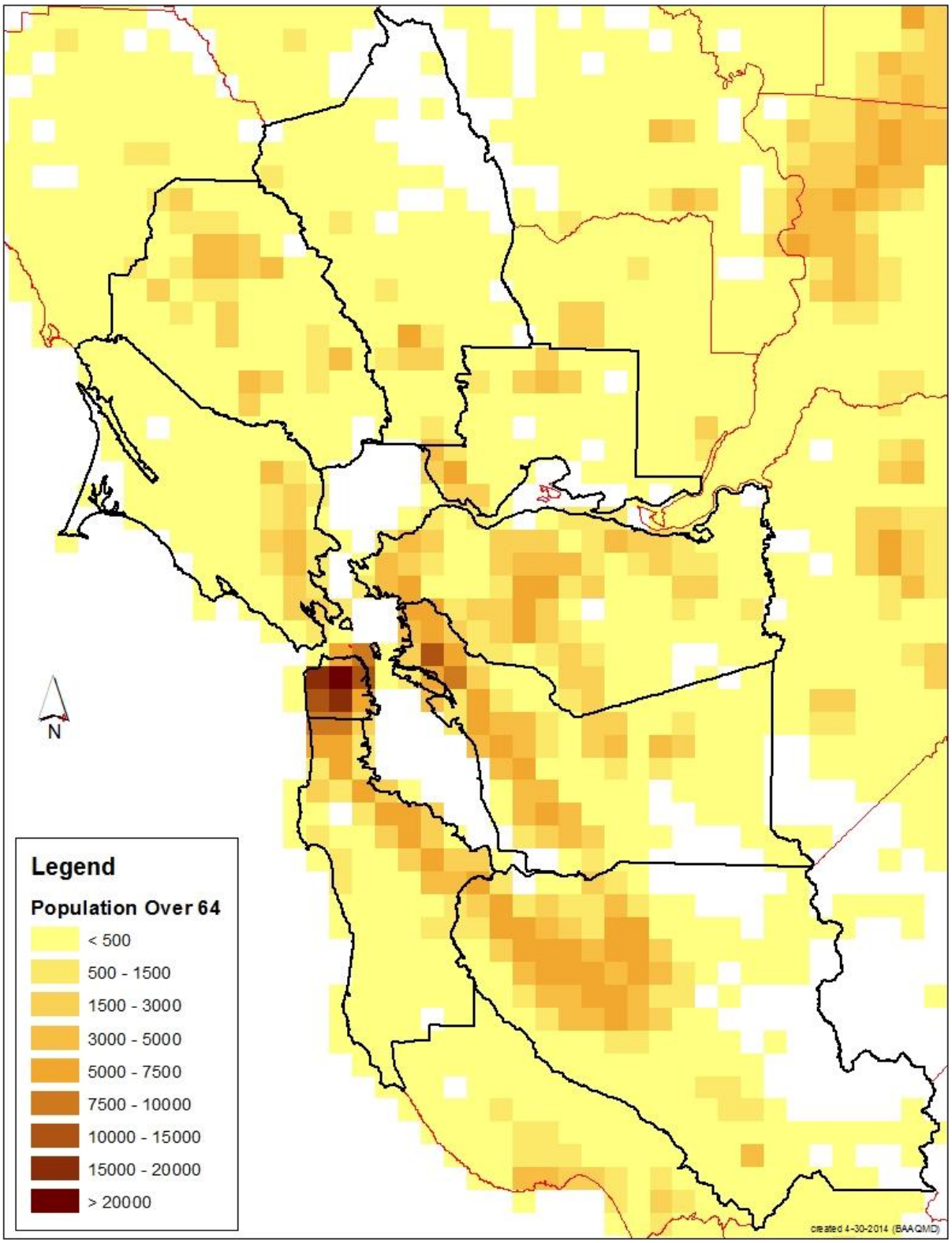

Figure 3. Gridded population of those over age 64 derived from 2010 Census block-level data.

6. BenMAP Application and Results

Execution of the BenMAP model occurs in three steps: estimating the change in incidence of each selected health endpoint, estimating the monetary impacts associated with those changes, and pooling results across multiple studies. Pooling is desirable to reduce uncertainty when more than one study or health impact function is available for a single health endpoint and they overlap in terms of their study populations (e.g., by age range). In this study, we elected to use the "all ages" functions alone (see Table 1) so that there was no overlap.

The following tables summarize the resulting change in incidence of the four health endpoints included in this study and the associated monetary valuations. Note that valuations associated with mortality represent the willingness to pay to avoid death whereas valuations associated with morbidity (costs of illness) are estimates of direct medical costs.

This analysis estimates that UFPM contributes to more than 800 premature deaths a year (see Table 3), a rate almost half of that attributed to PM2.5 (~1700) in a previous BAAQMD study (BAAQMD, 2011). The total value of the losses related to UFPM exposure is over $7 billion (in 2010 dollars) and is dominated by the mortality impacts. With regard to costs of illnesses linked to UFPM, our analysis shows an annual cost of more than $300 million, not accounting for other likely health endpoints such as missed school and work days. Hospital admissions for respiratory illness are by far the largest portion of annual costs of illness for the endpoints that were estimated.

Alameda County experiences the largest impacts, followed by Santa Clara County, despite the latter having a larger population. This result stands in contrast to Santa Clara County having the highest health impacts for PM2.5, a more regional pollutant. This suggests that the localized nature of UFPM can be very influential in determining public health impacts and thus warrants special consideration in identifying effective mitigation measures. Also, given its localized impacts, current information on PM2.5 transport, especially from the Central Valley, may not be applicable to UFPM. More studies are needed to quantify the impact of transport, if any, on UFPM levels and exposure.

Another important consideration is the seasonality of UFPM. Whereas PM2.5 is generally considered a wintertime pollutant due to both emissions and meteorology (as it pertains to secondary PM2.5 formation), UFPM is a year-round problem, especially near sources such as major transportation corridors.

Table 3. Estimated 2010 annual total public health impacts in the Bay Area attributable to UFPM.

County	Excess Mortality	Cardiovascular Hospital Admissions	Respiratory Hospital Admissions	Respiratory Emergency Room Visits
Alameda	193	255	2573	690
Contra Costa	124	151	1416	412
Marin	24	25	204	52
Napa	15	18	154	34
San Francisco	108	119	1089	217
San Mateo	77	91	720	209
Santa Clara	180	228	1929	527
Solano	42	61	466	146
Sonoma	45	43	372	106
Total	**808**	**991**	**8922**	**2393**

Table 4. Estimated 2010 annual monetary valuations associated with public health impacts attributed to UFPM in the Bay Area.

County	Excess Mortality (million)	Cardiovascular Hospital Admissions (thousand)	Respiratory Hospital Admissions (thousand)	Respiratory Emergency Room Visits
Alameda	$1,690	$9,992	$75,767	$267,982
Contra Costa	$1,092	$5,922	$41,788	$159,763
Marin	$208	$967	$6,094	$20,273
Napa	$129	$698	$4,497	$13,101
San Francisco	$944	$4,663	$32,127	$84,296
San Mateo	$679	$3,554	$21,259	$81,153
Santa Clara	$1,578	$8,952	$57,166	$204,506
Solano	$369	$2,365	$13,646	$56,845
Sonoma	$395	$1,679	$10,881	$41,210
Total	**$7,084**	**$38,791**	**$263,224**	**$929,128**

Note: Values are given in 2010 dollars.

7. Future Work

As discussed in Section 4 above, obtaining spatially resolved concentration data is critical to assessing human exposure, especially for a pollutant such as UFPM. Because it is impractical to establish a monitoring network dense enough to produce data with the level of resolution desired, computer simulation plays a very important role. The BAAQMD has begun modeling UFPM concentrations using tools and data that were developed mainly for PM2.5 modeling; however, we have also established a collaborative project with the University of California at Davis to develop enhanced emissions inventory and modeling techniques. The anticipated outcome of this work is a set of best practices for the BAAQMD to estimate emissions of UFPM and ambient UFPM levels. The current resolution of the horizontal grid is 4 km, and we expect this resolution to increase significantly as progress is made. This project is planned to be completed by the end of 2015.

The University of California at Davis is also planning to establish a speciated UFPM measurement station in the Bay Area as part of a field campaign funded by the California Air Resources Board (CARB). OEHHA will be also a collaborator in the project. OEHHA will use data from these measurements to perform California-specific epidemiologic studies to tie health effects to UFPM component concentrations. For these reasons, the BAAQMD is actively supporting this proposed project. At the same time, the BAAQMD has been internally discussing two options aimed at maximizing the usefulness of the CARB-funded measurements. One option is to establish another speciated measurement station which would operate concurrently with the CARB station (but at a different site to provide additional spatial coverage). The other option is to fund three additional speciated stations which would operate on a short-term basis, but at least for four months. The former alternative would provide year-round measurements while the latter would allow capture of concentration gradients between freeways and at select distances away from the freeways. The BAAQMD will use results obtained from the analysis of these data to identify major UFPM sources in the Bay Area and evaluate UFPM models.

8. References

BAAQMD, 2010. Ultrafine particulate matter study in the San Francisco Bay Area – Part I: study plan [Available at http://www.baaqmd.gov/~/media/Files/Planning%20and%20Research/Research%20and%20Modeling/Ultrafine%20Particulate%20Matter%20Study%20Plan.ashx]. August.

BAAQMD, 2011. Health impact analysis of fine particulate matter in the San Francisco Bay Area [Available at http://www.baaqmd.gov/~/media/Files/Planning%20and%20Research/Research%20and%20Modeling/Cost%20analysis%20of%20fine%20particulate%20matter%20in%20the%20Bay%20Area.ashx]. September.

EPA, 2012. BenMAP Environmental Benefits Mapping and Analysis Program – User's Manual, Prepared for the Office of Air Quality Planning and Standards, US EPA by Abt Associates Inc. [Available at http://www.epa.gov/airquality/benmap/models/BenMAPManualOct2012.pdf]. October.

