Long-term Exposure to \(\text{PM}_{2.5}\) and Incidence of Acute Myocardial Infarction

Citation
Madrigano, Jaime, Itai Kloog, Robert Goldberg, Brent A. Coull, Murray A. Mittleman, and Joel Schwartz. 2013. Long-term exposure to pm2.5 and incidence of acute myocardial infarction. Environmental Health Perspectives 121(2): 192-196.

Published Version
doi:10.1289/ehp.1205284

Permanent link
http://nrs.harvard.edu/urn-3:HUL.InstRepos:11011815

Terms of Use
This article was downloaded from Harvard University’s DASH repository, and is made available under the terms and conditions applicable to Other Posted Material, as set forth at http://nrs.harvard.edu/urn-3:HUL.InstRepos:dash.current.terms-of-use#LAA

Share Your Story
The Harvard community has made this article openly available. Please share how this access benefits you. Submit a story.

Accessibility
Long-term Exposure to PM$_{2.5}$ and Incidence of Acute Myocardial Infarction

Jaime Madrigano,$^{1,2,3}$ Itai Klooog,$^3$ Robert Goldberg,$^4$ Brent A. Coull,$^{3,5}$ Murray A. Mittleman,$^{6,7}$ and Joel Schwartz$^{3,7}$

$^1$The Earth Institute, and $^2$Mailman School of Public Health, Columbia University, New York, New York, USA; $^3$Department of Environmental Health, Harvard School of Public Health, Boston, Massachusetts, USA; $^4$University of Massachusetts Medical School, Worcester, Massachusetts, USA; $^5$Department of Biostatistics, Harvard School of Public Health, Boston, Massachusetts, USA; $^6$Cardiovascular Epidemiology Research Unit, Beth Israel Deaconess Medical Center, Boston, Massachusetts, USA; $^7$Department of Epidemiology, Harvard School of Public Health, Boston, Massachusetts, USA

**Background:** A number of studies have shown associations between chronic exposure to particulate air pollution and increased mortality, particularly from cardiovascular disease, but fewer studies have examined the association between long-term exposure to fine particulate air pollution and specific cardiovascular events, such as acute myocardial infarction (AMI).

**Objective:** We examined how long-term exposure to area particulate matter affects the onset of AMI, and we distinguished between area and local pollutants.

**Methods:** Building on the Worcester Heart Attack Study, an ongoing community-wide investigation examining changes over time in myocardial infarction incidence in greater Worcester, Massachusetts, we conducted a case–control study of 4,467 confirmed cases of AMI diagnosed between 1995 and 2003 and 9,072 matched controls selected from Massachusetts resident lists. We used a prediction model based on satellite aerosol optical depth (AOD) measurements to generate both exposure to particulate matter ≤ 2.5 μm in diameter (PM$_{2.5}$) at the area level (10 × 10 km) and the local level (100 m) based on local land use variables. We then examined the association between area and local particulate pollution and occurrence of AMI.

**Results:** An interquartile range (IQR) increase in area PM$_{2.5}$ (0.59 μg/m$^3$) was associated with a 16% increase in the odds of AMI (95% CI: 1.04, 1.29). An IQR increase in total PM$_{2.5}$ (area + local, 1.05 μg/m$^3$) was weakly associated with a 4% increase in the odds of AMI (95% CI: 0.96, 1.11).

**Conclusions:** Residential exposure to PM$_{2.5}$ may best be represented by a combination of area and local PM$_{2.5}$, and it is important to consider spatial gradients within a single metropolitan area when examining the relationship between particulate matter exposure and cardiovascular events.