APPENDIX A
Derivation of NO_2-UFPM Correlations

A1. Background and Synopsis

We wished to estimate ambient UFPM concentrations in the Bay Area in order to apply BenMAP to estimate the health impacts of UFPM on Bay Area residents. UFPM has been measured at four sites; with such limited information, it is not possible to estimate representative UFPM levels and exposure across the entire Bay Area. In contrast to UFPM, more extensive ambient measurement data exist for other pollutants, and these pollutants have also been simulated for a grid covering the region using the US EPA's Community Multi-scale Air Quality (CMAQ) model; therefore, we considered estimating UFPM from one of these other pollutants.

Among the set of pollutants considered (CO, NO, NO_2, NOx, O_3, and $PM_{2.5}$), NO_2 had the best overall correlation. Using ambient UFPM and NO_2 measurements at the four sites, we first estimated the relationship between UFPM and NO_2. (See Section A2. Prediction of UFPM from NO_2.)

Comparison between simulations and observations showed that the model overpredicts NO_2 if the ambient NO_2 is above 10 ppb. (See Section A3. Correcting Simulated NO_2.) We then corrected modeled NO_2 values based on comparisons with observed values. We used a simple correction that seemed to fit the data well, namely, for any simulated NO_2 value >10, we replaced it with 10 + 40% of its excess above 10 [that is, $y = 10 + 0.4*(x-10)$, if $x > 10$]. Finally, we computed the PM season quarterly averages of these adjusted NO_2 values and applied the conversion formulas from Section A2 to estimate quarterly UFPM.

A2. Prediction of UFPM from NO_2

To predict UFPM from NO_2, we wanted to develop formulas that are applicable at all Bay Area locations. Figure A1 shows a plot of 24-hour average UFPM vs. NO_2 for the four measurement sites. Although there were statistically significant differences among sites in their UFPM-NO_2 relationships, there was still a reasonably similar pattern. Thus, we pooled the sites to establish prediction equations.

We applied linear regressions separately for the four PM seasons simulated by CMAQ: “winter” (Nov 16 – Feb 15), “spring” (Feb 16 – May 15), “summer” (May 16 – August 15), and “fall” (August 16 – November 15).

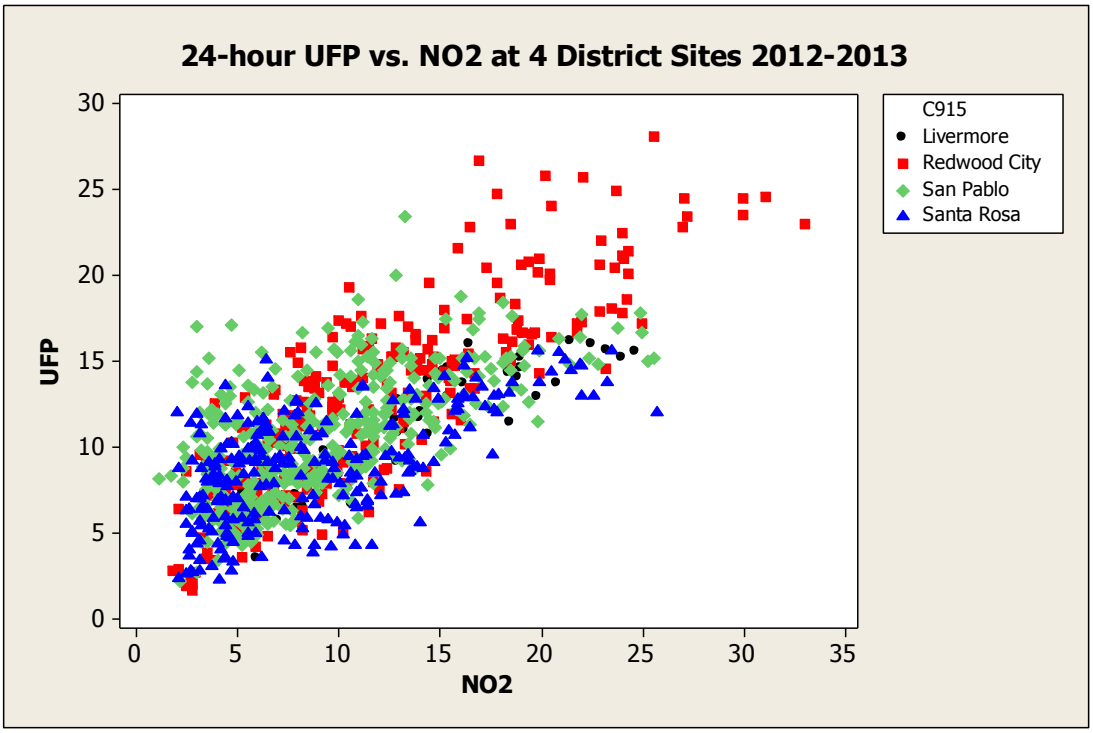

Figure A1. Bay Area 24-hour average UFPM values vs. NO_2 at four sites. (Note: Livermore values were limited to those after October 2012.)

We first fit different slopes and intercepts for each season. The adjusted R^2 value was 55.9%. We found that we could do almost as well with four independent variables: NO_2 and separate intercepts for winter and fall combined, spring, and summer. The adjusted R^2 value for this regression was 55.4%. Results are shown in Table A1.

Table A1. Estimated slopes and intercepts for each season.

Season	Estimation Equation (standard error)
Spring	NO_2 * 0.631 (0.020) + 4.58 (0.26)
Summer	NO_2 * 0.631 (0.020) + 5.47 (0.21)
Winter and fall together	NO_2 * 0.631 (0.020) + 3.57 (0.29)

The regression equation was:

UFPM = 3.57 - 0.983 C971 + 2.07 C972 + 1.43 C973 + 0.690 C975 + 0.520 C976 + 0.711 C977 + 0.651 C978

where C971 through C978 are constants defined in Table A2; 948 cases were used, 1659 cases contained missing values. Analysis of variance is shown in Table A3.

Table A2. Constants defined in the regression equation.

Predictor	Coeff	SE Coeff	T	P
Constant	3.5654	0.5133	6.95	0.000
C971	-0.9834	0.7200	-1.37	0.172
C972	2.0683	0.6684	3.09	0.002
C973	1.4322	0.6619	2.16	0.031
C975	0.68984	0.03169	21.77	0.000
C976	0.52045	0.04038	12.89	0.000
C977	0.71080	0.06487	10.96	0.000
C978	0.65069	0.04848	13.42	0.000

s = 2.87974, R^2 = 56.2%, R^2 (adjusted) = 55.9%

Table A3. Analysis of variance.

Source	DF	SS	MS	F	P
Regression	7	10,004.8	1429.3	172.35	0.000
Residual error	940	7795.3	8.3		
Total	947	17,800.2			

A3. Correcting Modeled NO_2

Before using the modeled (i.e., gridded) NO_2 data, we checked the quality of these data. We investigated the relationship between the simulated and observed ambient NO_2 as follows. We used the set of monitors that had NO_2 data on the days modeled by CMAQ in 2010 and 2011 and found the NO_2 for the grid square each monitor was in. For each site, we matched the set of modeled days with the set of days with NO_2 measurements, comparing 24-hour averages. The correlations between modeled and ambient measurements were reasonably good (Figure A2). Figure A3 shows the means of ambient and modeled NO_2 on matched days. The model appears to overpredict when the ambient mean is more than 10 ppb. A line is shown that is close to the linear regression line that uses a breakpoint at 10 ppb.[2] This line was used to adjust modeled NO_2 data to better represent ambient NO_2.

[2] The regression excluded data for San Rafael (sr), which is something of an outlier.

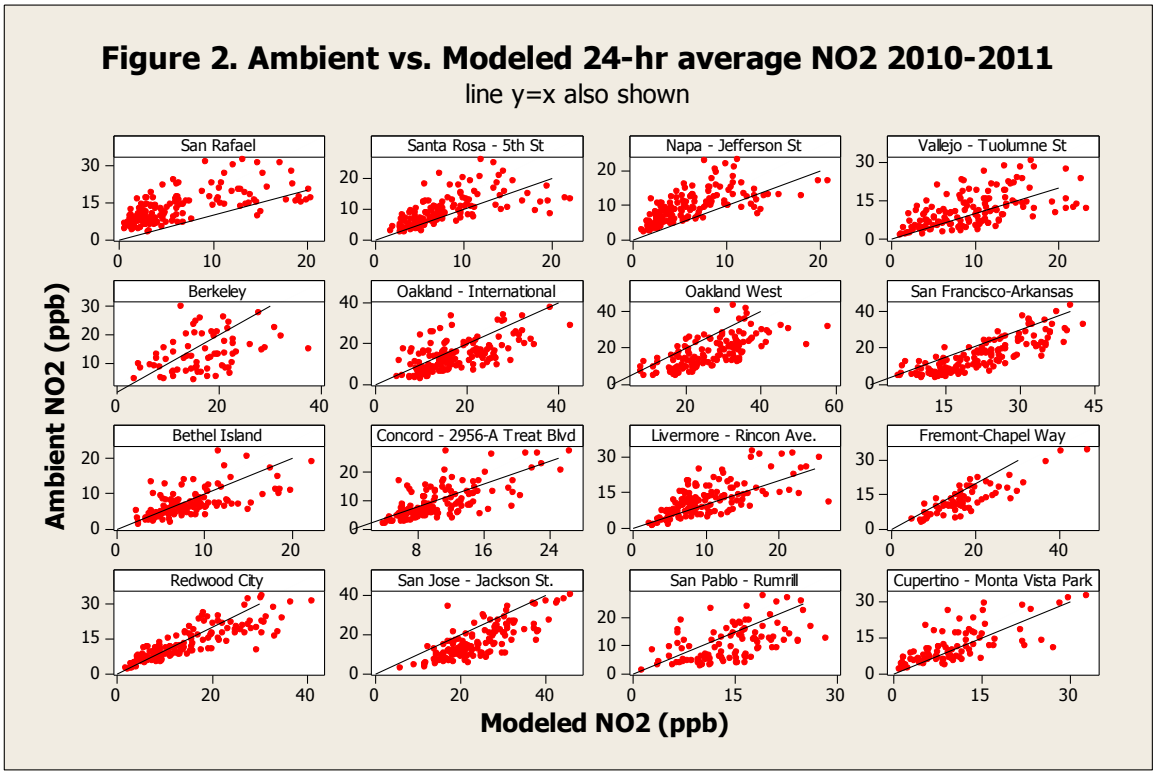

Figure A2. Correlation between ambient and modeled NO_2 at measurement stations.