**Key words:** air pollution. *Environ Health Perspect* 121:192–196 (2013). http://dx.doi.org/10.1289/ehp.1205284 [Online 29 November 2012]

Several studies have shown associations between chronic exposure to particulate air pollution and increased mortality, particularly from cardiovascular disease (Dockery et al. 1993; Pope et al. 2004; Puett et al. 2009). Fewer studies, however, have examined the association between long-term exposure to fine particulate air pollution, such as particulate matter ≤ 2.5 μm in diameter (PM$_{2.5}$), and specific cardiovascular outcomes, such as acute myocardial infarction (AMI). A systematic review of the association between air pollution and the incidence of MI concluded that the evidence for long-term effects, in contrast to short-term effects, of air pollution on MI risk is limited and few conclusions could be drawn (Bhaskaran et al. 2009). This may be in part because of the limited number of AMIs in many cohort studies.

Furthermore, spatial gradients within metropolitan areas are increasingly being identified as important in the association between particulate air pollution and health outcomes. Findings suggest that spatial gradients within cities might be as large, or larger, as those between cities (Hoek et al. 2002; Jerrett et al. 2005). In one of the few cohort studies that has investigated long-term exposure to PM$_{2.5}$ and incidence of cardiovascular events, a larger association with AMI was found for an exposure increase of 10 μg/m$^3$ within cities than between cities (Miller et al. 2007). The hazard ratio for AMI did not reach statistical significance, but this study had limited statistical power because of the relatively small number (n = 584) of events. This limitation is a common problem for even large cohort studies; the incidence of AMI in a decade is not high enough to produce a large number of cases. In such circumstances, case–control studies are an attractive alternative.

We previously found an association between traffic particles and occurrence of AMI in case–control studies within a single metropolitan area (Tonne et al. 2007, 2009). Our earlier analyses included indicators of traffic as a proxy for long-term exposure to traffic pollutants as well as a latent-variable approach to model residential exposure to traffic particles. Hence, it did not capture any effects of particles other than primary traffic particles. To gain a better understanding of how long-term exposure to area particulate matter affects the onset of AMI, and to distinguish between area and local pollutants, we examined both of these measures simultaneously in our analysis. In the present study, we used a PM$_{2.5}$-prediction model based on satellite aerosol optical depth (AOD) measurements (Klooog et al. 2011). The model generates area particulate air pollution predictions in addition to local particulate pollution based on local land use variables, both of which are assigned according to residential address. We then examined the association between both area and local particulate pollution and incidence of AMI using a case–control study design.

**Methods**

**Study population.** Cases of AMI included in this study were drawn from the Worcester Heart Attack Study, an ongoing community-wide investigation examining changes over time in the incidence and case-fatality rates of independently confirmed cases of AMI in residents of the greater Worcester, Massachusetts, area who were hospitalized with MI at all area medical centers. The details of this study have been described previously (Floyd et al. 2009; Goldberg et al. 1988, 1999). In brief, during the 5 years under study for the present investigation (1995, 1997, 1999, 2001, and 2003), the medical records of the 11 acute care general hospitals serving residents of the Worcester metropolitan area were searched for patients with a possible discharge diagnosis of AMI. The records were reviewed and validated according to diagnostic criteria described previously (Floyd et al. 2009; Goldberg et al. 1988), and at least two of the following criteria were required for inclusion in the original study: a suggestive clinical history, increased serum biomarker levels above each hospital’s normal range, and serial electrocardiographic findings indicative of AMI. The present study: a suggestive clinical history, increased serum biomarker levels above each hospital’s normal range, and serial electrocardiographic findings indicative of AMI. The present study was supported by the National Institutes of Health (grant RO1 HL35434), and the U.S. Environmental Protection Agency (EPA; grant RD 8347980). The contents of this article are solely the responsibility of the authors and do not necessarily represent the official views of the U.S. EPA. Further, the U.S. EPA does not endorse the purchase of any commercial products or services mentioned in the publication.

The authors declare they have no actual or potential competing financial interests.

Received 29 March 2012; accepted 29 September 2012.
In a second stage, we estimated exposures on
with random slopes for day and nested regions.

monitor and AOD values, using mixed models
each day using data from grid cells with both
major roads, percent of open space, point emis
tics for each monitor and a smooth function of
percent of open spaces, elevation, and traffic
ture within census block group and census

areas). The study area sections were central Worcester, the
northern suburbs, and the southern suburbs.