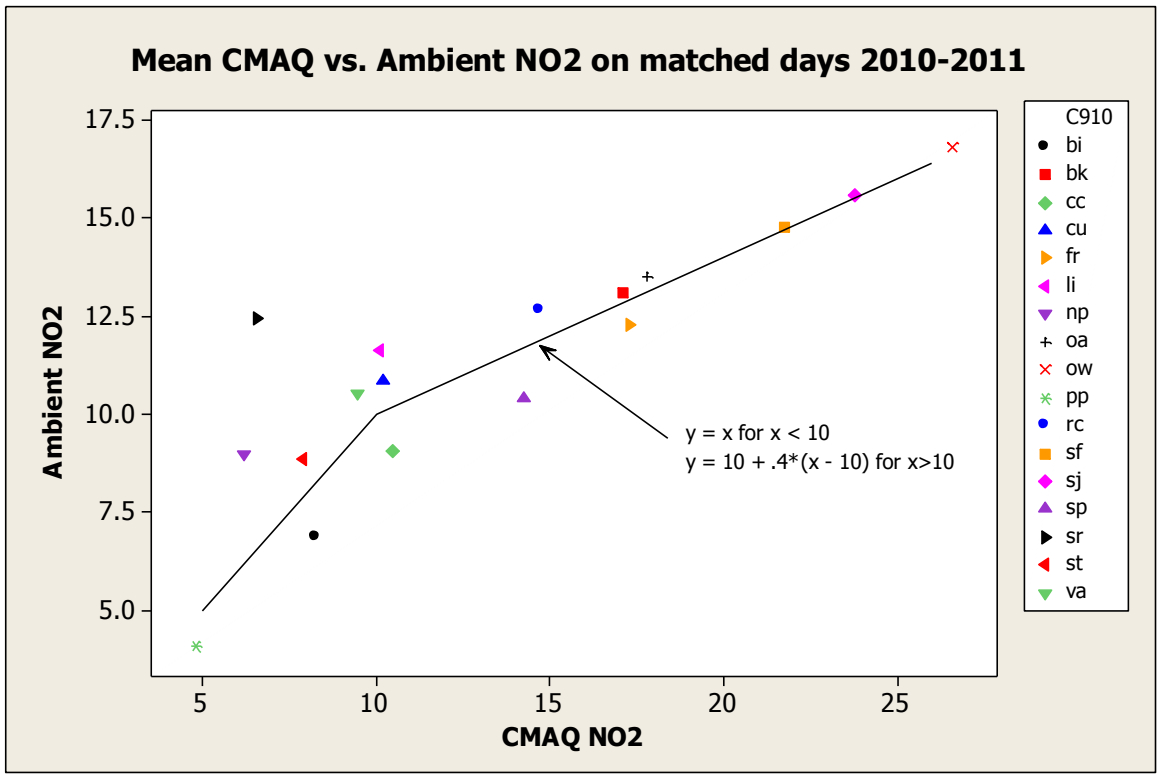

Figure A3. Correlation between ambient and modeled NO_2 on matched days.

A4. Estimating Seasonal UFPM

For each grid square, CMAQ-modeled NO_2 was averaged for each of the four PM seasons, with any average value >10 ppb adjusted using the formula found in Section A3. The seasonal regression fits from Section A2 were then applied to estimate UFPM for each PM season, and the four seasonal means were averaged to provide an estimate of the annual UFPM concentration. These values are plotted in Figure A4.

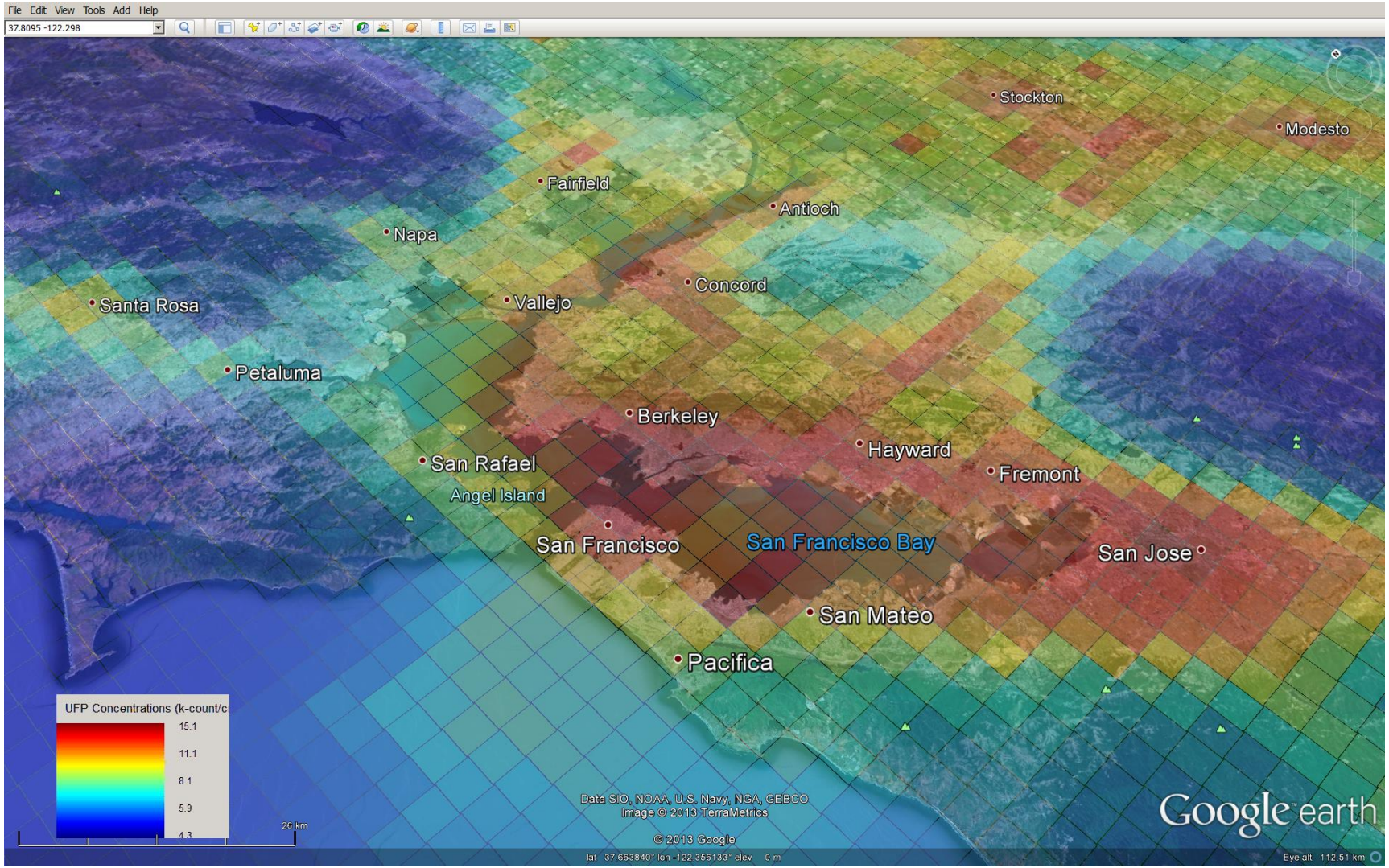

Figure A4. Estimated annual mean (2010-2011) UFPM concentrations (k-count/cm^3)

Ultrafine Particulate Matter in the San Francisco Bay Area
Part II: Compilation of Concentration-Response Functions

1. Background

Exposure to UFPM, defined as particles less than 0.1 µm in diameter, is suspected to be related to increased morbidity and mortality. UFPM have a stronger potential for significant health effects because they have a larger surface area per volume than larger particles and therefore more potential for biological activity (Oberdorster et al., 2005). Many epidemiologic and toxicologic studies of more subtle responses have shown associations of UFPM with cardiovascular and respiratory effects. An example of an epidemiologic study is a population-based, prospective cohort study of approximately 5000 randomly selected 45- to 75-year-old participants in urban Germany (Hertel et al., 2010). After adjusting for temperature and season, the researchers reported statistically significant increases in C-reactive protein levels, a marker of inflammation, after short-term exposures to UFPM (Hertel et al., 2010). Another example is a panel study of 57 adult asthmatics in Helsinki; increased daily UFPM levels were associated with decreased peak expiratory flow (Penttinen et al., 2001). A retrospective study of approximately 24,000 emergency room visits in Leipzig, Germany reported a statistically significant association of UFPM levels and hypertension, but no consistent association with larger particles (Franck et al., 2011). Toxicological effects, such as greater lung inflammation (Baggs et al., 1997), greater neutrophil flow into the lung (Brown et al., 2001), and systemic microvascular dysfunction (Nurkiewicz et al., 2011) have also been reported.

Animal studies have shown that nanoparticles, defined as particles between 0.001 and 0.1 micrometers in diameter, are translocated to the brain (Shi et al., 2013). For ethical and technical reasons, no experimental human studies have attempted to show this translocation to the brain, nor is the exact mechanism behind UFPM travel to organs known. A recent review (Shannahan et al., 2012) concludes that the activation of mast cells by inhalation of UFPM is a likely mechanism for adverse cardiovascular effects.

Given these epidemiologic and toxicologic findings, there is interest in quantifying the potential effects of UFPM. While this is a challenging endeavor with large uncertainties, we have attempted to derive concentration-response functions from the epidemiologic literature for use in such an effort.