Cases’ residential addresses at the time of
AMI were collected from the review of hospital
medical records, and the controls’ residential
addresses were extracted from the resident lists.
Addresses were sent to a commercial firm for
goecoding (Mapping Analytics, Rochester, NY).

were generated by a novel exposure model developed recently by
Kloog et al. (2011) for assessing tempo-
day combinations without AOD data (the second stage models), our model performance
was excellent (mean out-of-sample $R^2 = 0.81$). Importantly, these $R^2$ are for daily observa-
tions, rather than monthly or yearly values.

To correct for bias we regressed the measured
PM$_{2.5}$ values against the predicted values in
each site on each day.

To estimate traffic particle exposures at
the local level, we used local (100 m) land use
terms (distance to primary highways, distance to
point source emissions, population density,
percent of open spaces, elevation, and traffic
density) to model the difference between the
10 × 10 km grid cell predictions and moni-
tored values. We regressed the residuals for
each monitor against local land use characteris-
tics for each monitor and a smooth function of
traffic density. The local PM$_{2.5}$ term provides
an estimate of traffic-related local particulate
pollution that is spatio temporally correlated
with traffic and local PM$_{2.5}$.

Finally, as an estimate of the total
outdoor PM$_{2.5}$ exposure at residential location,
we summed the local and area PM$_{2.5}$ terms.

Because our exposure varied
spatially, confounding by spatially varying
covariates was an issue. We obtained area-
based measures of socioeconomic status (SES)
from the year 2000 census at the block group level (U.S. Census Bureau 2000b). The follow-
ing SES measures were obtained: proportion of
the population with 1999 income below
the federally defined poverty level, median
household income in 1999, and percentage
of persons ≥ 25 years of age whose highest
degree was less than a high school diploma or
its equivalent. Census block groups have a
population of about 1,500 individuals and are
defined by the Census Bureau as small statis-
tical subdivisions of counties with generally
stable boundaries, designed to have relatively
small geographic areas (U.S. Census Bureau 2000a).

area. Although we matched on 10-year age
groups, we included age in our models as a
continuous, linear term, thus controlling more
finely for this covariate. We also included all
higher-order (2- and 3-way) interaction terms
for the matching factors in our models. Next,
we included measures of block group popula-
tion density and SES, distance to the near-
est large supermarket, and distance to nearest
recreation area in our models. Finally, we
used generalized estimating equations (GEEs)
assuming an exchangeable correlation struc-
ture within census block group and census
tract to account for any remaining correlation
among subjects in the same block group (or
census tract) not captured by model covari-
ates. We ran two sets of models: the first with
separate terms for area and local PM$_{2.5}$, and
the second with a term for their sum. In addi-
tion, we repeated GEE models restricted to
first (vs. any) AMI, and after stratifying by
section of the study area, and by time period
(1995, 1997, and 1999; or 2001 and 2003). All
models were conducted using PROC
GENMOD in SAS version 9.2 (SAS Institute Inc., Cary, NC).

Results
Exposure and covariate information by study
area section for cases and controls is presented in
Table 1. Figure 1 shows the residential loca-
tion for our study subjects according to their
10 × 10 km pollution grid cell. Exposure was
divided into two parts: a) area PM$_{2.5}$ predicted
for the 10 × 10 km grid cell that each case or
control lived in, and b) local PM$_{2.5}$ from the
local land use prediction model. In the year

socioeconomic inequalities in health outcomes
(Krieger et al. 2002).

individual lifestyle factors, such as dietary
patterns, obesity, and level of exercise, may be
related with place of residence. Although
such lifestyle factors were unavailable for the
cases and controls in our study, we attempted
to control for such factors by proxy. Obesity
prevalence, as well as fruit and vegetable con-
sumption, have been associated with distance
to large supermarkets (defined as having
> 50 employees) in metropolitan areas (Michimi
and Wimberly 2010), whereas access to parks,
walking and jogging trails, and enjoyable scen-
ery have been associated with physical activ-
ity behavior (Brownson et al. 2001). ArcGIS
version 10.1 (ESRI, Redlands, CA) was used to
calculate the straight-line distance between
residential addresses and large supermarkets.

locations of large supermarkets were available
from the 2006 InfoUSA Business Listing File
from ESRI’s Business Analyst Extension. Data
on recreation areas was downloaded from the
MassGIS web site (MassGIS 2012). These data
were geocoded using geocoding (Mapping Analytics, Rochester, NY).