2. Issues

There are many difficulties associated with assessing the effects of UFPM, including: (1) the spatial heterogeneity of the particles, which makes it difficult to measure population exposure over a wide area (HEI, 2010); often only one monitor is used to represent a

sufficiently wide spatial area, such as a city or county, to ensure a large enough population for an epidemiological study, (2) the need to generalize to a larger population when panel studies (e.g. school-based, indoor or personal monitoring) are designed, (3) the need to distinguish independent effects of UFPM since they are often moderately to highly correlated with those of other particulate matter (PM) sizes (PM1, PM2.5), PM species (e.g., elemental carbon), or gases (e.g., NO_2), (4) the difficulty extrapolating results from countries in Europe or Asia to the U.S. since these countries often have UFPM concentrations with a much higher proportion from diesel or with different exposure characteristics, (5) different definitions for UFPM (for example, many studies have used a metric of total particle number count or count over specific ranges (e.g., 0.03–0.1 µm) instead of counts for 0.1 µm or smaller particles), and (6) the lack of any studies on the long-term health effects of UFPM.

3. Assumptions

We decided to take a worst-case scenario approach so we assumed that (1) the monitor adequately characterized the UFPM exposure although UFPM is known to blend into background levels beyond 300 m (daytime) and 500 m (nighttime) from a roadway (HEI, 2010) and (2) results could be attributed to UFPM despite moderate to strong correlations with other pollutants.

4. Approach

We conducted a literature search to identify published peer-reviewed articles on UFPM and health using these search terms: (ultrafine particles or particle number concentration or PM0.1 or UFP) and (epidemiology or health or effects or toxicology). We also searched the references of these articles.

We considered results from PM2.5 and NO_2 since these pollutants are usually reported and are often derived from the same source as UFPM. We used results from single-pollutant models but considered the results from these other pollutants when the correlations with UFPM were moderate to low. We excluded studies where the correlation with PM2.5 was 0.8 or greater (e.g., Adar et al., 2007). We excluded cross-sectional studies given the difficulty of determining the timing of the exposure and the outcome. We also excluded studies with subclinical outcomes (e.g., lung function changes or C-reactive protein levels) or outcomes such as decreased heart rate variability since the aim is to quantify the costs and benefits of reducing UFPM concentrations, which requires outcomes where these can be measured. If more than one study existed on the same population for the same outcome, we included the study that covered the greater number of years.

We evaluated the suitability of these studies for estimating Bay Area concentration-response functions using the following: similarity to the Bay Area UFPM levels (daily summer averages ranging from 8000 to 11,000 particles/cm^3), lower correlations of UFPM with other pollutants, larger study size, and multi-city studies (since this increases the likelihood that results for a single city were not obtained by chance). For quality of hospitalization studies, we also considered whether the date of symptom onset was used instead of date of admission, and whether scheduled visits were included in the hospitalizations.

We included studies of hospitalizations, emergency room visits, and mortality. We limited the studies to those measuring particle counts per unit volume of air for ease of comparison and converted all effect estimates to percent increase (excess risk) per 10,000 particles/cm^3 increase and 95% confidence interval (CI). We included studies that measured counts of all particles (not just those in the UFPM range) because UFPM are the dominant contributors to particle counts. Although there were few studies of the same outcome and age group, we performed a meta-analysis on studies that best met our criteria for suitability using the random effects model (StataCorp LP 2011, metan command). Studies were weighted by the inverse of their standard error.

We report an I^2 statistic for the meta-analysis, which describes the percentage of the variability in effect estimates that is due to statistical heterogeneity, a measure of the degree of inconsistency in the studies' results, rather than sampling error (chance). Given our assumptions and the lack of studies for any given health outcome, our estimates of the UFPM effect on adverse health outcomes are very preliminary.

If a paper reported results for a cardiovascular outcome and a respiratory outcome, or for two age ranges for an outcome, then we treated that paper as reporting two studies. If a study reported results for more than one size fraction of particles, we chose the fraction that most closely corresponded to particles less than 0.1 µm. We reviewed 24 morbidity studies and 14 mortality studies. Figures 1 and 2 summarize the details of these studies. All of the studies took place in Europe, except for three in China and two in the U.S. (Atlanta, GA). The predominant race for all of the European study areas was white. All the studies controlled for important covariates related to UFPM and the health outcome. These covariates included meteorology (e.g., temperature, relative humidity, barometric pressure) and a variable related to the date (e.g., day of week, day of month). Some estimates were based on same-day UFPM exposure, (lag0), as well as exposures one day before (lag1) and up to 10 days (lag10) before the emergency room visit, hospitalization or death. Other estimates were based on cumulative days of UFPM exposure before the emergency room visit, hospitalization or death. For example, three days of UFPM exposure (the same day, 1 day before, and 2 days before) would be lag0-2. The longest

cumulative daily exposure was 11 days (lag0-10). Our concentration-response functions are reported without specifying a lag since this varied greatly between studies.

Most of the studies reviewed used a standard time-series study design and a few used a case-crossover study design. These two designs often produce similar results and are widely accepted approaches for air pollution health studies. The time-series study design compares daily outcome counts (e.g., hospitalizations, deaths) with exposure measurements collected at regular time intervals. Confounding factors that vary over time (e.g., seasonality, temperature) are added as covariates to the model. The case-crossover design is similar to a matched case-control study. Each case serves as its own control. Thus, measured and unmeasured confounders, such as smoking habits or time-activity patterns, are controlled for by design. All the case-crossover studies in Figure 1 used a time-stratified refinement, which limits the bias introduced when selecting control periods. This refinement randomly selects control periods before and after the case period, usually by selecting control periods in the same month and year that the case period occurred.

5. Prior Expert Reviews

As a starting point, we examined two papers by a panel of peer-selected European experts from different disciplines (epidemiology, toxicology and clinical medicine) (Knol et al., 2009 and Hoek et al., 2010) who considered literature published from 1995 to January 2008. Most of the experts on this panel determined there was a medium to high likelihood of a causal relationship between short-term ambient UFPM exposure and all-cause mortality, cardiovascular and respiratory hospital admissions, worsening of asthma symptoms, and lung function decrements (Knol et al., 2009). For all-cause mortality, several experts relied on a study by Stolzel et al. (2007) (Hoek et al., 2010). Overall, the experts estimated a 3% increase in all-cause mortality for a 10,000 particles/cm^3 increase in UFPM concentration, with a range from 1% to 12%. Cardiovascular and respiratory hospital admissions were each estimated at a 2% increase. Cardiovascular hospital admissions were based on the studies by Metzger et al. (2004), Andersen et al. (2008) and Lanki et al. (2006). Respiratory hospital admissions were based on the studies by Peel et al. (2005), Andersen et al. (2008), and Halonen et al. (2008).

A significant source of uncertainty indicated by the experts included the lack of long-term studies to quantitatively assess the relationship between UFPM and all-cause mortality. Reasons for uncertainty in relating UFPM to adverse health effects included the limited number of epidemiologic studies and exposure misclassification.

Another review by Araujo and Nel (2009) focused on PM and atherosclerosis. These researchers offer several reasons why UFPM is more pro-atherogenic than PM2.5. These

include (1) larger numbers of particles and larger surface-to-mass ratio, leading to larger bioavailable surface, (2) higher content of organic carbon and pro-oxidative polycyclic aromatic hydrocarbons, which can lead to oxidative stress and inflammation, and (3) greater fractional deposition deeper into the lung, which could lead to greater retention and therefore higher cellular uptake.

The U.S. EPA Integrated Science Assessment (2009) reviewed about 40 studies that examined health effects and UFPM exposure. The study reported inconsistent results, but considering toxicological findings, found suggestive evidence of a causal relationship between short-term UFPM exposure and respiratory and cardiovascular effects.

The Health Effects Institute recently published a review by a special panel of six contributors and ten peer reviewers on the health effects of UFPM (HEI, 2013). The conclusion was that "while selected studies show evidence for UFPM effects, the current evidence, when considered together, is not sufficiently strong to conclude that short-term exposures to UFPMs have effects that are dramatically different from those of larger particles." Also noted was that the lack of strong evidence for an independent effect of UFPM does not rule out the existence of an effect.

Thus, although there is disagreement and considerable uncertainty, we began with the premise that UFPM causes adverse human health effects for both cardiovascular and respiratory endpoints. Below we review the studies used for each outcome proposed for use in a health impact assessment, including cardiovascular morbidity and mortality, respiratory morbidity and mortality, and all-cause mortality. All-effect estimates are per 10,000 particles/cm^3, and unless otherwise noted, the effect estimates apply to all ages.

6. Cardiovascular Morbidity

The 12 cardiovascular-related morbidity studies had central effect estimates of UFPM exposure from -0.5 to 40%. Five studies examined the broad category of all cardiovascular outcomes, while seven studies examined more specific cardiovascular endpoints including stroke, arrhythmia and acute myocardial infarction. Ten studies took place in Europe, one in the U.S. and one in China. Most studies had UFPM levels comparable to the Bay Area.

7. Specific Cardiovascular Morbidities

We briefly reviewed six studies for specific cardiovascular morbidities, but did not make concentration-response function estimates since we used "all cardiovascular hospitalization" as an outcome. Nevertheless, these studies provide support for a cardiovascular morbidity outcome. In a Rome study of emergency room visits related to heart failure for patients 35 years and older, Belleudi et al. (2010) reported a 2.8% (95% CI: 0.3, 5.5) increase at lag0-6. A Helsinki study of arrhythmia hospitalizations in patients

65 years and older reported a UFPM effect estimate of 16.6% (CI: 1.3, 32.5) at lag0-4, but the UFPM effect could not be separated from an effect due to NO_2 (Halonen et al., 2009). Lanki et al. (2006) studied the first acute myocardial infarction hospitalizations of patients 35 years and older in three European cities. They reported a UFPM effect estimate of 1.3% (CI: 0, 2.6) at lag0. Andersen et al. (2010), describing a study in Copenhagen, reported a 40% (CI: 11, 77) increase in mild strokes at lag4, and a decrease in severe strokes (-21%, CI: -42, 5) at lag4. For most hospitalization studies, the date of hospitalization is known but not the date of symptom onset. In Andersen et al. (2010), for 75% of stroke cases, the date of symptom onset was reported in the analysis, allowing a better exposure assessment. Although NO_x is moderately correlated with UFPM, when NO_x was added to the model for mild stroke, the UFPM estimate remained about the same while the NO_x estimate decreased. Another much larger Helsinki study, limited to patients 65 years and older, reported a 10.5% (CI: -4.2, 25.7) increase in stroke hospitalizations at lag0-4 (Halonen et al., 2009). UFPM and NO_2 were moderately correlated; the estimate for NO_2 was positive but not significant. These cardiovascular morbidity studies taken together lend support to a positive effect of elevated UFPM on cardiovascular hospitalizations and emergency room visits.

8. All-Cardiovascular Hospitalizations

Six studies were considered for all-cardiovascular hospitalizations. Since approximately 60% of cardiovascular patients are transferred from the emergency room to the hospital (based on 2005-2009 emergency room and hospitalization data in the Bay Area), we included emergency room visit studies with the cardiovascular hospitalization studies. The following are the studies we did not use for our summary estimate. A study of UFPM and cardiovascular emergency room visits for all ages in Atlanta, GA did not find a positive association [-0.5% CI: (-1.2, 0.2) at lag0-2] (Metzger et al., 2004). The levels of UFPM were much greater than those recently measured in the Bay Area. The number of days of missing UFPM measurements (44%) may have contributed to the null findings. Liu et al. (2013) reported an 8.0% (CI: 1.2, 15.1 at lag0-10) increase in emergency room visits for all ages in a Beijing population. No co-pollutant information was provided and the UFPM levels were much greater than those recently measured in the Bay Area. Branis et al. (2010), studying cardiovascular hospitalizations in Prague, reported an effect of 11.6% (CI: 4.1, 19.5) at lag0-6, but the UFPM effect could not be separated to be considered independently from PM2.5. An Andersen et al. (2008) study in Copenhagen was limited to age 65 years and older but could be included with all ages since most effects occur in this age group. This study found no relationship between UFPM and cardiovascular hospitalizations (0% (CI: -2.5, 5.2)). Planned hospital admissions were included (the authors estimate these at 20% of the hospital admissions), which would lead to greater exposure misclassification.

The two studies that best meet our criteria were Atkinson et al. (2010) and von Klot et al. (2005). Atkinson et al. (2010) was the largest study among the all-cardiovascular morbidity studies and UFPM appeared to have an effect independent of PM2.5. This London study reported a small, not statistically significant effect [0.6% (CI: -0.4, 1.7)] at lag1. A study of five European cities examined the relationship between UFPM and several specific cardiovascular hospitalization outcomes combined (acute myocardial infarction, angina pectoris, dysrhythmia, and heart failure) (von Klot et al., 2005). Since these specific cardiovascular hospitalizations cover the majority of cardiovascular hospitalizations, we also included this study for all-cardiovascular hospitalizations (based on 2005-2008 CA hospitalization data). In this multi-city study, the UFPM effect for these combined cardiovascular outcomes among incident myocardial infarction patients aged 35 years and older was estimated at 2.6% (CI: 0.5, 4.8) at lag0, but the UFPM effect could not be separated from that of NO_2 (von Klot et al., 2005). We performed a meta-analysis, which resulted in an estimate for all-cardiovascular hospitalizations of 1.4% (CI: -0.5, 3.3), although a moderate level of statistical heterogeneity exists (see Figure 1). This estimate is similar to that in the review by Hoek et al. (2010) of 2%. Our estimate for all-cardiovascular hospitalizations is supported by findings of effects on several specific cardiovascular diseases.

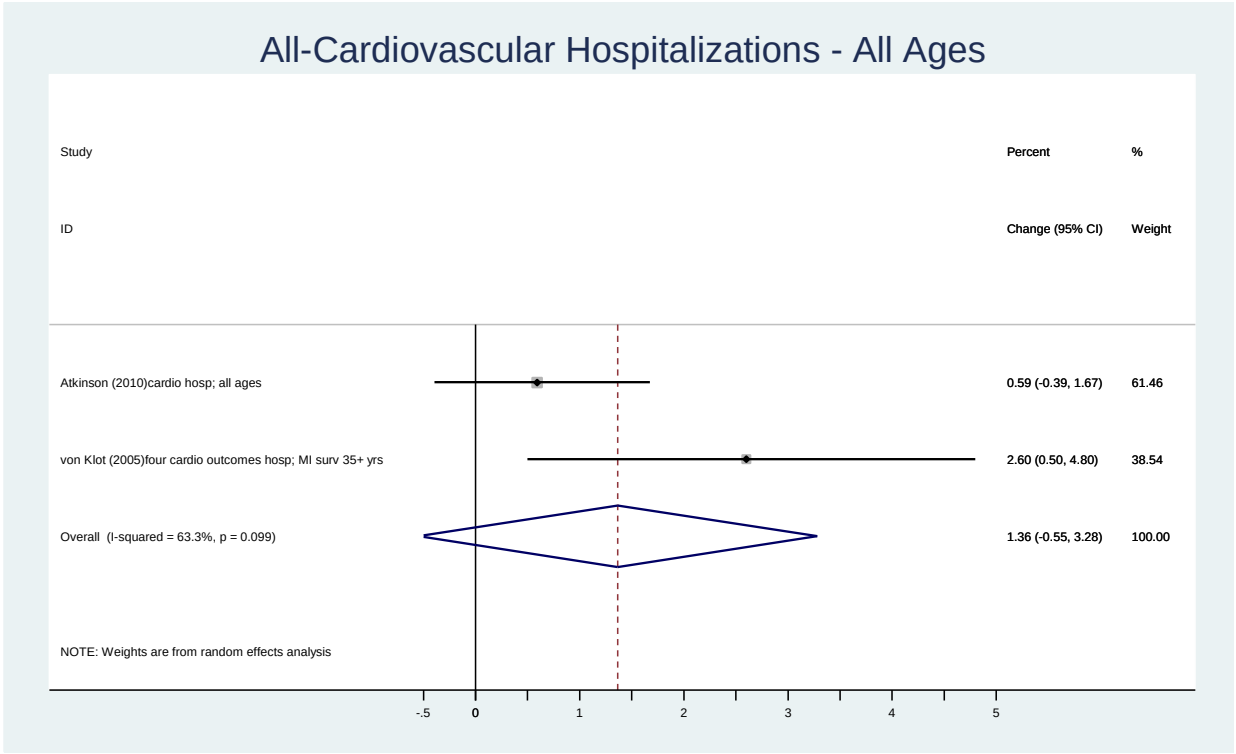

Figure 1. Meta-analysis of cardiovascular hospitalizations.

9. Respiratory Morbidity

Twelve studies estimated UFPM effects for respiratory-related emergency room visits or hospitalizations. The central effect estimates in these studies ranged from 0.6% to 32%. We mention the following studies but did not use them for concentration-response functions since there was only one study for each specific respiratory outcome. Halonen et al. (2009) reported a UFPM effect on pneumonia hospitalizations for ages 65 years and older in Helsinki of 15.6% (CI: 0.7, 31.2). Belleudi et al. (2010) reported that for Romans 35 years and older, 1.7% (CI: 0.1, 3.4) of emergency room visits for chronic obstructive pulmonary disease were related to UFPM. Iskandar et al. (2012) examined asthma hospitalizations in Copenhagen and reported that 16.5% (CI: -5.2, 41.0) of them were related to UFPM for patients 18 years old and younger. These studies taken together lend support to a positive effect on respiratory hospitalizations and emergency room visits with increasing levels of UFPM.

10. All-Respiratory Emergency Room Visits

Three of the five studies that examined all-respiratory morbidity effects used an emergency room visit as the outcome. Only about 20% of respiratory emergency room visits go on to hospitalizations (based on 2005-2009 emergency room and hospitalization data in the Bay Area), so we treated emergency room visits and hospitalizations separately. The emergency room visit studies involved three age groups. Leitte et al. (2011), a study in Beijing, reported results for all ages (23.8% CI: 0.0, 54.7 at lag0-3) but the UFPM levels were much higher than those recently measured in the Bay Area. Atkinson et al. (2010) reported similar results for Londoners 65 years and older (1.3% CI: -0.1, 2.7 lag4) and under 15 years (1.6% CI: -0.2, 3.5 lag2). The Atkinson et al. (2010) study better fits our criteria than the Beijing study since the UFPM levels were more similar to the Bay Area's. We estimated the effect of UFPM on respiratory emergency room visits using these studies. We performed a meta-analysis of these two age categories, resulting in an estimate for all-respiratory emergency room visits of 1.4% (CI: 0.3, 2.5) for all ages (see Figure 2). No statistical heterogeneity occurred when combining these two studies.

Several studies examined asthma emergency room visits. We decided against using them for deriving concentration response functions since they are a subset of all-respiratory emergency room visits and therefore would lead to double counting. The results of these studies support a positive association of increased asthma emergency room visits with increasing levels of UFPM. Peel et al. (2005), summarizing a study that took place in Atlanta, GA, reported results for all-ages asthma emergency room visits (0.6% CI: 0.2, 1.0 at lag4), but the UFPM levels were much higher than those recently measured in the Bay Area and 44% of the days were missing UFPM measurements. Halonen et al. (2008) reported UFPM results for Helsinki asthma emergency room visits for three age groups:

under age 15 years (31.5% CI: 16.2, 47.3 at lag4), age 15-64 years (13.0% CI: 0.3, 26.0 at lag0), and age 65 years and older (12.4% CI: -5.3, 30.9 at lag0). The UFPM effect could not be clearly distinguished from that of PM2.5 or NO_2.