Statistical analysis. We first ran logistic
regression models adjusted only for the match-
ing factors—age, sex, and section of the study
area. Although we matched on 10-year age
groups, we included age in our models as a
continuous, linear term, thus controlling more
finely for this covariate. We also included all
higher-order (2- and 3-way) interaction terms
for the matching factors in our models. Next,
we included measures of block group popula-
tion density and SES, distance to the near-
est large supermarket, and distance to nearest
recreation area in our models. Finally, we
used generalized estimating equations (GEEs)
assuming an exchangeable correlation struc-
ture within census block group and census
tract to account for any remaining correlation
among subjects in the same block group (or
census tract) not captured by model covari-
ates. We ran two sets of models: the first with
separate terms for area and local PM$_{2.5}$, and
the second with a term for their sum. In addi-
tion, we repeated GEE models restricted to
first (vs. any) AMI, and after stratifying by
section of the study area, and by time period
(1995, 1997, and 1999; or 2001 and 2003). All
models were conducted using PROC
GENMOD in SAS version 9.2 (SAS Institute Inc., Cary, NC).

Results
Exposure and covariate information by study
area section for cases and controls is presented in
Table 1. Figure 1 shows the residential loca-
tion for our study subjects according to their
10 × 10 km pollution grid cell. Exposure was
divided into two parts: a) area PM$_{2.5}$ predicted
for the 10 × 10 km grid cell that each case or
control lived in, and b) local PM$_{2.5}$ from the
local land use prediction model. In the year

socioeconomic inequalities in health outcomes
(Krieger et al. 2002).

individual lifestyle factors, such as dietary
patterns, obesity, and level of exercise, may be
related with place of residence. Although
such lifestyle factors were unavailable for the
cases and controls in our study, we attempted
to control for such factors by proxy. Obesity
prevalence, as well as fruit and vegetable con-
sumption, have been associated with distance
to large supermarkets (defined as having
> 50 employees) in metropolitan areas (Michimi
and Wimberly 2010), whereas access to parks,
walking and jogging trails, and enjoyable scen-
ery have been associated with physical activ-
ity behavior (Brownson et al. 2001). ArcGIS
version 10.1 (ESRI, Redlands, CA) was used to
calculate the straight-line distance between
residential addresses and large supermarkets.

locations of large supermarkets were available
from the 2006 InfoUSA Business Listing File
from ESRI’s Business Analyst Extension. Data
on recreation areas was downloaded from the
MassGIS web site (MassGIS 2012). These data
were geocoded using geocoding (Mapping Analytics, Rochester, NY).

Statistical analysis. We first ran logistic
regression models adjusted only for the match-
ing factors—age, sex, and section of the study
area. Although we matched on 10-year age
groups, we included age in our models as a
continuous, linear term, thus controlling more
finely for this covariate. We also included all
higher-order (2- and 3-way) interaction terms
for the matching factors in our models. Next,
we included measures of block group popula-
tion density and SES, distance to the near-
est large supermarket, and distance to nearest
recreation area in our models. Finally, we
used generalized estimating equations (GEEs)
assuming an exchangeable correlation struc-
ture within census block group and census
tract to account for any remaining correlation
among subjects in the same block group (or
census tract) not captured by model covari-
ates. We ran two sets of models: the first with
separate terms for area and local PM$_{2.5}$, and
the second with a term for their sum. In addi-
tion, we repeated GEE models restricted to
first (vs. any) AMI, and after stratifying by
section of the study area, and by time period
(1995, 1997, and 1999; or 2001 and 2003). All
models were conducted using PROC
GENMOD in SAS version 9.2 (SAS Institute Inc., Cary, NC).