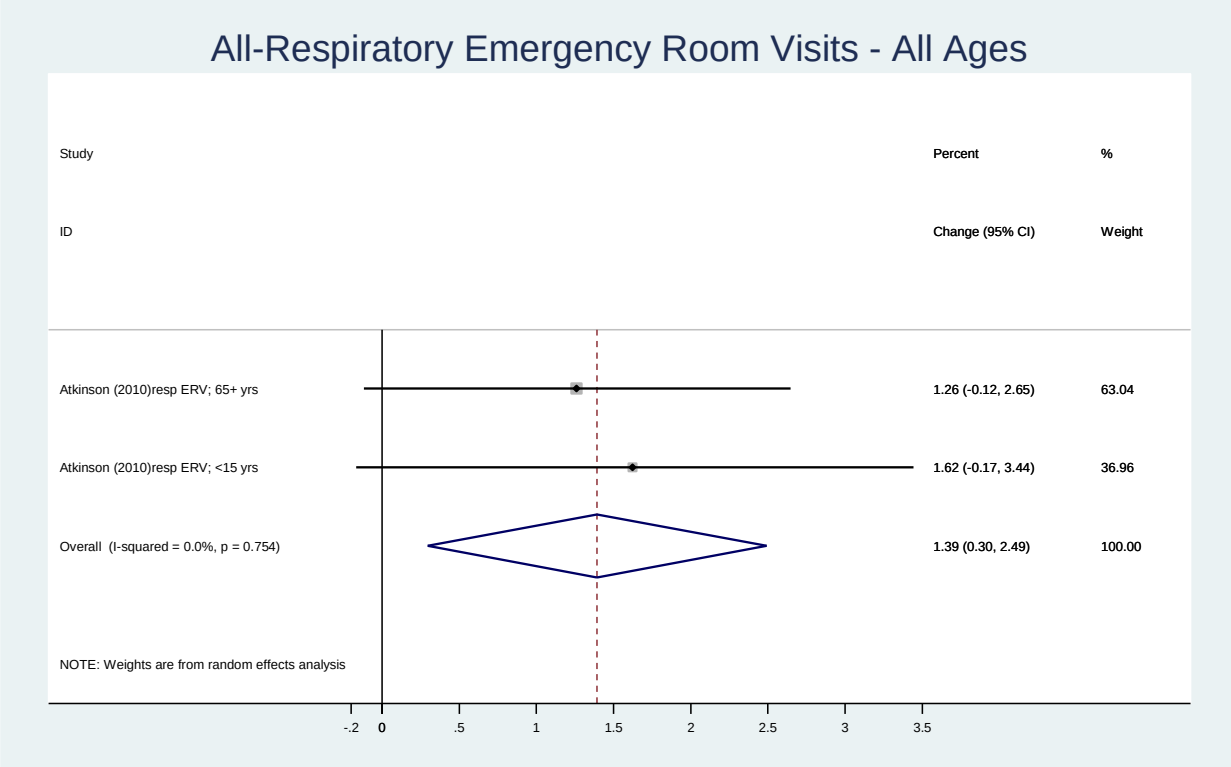

Figure 2. Meta-analysis of respiratory emergency room visits.

11. All-Respiratory Hospitalizations

Two studies reported results for all-respiratory hospitalizations. The Copenhagen study reported results for ages 65 years and older (10.6% CI: 0.0, 18.9 at lag0-4), but when either NO_2 or PM2.5 was added to the model, the central effect estimates for UFPM became zero or negative, indicating that the UFPM effect was not independent of these pollutants (Andersen et al., 2008). The Prague study reported results for all ages (19.5% CI: 7.2, 34.4 at lag0-3) (Branis et al., 2010). The PM2.5 results for the Prague study were also significant; therefore, the UFPM effect could not be ruled out as being related to those of PM2.5. The Prague study best meets our criteria since the UFPM effects were greatly attenuated in the Copenhagen study when co-pollutants were added. The Prague study estimate is much higher than the 2% of the review by Hoek et al. (2010). That review combined hospitalizations and emergency room visits and also combined specific

respiratory outcomes. Also, that review appeared before additional respiratory morbidity studies were published that reported high effects (Branis et al., 2010, Leitte et al., 2011, and Iskandar et al., 2012).

12. All-Cardiovascular Mortality

Seven studies examined cardiovascular-related mortality and UFPM exposure. The central effect estimates ranged from -1.2% to 17%. The three studies that reported a UFPM effect for all-cardiovascular mortality also reported a UFPM effect for all-cause mortality. In each instance, the all-cardiovascular effect was greater than the all-cause mortality effect (Atkinson et al., 2010, Branis et al., 2010, and Peters et al., 2009). Studies that limited cardiovascular deaths to ages 15 years and older or to ages 65 years and older were considered with all-ages studies since few cardiovascular deaths occur below the age of 15 years and most occur at ages 65 years and older (based on California mortality data in 2003). The study that limited deaths examined to ischemic heart disease were considered with all-cardiovascular mortality since ischemic heart disease is the cause of the majority of cardiovascular deaths (based on California mortality data in 2003).

The following studies were not included in our summary estimates for cardiovascular mortality. Forastiere et al. (2005) examined out-of-hospital deaths from ischemic heart disease and reported a UFPM effect of 3.0% (CI: 0.6, 5.5) at lag0-1. The UFPM levels were considerably higher than those recently measured in the Bay Area. The Breitner et al. (2011) study in Beijing of ages 15 years and older reported a UFPM effect of 6.5% (CI: 1.9, 11.2) at lag2. The UFPM levels were much higher than those recently reported in the Bay Area and no co-pollutant information was provided.

The four studies that best met our criteria (race/ethnicity demographics and UFPM levels similar to the Bay Area) were Atkinson et al. (2010), Branis et al. (2010), Halonen et al. (2009) and Peters et al. (2009). Atkinson et al. (2010), describing a large study in London, reported a UFPM effect of 2.2% (CI: 0.6, 3.7) at lag1. Branis et al. (2010), describing a study in Prague, reported 4.0% (CI: -3.0, 11.6) at lag2. Peters et al. (2009), describing a study in Erfurt, reported 3.2% (CI: 0.2, 6.2) at lag4. Another all-cardiovascular study of ages 65 years and older in Finland reported UFPM effects of -1.2% (CI: -8.7, 6.5) at lag2 (Halonen et al., 2009). Based on a meta-analysis of these studies, we estimated the UFPM effect of all-cardiovascular mortality to be 2.3% (CI: 1.0, 3.7) for all ages (see Figure 3). No statistical heterogeneity occurred when combining these studies.

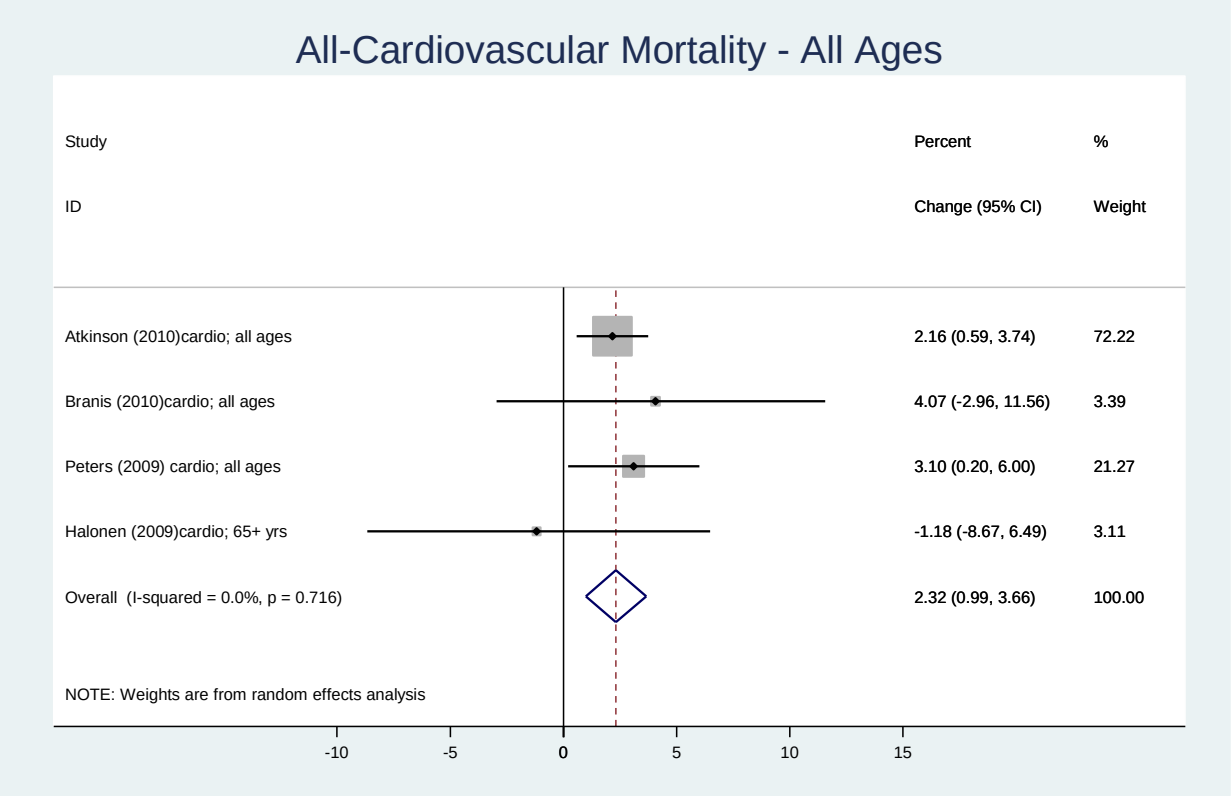

Figure 3. Meta-analysis of cardiovascular mortality.

A study in Helsinki, limited to stroke deaths at ages 65 years and older in the warm season, reported a UFPM effect of 17.0% (CI: -2.3, 38.3) at lag1 (Kettunen et al., 2007). Similar to hospitalization, the effect was much higher for stroke than other cardiovascular mortalities. This lends support to the findings for stroke hospitalizations and to cardiovascular mortality. Since there was only one study for this outcome, we did not estimate a concentration-response function.

13. All-Respiratory Mortality

Four studies examined all-respiratory mortality and UFPM. We considered a study that limited deaths to 65 years and older an all-ages study, since the majority of respiratory deaths occur in this age group. We did not include a study in Beijing, limited to 20 years old and older, reporting a UFPM effect of 2.3% (CI: -2.5, 7.5) because the UFPM levels were considerably higher than those recently measured in the Bay Area.

The following three studies best met our criteria. None of the studies reported statistically significant results. Atkinson et al. (2010) reported a UFPM effect of 2.3% (CI: -0.2, 4.8) at lag1 for all ages. Branis et al. (2010) reported 6.1% (CI: -12.3, 28.0) at lag2. Halonen et al. (2009), for age 65 years and older, reported -0.4% (-16.4, 16.2) at lag2. Based on meta-analysis of these studies, we estimated the UFPM effect of all-respiratory

mortality to be 2.3% (CI: -0.1, 4.7) for all ages (see Figure 4). No statistical heterogeneity occurred when combining these studies.

Figure 4. Meta-analysis of respiratory mortality.

14. All-Cause Mortality

All three of the studies of all-cause mortality and UFPM exposure took place in Europe, where UFPM levels were similar to those recently measured in the Bay Area, and there was no evidence that NO_2 or PM2.5 was confounding the results. Atkinson et al. (2010) reported a UFPM effect of 1.4% (CI: 0.5, 2.4) at lag1, Branis et al. (2010) reported 3.0% (CI: -2.0, 8.3) at lag2, and Peters et al. (2009) reported 3.0% (CI: 0.3, 5.5) at lag4. The results of these studies were similar to the Hoek et al. (2010) estimate of 3%. We considered the three studies to similarly meet our criteria, although Atkinson et al. (2010) was a much larger study. We performed a meta-analysis, which resulted in an estimate for all-cause mortality of 1.6% (CI: 0.7, 2.5) for all ages (see Figure 5). No statistical heterogeneity occurred when combining these three studies.

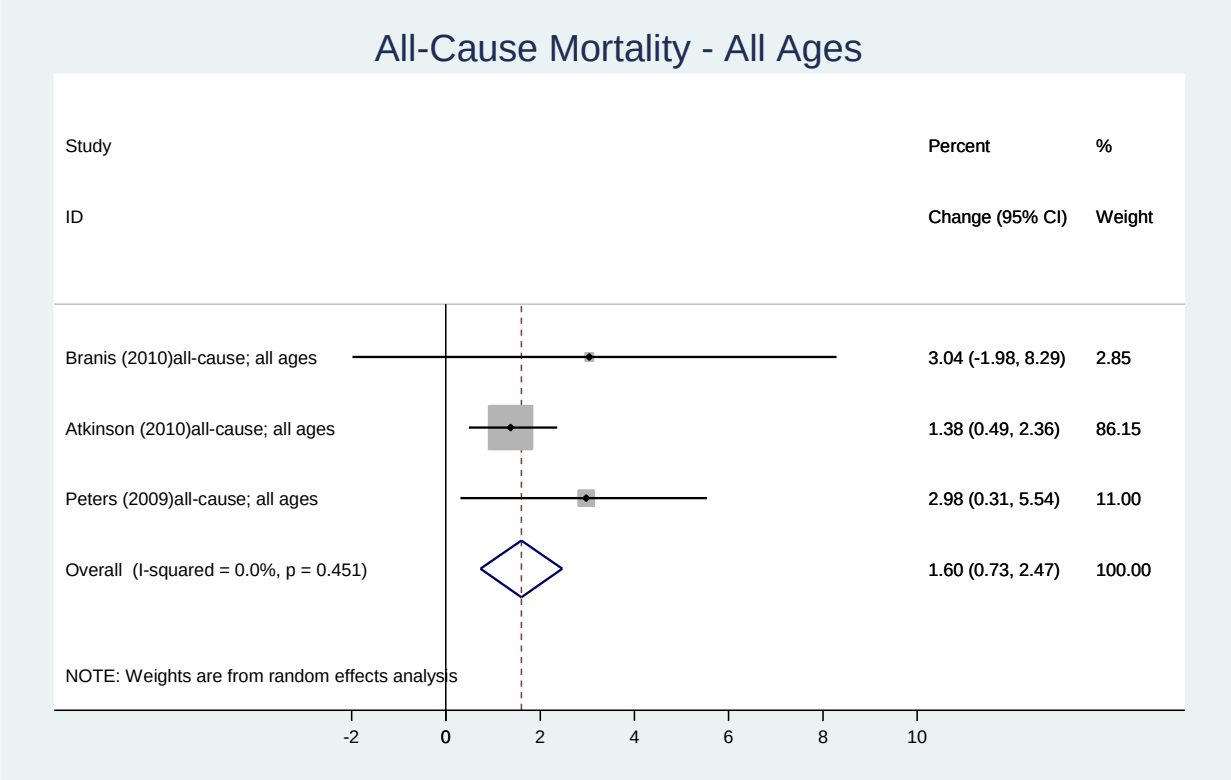

Figure 5. Meta-analysis of all-cause mortality.

15. Results and Recommendations

There are not enough studies to determine if a threshold exists below which there would be minimal adverse health effects, or above which adverse health effects would not greatly increase. We plotted average UFPM study levels with excess risk for health effects. Since the studies reported different size ranges of particles, we estimated a common metric of <0.1 µm/cm^3. The factors for converting the size ranges to a common metric were based on a size distribution curve (Andersen et al., 2008; Figure 1), as well as studies that reported both size ranges (Breitner et al., 2011, Leitte et al. 2011, and Halonen et al. 2009, 2008). The only outcome that displayed a fairly consistent dose-response relationship was cardiovascular mortality (see Figure 6).

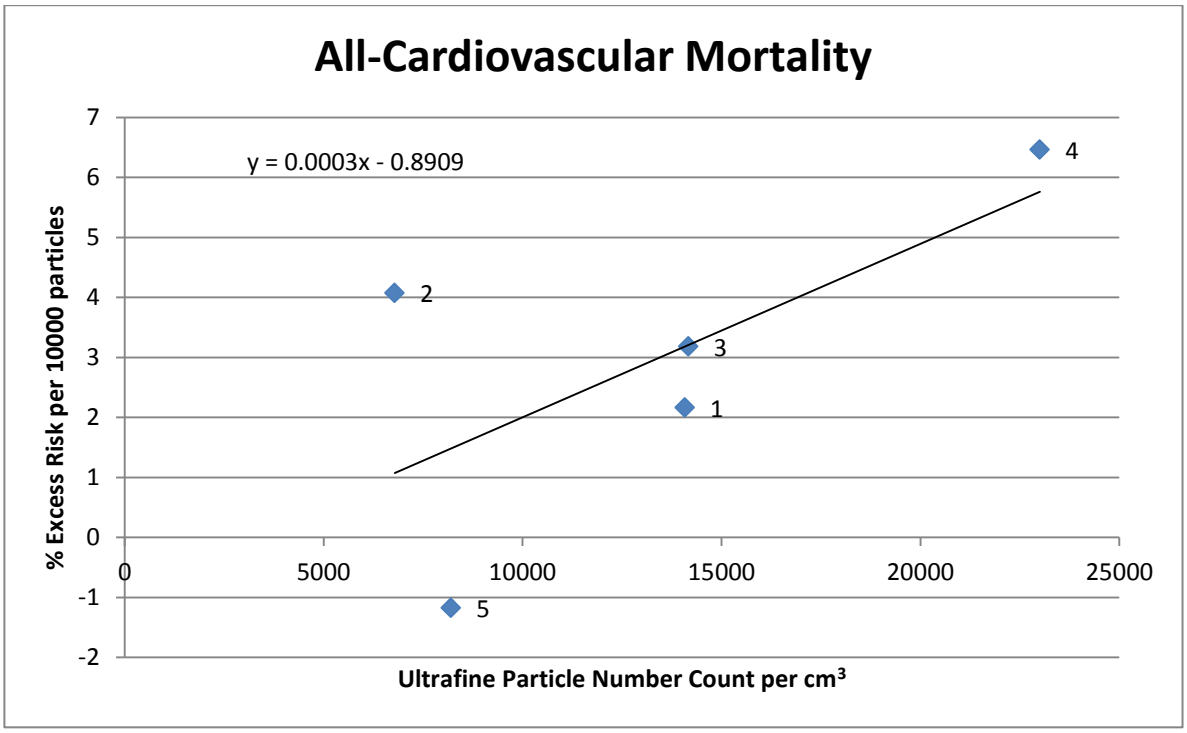

Figure 6. Distribution of percent increased risk for all-cardiovascular mortality by study's average level of UFPM count per cm^3. Labels correspond to 1. Atkinson et al., 2000, 2. Branis et al., 2010, 3. Peters et al., 2009, 4. Breitner et al., 2011, and 5. Halonen et al., 2009.

Table 1 shows the results of our estimates for the concentration-response functions for the Bay Area. Our estimates for the UFPM effect on health outcomes in the Bay Area have great uncertainty and we have assumed a worst-case scenario. Specifically, when studies have reported effects for both UFPM and other correlated co-pollutants, we have assumed that UFPM are the pollutant responsible. To have better estimates, there is a need for additional UFPM studies using several monitors for exposure assessment, a more consistent size range of particles examined, and population demographics and UFPM levels similar to the Bay Area.

Table 1. Estimated excess risk associated with a 10,000 particles/cm^3 increase in UFPM for the Bay Area.

Outcome	Age Group	Estimate (95% CI)
All cardiovascular hospitalizations	All	1.4% (-0.5, 3.3)
All respiratory hospitalizations	All	19.0% (6.7, 31.2)
All respiratory emergency room visits	<15 yrs	1.6% (-0.2, 3.5)
	≥65 yrs	1.3% (-0.1, 2.7)
	All*	1.4% (0.3, 2.5)
All-cardiovascular mortality	All	2.3% (1.0, 3.7)
All-respiratory mortality	All	2.3% (-0.2, 4.8)
All-cause mortality#		1.6% (0.7, 2.5)

*An “all ages” estimate can be used in place of the age-specific results.

#An “all-cause” estimate can be used in place of the respiratory plus cardiovascular estimates.

16. References

Adar, S.D., Gold, D.R., Coull, B.A., Schwartz, J., Stone, P.H., Suh, H., 2007. Focused exposures to airborne traffic particles and heart rate variability in the elderly. Epidemiology 18 (1), 95-103.

Andersen, Z.J., Olsen, T.S., Andersen, K.K., Loft, S., Ketzel, M., Raaschou-Nielsen, O., 2010. Association between short-term exposure to ultrafine particles and hospital admissions for stroke in Copenhagen, Denmark. Eur Heart J 31 (16), 2034-2040.

Andersen, Z.J., Wahlin, P., Raaschou-Nielsen, O., Ketzel, M., Scheike, T., Loft, S., 2008. Size distribution and total number concentration of ultrafine and accumulation mode particles and hospital admissions in children and the elderly in Copenhagen, Denmark. Occup Environ Med 65 (7), 458-466.