Results
Exposure and covariate information by study
area section for cases and controls is presented in
Table 1. Figure 1 shows the residential loca-
tion for our study subjects according to their
10 × 10 km pollution grid cell. Exposure was
divided into two parts: a) area PM$_{2.5}$ predicted
for the 10 × 10 km grid cell that each case or
control lived in, and b) local PM$_{2.5}$ from the
local land use prediction model. In the year
In the present analysis, we observed an association between long-term exposure to area PM$_{2.5}$ and occurrence of AMI. In two prospective studies of women, one across the United States and one in the Northeast and Midwest regions of the country, elevated, but not statistically significant, hazard ratios were found for incident MI in association with an increase of 10 μg/m$^3$ of PM$_{2.5}$, with exposure based on either nearest monitor (Miller et al. 2007) or a spatiotemporal regression model (Puett et al. 2009). The relatively small number of incident cases in the two studies (< 1,000 in each) may partly explain these findings. In contrast, the present study included > 4,000 incident cases of AMI. Previous analyses (Tonne et al. 2007, 2009) of the Worcester Heart Attack Study, a population-based case–control study, indicated that exposure to traffic particles was associated with occurrence of AMI. In the present study, we found an association between the occurrence of AMI and exposure to regional PM$_{2.5}$.

**Discussion**

In the present analysis, we observed an association between long-term exposure to area PM$_{2.5}$, a regional air pollutant, and occurrence of AMI. Although several studies have found associations between long-term exposure to PM$_{10}$ or PM$_{2.5}$ and cardiovascular disease mortality (Dockery et al. 1993; Krewski et al. 2009; Miller et al. 2007; Puett et al. 2009), few have looked at specific outcomes such as AMI. In two prospective studies of women, one across the United States and one in the Northeast and Midwest regions of the country, elevated, but not statistically significant, hazard ratios were found for incident MI in association with an increase of 10 μg/m$^3$ of PM$_{2.5}$, with exposure based on either nearest monitor (Miller et al. 2007) or a spatiotemporal regression model (Puett et al. 2009). The relatively small number of incident cases in the two studies (< 1,000 in each) may partly explain these findings. In contrast, the present study included > 4,000 incident cases of AMI. Previous analyses (Tonne et al. 2007, 2009) of the Worcester Heart Attack Study, a population-based case–control study, indicated that exposure to traffic particles was associated with occurrence of AMI. In the present study, we found an association between the occurrence of AMI and exposure to regional PM$_{2.5}$.
while controlling for fine-scale variation in particulate air pollution that may be due to local traffic. We modeled exposure of PM$_{2.5}$ based on daily measurements of AOD in 32 grid cells across Worcester County. The use of actual spatially resolved measurements is an important advantage over land use regression (LUR), which is calibrated using space- and time-limited monitoring data, and our model performed better in out-of-sample validation than reported previously in other LUR-based models (Kloog et al. 2011). LUR models are calibrated only at measuring sites; our model benefits by incorporating physical measurements (via satellite data) over the entire spatial domain. In addition, satellite AOD data may be used to fit LUR models in locations without ground monitors, and may reduce bias due to non-random placement of monitors.

We separated estimates for local- and area-level pollution in our modeling. The first phase used the model developed by Kloog et al. (2011) to estimate average PM$_{2.5}$ concentrations on a 10 km grid. In the second phase, we took the residuals between the actual monitored value in each grid and the predicted mean value for each grid, which presumably reflect the influence of local conditions near each monitoring site, and regressed them against land use terms within 100 m of the monitor to account for the effects of these local sources. This model was then used to estimate local particle concentrations at the addresses of study participants. Because the land use regression is fit to the difference between the monitoring site and the addresses, the contribution is independent of the grid cell value, allowing us to examine the different sources of particle exposure with less collinearity in our model. A unique advantage of this approach is that it allows us to look at these exposure metrics separately and together, allowing for a best estimate of a subject’s residential outdoor PM$_{2.5}$ exposure. Because the measure of total PM$_{2.5}$ comprised two estimates with different spatial variability, it had little correlation with area SES characteristics, such as percent families living in poverty, and therefore the association between this metric and AMI may suffer less from residual confounding.