Araujo, J.A., Nel, A.E., 2009. Particulate matter and atherosclerosis: role of particle size, composition and oxidative stress. Part Fibre Toxicol 6, 24.

Atkinson, R.W., Fuller, G.W., Anderson, H.R., Harrison, R.M., Armstrong, B., 2010. Urban ambient particle metrics and health: a time-series analysis. Epidemiology 21 (4), 501-511.

Belleudi, V., Faustini, A., Stafoggia, M., Cattani, G., Marconi, A., Perucci, C.A., Forastiere, F., 2010. Impact of fine and ultrafine particles on emergency hospital admissions for cardiac and respiratory diseases. Epidemiology 21 (3), 414-423.

Branis, M., Vyskovska, J., Maly, M., Hovorka, J., 2010. Association of size-resolved number concentrations of particulate matter with cardiovascular and respiratory hospital admissions and mortality in Prague, Czech Republic. Inhal Toxicol 22 Suppl 2, 21-28.

Breitner, S., Liu, L., Cyrys, J., Bruske, I., Franck, U., Schlink, U., Leitte, A.M., Herbarth, O., Wiedensohler, A., Wehner, B., Hu, M., Pan, X.C., Wichmann, H.E., Peters, A., 2011. Sub-micrometer particulate air pollution and cardiovascular mortality in Beijing, China. The Science of the total environment 409 (24), 5196-5204.

Brown, D.M., Wilson, M.R., MacNee, W., Stone, V., Donaldson, K., 2001. Size-dependent proinflammatory effects of ultrafine polystyrene particles: a role for surface area and oxidative stress in the enhanced activity of ultrafines. Toxicol Appl Pharmacol 175 (3), 191-199.

Forastiere, F., Stafoggia, M., Picciotto, S., Bellander, T., D'Ippoliti, D., Lanki, T., von Klot, S., Nyberg, F., Paatero, P., Peters, A., Pekkanen, J., Sunyer, J., Perucci, C.A., 2005. A case-crossover analysis of out-of-hospital coronary deaths and air pollution in Rome, Italy. Am J Respir Crit Care Med 172 (12), 1549-1555.

Franck, U., Odeh, S., Wiedensohler, A., Wehner, B., Herbarth, O., 2011. The effect of particle size on cardiovascular disorders--the smaller the worse. Sci Total Environ 409 (20), 4217-4221.

Halonen, J.I., Lanki, T., Yli-Tuomi, T., Kulmala, M., Tiittanen, P., Pekkanen, J., 2008. Urban air pollution, and asthma and COPD hospital emergency room visits. Thorax 63 (7), 635-641.

Halonen, J.I., Lanki, T., Yli-Tuomi, T., Tiittanen, P., Kulmala, M., Pekkanen, J., 2009. Particulate air pollution and acute cardiorespiratory hospital admissions and mortality among the elderly. Epidemiology 20 (1), 143-153.

Health Effects Institute, 2010. Traffic-Related Air Pollution: A Critical Review of the Literature on Emissions, Exposure, and Health Effects. Health Effects Institute, Boston, MA.

Health Effects Institute, 2013. Understanding the Health Effects of Ambient Ultrafine Particles: HEI Review Panel on Untrafine Particles. Health Effects Institute, Boston, MA.

Hertel, S., Viehmann, A., Moebus, S., Mann, K., Brocker-Preuss, M., Mohlenkamp, S., Nonnemacher, M., Erbel, R., Jakobs, H., Memmesheimer, M., Jockel, K.H., Hoffmann, B., 2010. Influence of short-term exposure to ultrafine and fine particles on systemic inflammation. Eur J Epidemiol 25 (8), 581-592.

Iskandar, A., Andersen, Z.J., Bonnelykke, K., Ellermann, T., Andersen, K.K., Bisgaard, H., 2012. Coarse and fine particles but not ultrafine particles in urban air trigger hospital admission for asthma in children. Thorax 67 (3), 252-257.

Kettunen, J., Lanki, T., Tiittanen, P., Aalto, P.P., Koskentalo, T., Kulmala, M., Salomaa, V., Pekkanen, J., 2007. Associations of fine and ultrafine particulate air pollution with stroke mortality in an area of low air pollution levels. Stroke 38 (3), 918-922.

Ketzel, M., Wåhlin, P., Berkowicz, R., Palmgren, F., 2003. Particle and trace gas emission factors under urban driving conditions in Copenhagen based on street and roof-level observations. Atmospheric Environment 37 (20), 2735-2749.

Knol, A.B., de Hartog, J.J., Boogaard, H., Slottje, P., van der Sluijs, J.P., Lebret, E., Cassee, F.R., Wardekker, J.A., Ayres, J.G., Borm, P.J., Brunekreef, B., Donaldson, K., Forastiere, F., Holgate, S.T., Kreyling, W.G., Nemery, B., Pekkanen, J., Stone, V., Wichmann, H.E., Hoek, G., 2009. Expert elicitation on ultrafine particles: likelihood of health effects and causal pathways. Part Fibre Toxicol 6, 19.

Lanki, T., Pekkanen, J., Aalto, P., Elosua, R., Berglind, N., D'Ippoliti, D., Kulmala, M., Nyberg, F., Peters, A., Picciotto, S., Salomaa, V., Sunyer, J., Tiittanen, P., von Klot, S., Forastiere, F., 2006. Associations of traffic related air pollutants with hospitalisation for first acute myocardial infarction: the HEAPSS study. Occup Environ Med 63 (12), 844-851.

Leitte, A.M., Schlink, U., Herbarth, O., Wiedensohler, A., Pan, X.C., Hu, M., Richter, M., Wehner, B., Tuch, T., Wu, Z., Yang, M., Liu, L., Breitner, S., Cyrys, J., Peters, A., Wichmann, H.E., Franck, U., 2011. Size-segregated particle number concentrations and respiratory emergency room visits in beijing, china. Environ Health Perspect 119 (4), 508-513.

Leitte, A.M., Schlink, U., Herbarth, O., Wiedensohler, A., Pan, X.C., Hu, M., Wehner, B., Breitner, S., Peters, A., Wichmann, H.E., Franck, U., 2012. Associations between size-segregated particle number concentrations and respiratory mortality in Beijing, China. Int J Environ Health Res 22 (2), 119-133.

Liu, L., Breitner, S., Schneider, A., Cyrys, J., Brüske, I., Franck, U., Schlink, U., Marian Leitte, A., Herbarth, O., Wiedensohler, A., Wehner, B., Pan, X., Wichmann, H.E., Peters, A., 2013. Size-fractioned particulate air pollution and cardiovascular emergency room visits in Beijing, China. Environ Res 121, 52-63.

Metzger, K.B., Tolbert, P.E., Klein, M., Peel, J.L., Flanders, W.D., Todd, K., Mulholland, J.A., Ryan, P.B., Frumkin, H., 2004. Ambient air pollution and cardiovascular emergency department visits. Epidemiology 15 (1), 46-56.

Oberdorster, G., 2005. Nanotoxicology: An emerging discipline evolving from studies of ultrafine particles. Environ Health Perspect 118 (9), 823-839.

Peel, J.L., Tolbert, P.E., Klein, M., Metzger, K.B., Flanders, W.D., Todd, K., Mulholland, J.A., Ryan, P.B., Frumkin, H., 2005. Ambient air pollution and respiratory emergency department visits. Epidemiology 16 (2), 164-174.

Penttinen, P., Timonen, K.L., Tiittanen, P., Mirme, A., Ruuskanen, J., Pekkanen, J., 2001. Ultrafine particles in urban air and respiratory health among adult asthmatics. Eur Respir J 17 (3), 428-435.

Peters, A., Breitner, S., Cyrys, J., Stolzel, M., Pitz, M., Wolke, G., Heinrich, J., Kreyling, W., Kuchenhoff, H., Wichmann, H.E., 2009. The influence of improved air quality on mortality risks in Erfurt, Germany. Res Rep Health Eff Inst (137), 5-77; discussion 79-90.

Ruckerl, R., Phipps, R.P., Schneider, A., Frampton, M., Cyrys, J., Oberdorster, G., Wichmann, H.E., Peters, A., 2007. Ultrafine particles and platelet activation in patients with coronary heart disease--results from a prospective panel study. Part Fibre Toxicol 4, 1-14.

Shannahan, J.H., Kodavanti, U.P., Brown, J.M., 2012. Manufactured and airborne nanoparticle cardiopulmonary interactions: a review of mechanisms and the possible contribution of mast cells. Inhal Toxicol 24 (5), 320-339.

Shi, H., Magaye, R., Castranova, V., Zhao, J., 2013. Titanium dioxide nanoparticles: a review of current toxicological data. Part Fibre Toxicol 10, 1-15.

StataCorp LP, 2011. STATA, version 12. StataCorp, College Station, TX.

Stolzel, M., Breitner, S., Cyrys, J., Pitz, M., Wolke, G., Kreyling, W., Heinrich, J., Wichmann, H.E., Peters, A., 2007. Daily mortality and particulate matter in different size classes in Erfurt, Germany. J Expo Sci Environ Epidemiol 17 (5), 458-467.

U.S. EPA, 2009. Integrated Science Assessment for Particulate Matter (Final Report) EPA/600/R-08/139F.

von Klot, S., Peters, A., Aalto, P., Bellander, T., Berglind, N., D'Ippoliti, D., Elosua, R., Hormann, A., Kulmala, M., Lanki, T., Lowel, H., Pekkanen, J., Picciotto, S., Sunyer, J., Forastiere, F., 2005. Ambient air pollution is associated with increased risk of hospital cardiac readmissions of myocardial infarction survivors in five European cities. Circulation 112 (20), 3073-3079.

Wichmann, H.E., Spix, C., Tuch, T., Wolke, G., Peters, A., Heinrich, J., Kreyling, W.G., Heyder, J., 2000. Daily mortality and fine and ultrafine particles in erfurt, germany part I: role of particle number and particle mass. Res Rep Health Eff Inst (98), 5-86; discussion 87-94.