In the northeastern United States, PM$_{2.5}$ is composed predominantly of secondary organics and sulfate aerosols. Sulfate aerosols are formed from the oxidation of sulfur dioxide (SO$_2$) emitted from fossil fuel combustion, and it is estimated that 70% of the SO$_2$ emissions in the United States are from electricity-generating facilities (U.S. Environmental Protection Agency 2009). Formation of secondary organic aerosols is not as fully understood as that of particulate sulfate, but a portion of their formation is attributed to aromatic hydrocarbon precursors under nitrogen oxide (NO$_x$)-limiting conditions, and NO$_x$ is, like SO$_2$, also emitted from fossil fuel combustion, including motor vehicle exhaust. Prior work in this cohort was focused on traffic-related air pollution, which was measured using exposure proxies and a latent variable model (Tonne et al. 2007, 2009). However, in the present analysis we were able to estimate personal exposure to total PM$_{2.5}$, which was not solely due to traffic. A key contribution of the present analysis is the finding that transported particles, as well as local traffic particles, are associated with cardiovascular disease.

Through the use of our spatiotemporal regression model, we also identified an association between AMI and a relatively small amount of variation in PM$_{2.5}$ exposure within a single New England metropolitan area over the course of a calendar year. These results are consistent with findings from the Women’s Health Initiative Observational Study, where the association between PM$_{2.5}$ and cardiovascular events was stronger within-cities than between-cities (Miller et al. 2007). Taken together, these findings indicate that it is important to examine variation in exposure within a single metropolitan area, even when examining regional air pollutants, such as PM$_{2.5}$. Our results were not attenuated when accounting for spatial dependence, possibly because of the varying spatial scales of our exposure metrics. As expected, local sources made the greatest contribution to variation in particulate matter exposure, and therefore local PM$_{2.5}$ accounted for most of the variation in total PM$_{2.5}$ in this single metropolitan area. However, there was enough variation in area PM$_{2.5}$ to detect an independent association with that exposure metric as well.

Fine control for socioeconomic factors at the block group level, which in urban areas is quite small, had little effect on associations with PM$_{2.5}$. This is consistent with a recent publication of Brochu et al. (2011), who showed that PM$_{2.5}$ concentrations were associated with measures of poverty, education, and income over long spatial scales representing regional and between-city differences, but not on the finer within-city spatial scale, suggesting that studies focusing on within-city spatial variation will have little confounding with SES measures. Indeed, we found low-to-moderate correlation between our exposure metrics and measures of socioeconomic characteristics at the population level.

In contrast to our previous analysis specifically examining traffic particles, we only found a weak association between our measure of local PM$_{2.5}$ pollution and occurrence of AMI. Our estimate of “residual” local variation in particulate matter can be thought of as the incremental effect, beyond that captured by area PM$_{2.5}$, of particulate air pollution. The fact that it represents only an incremental effect, or that it captures a different source of pollution, may explain this difference.

A number of mechanisms by which long-term exposure to PM$_{2.5}$ may impact cardiovascular disease have been proposed, such as progression of atherosclerosis, systemic inflammation, and alterations in immune function. Evidence for such mechanistic pathways exists in both the toxicology and epidemiology literature. Studies of apolipoprotein E-deficient

---

### Table 2. Relative odds (OR [95% CI]) of AMI among cases and controls.

| Model | Area PM$_{2.5}$ | Local PM$_{2.5}$ | Total PM$_{2.5}$ |
|-------|-----------------|------------------|-----------------|
| Area PM$_{2.5}$ only* | 1.15 (1.09, 1.21) | — | — |
| Area PM$_{2.5}$ and local PM$_{2.5}$ | 1.16 (1.10, 1.22) | 1.03 (1.00, 1.06) | 1.04 (1.01, 1.08) |
| Area PM$_{2.5}$ and local PM$_{2.5}$ | 1.12 (1.06, 1.18) | 1.03 (1.00, 1.07) | 1.04 (1.00, 1.07) |
| GEE models with exchangeable correlation within census block group* | 1.14 (1.04, 1.29) | 1.03 (0.97, 1.08) | 1.04 (0.96, 1.11) |
| GEE models with exchangeable correlation within census tract* | 1.18 (1.04, 1.35) | 1.03 (0.98, 1.09) | 1.03 (0.97, 1.10) |

OR per IQR of pollutant; the IQR was 0.59 μg/m$^2$ for area PM$_{2.5}$, 1.08 μg/m$^2$ for local PM$_{2.5}$, and 1.05 μg/m$^2$ for total PM$_{2.5}$.

*Adjusted for matching factors (age, sex, and study area section) and interaction terms of matching factors.

### Table 3. Relative odds (OR [95% CI]) of AMI among cases and controls.

| Stratification factor | Area PM$_{2.5}$ | Local PM$_{2.5}$ | Total PM$_{2.5}$ |
|----------------------|-----------------|------------------|-----------------|
| AMI order            |                 |                  |                 |
| First AMI            | 1.19 (1.06, 1.33) | 1.04 (1.00, 1.09) | 1.05 (1.00, 1.11) |
| Any AMI              | 1.16 (1.04, 1.29) | 1.03 (0.97, 1.10) | 1.04 (0.97, 1.11) |
| Study section        |                 |                  |                 |
| 1                    | 1.24 (1.04, 1.48) | 1.01 (0.96, 1.06) | 1.01 (0.95, 1.07) |
| 2                    | 1.18 (1.04, 1.35) | 1.06 (0.98, 1.14) | 1.06 (0.98, 1.13) |
| 3                    | 1.06 (0.83, 1.34) | 1.11 (0.99, 1.24) | 1.10 (0.99, 1.23) |
| Study period         |                 |                  |                 |
| 1995, 1997, 1999     | 1.10 (0.98, 1.24) | 1.03 (0.98, 1.08) | 1.03 (0.98, 1.09) |
| 2001, 2003           | 1.18 (1.05, 1.32) | 1.00 (0.96, 1.03) | 1.00 (0.96, 1.05) |

OR per IQR of pollutant; the IQR was 0.59 μg/m$^2$ for area PM$_{2.5}$, 1.08 μg/m$^2$ for local PM$_{2.5}$, and 1.05 μg/m$^2$ for total PM$_{2.5}$.

*Adjusted for matching factors (age, sex, and study area section) and interaction terms of matching factors, population density, SES, distance to large supermarket, and distance to recreation area.
(ApoE−/−) mice have linked exposure to concentrated air particles over 4–6 months with increased aortic atherosclerotic plaque (Chen and Nadziejko 2005). A more recent study of low density lipoprotein receptor–deficient (LDLR−/−) mice demonstrated that particle exposure increased oxidation of LDL, increased the thickness of the arterial wall, and promoted plaque growth and instability (Soares et al. 2009). In humans, long-term exposure to PM2.5 has been associated with increased carotid intima media thickness, a subclinical marker of coronary atherosclerosis, in two cross-sectional studies in the United States (Diez Roux et al. 2008; Künzli et al. 2005) and one in Germany (Bauer et al. 2010). Other studies have also reported associations of particles with various markers of chronic atherosclerosis (Adar et al. 2010; Allen et al. 2009). These studies suggest that our findings of an association between long-term exposure to PM2.5 and occurrence of AMI are biologically plausible.

In the present population-based study, we observed an association between AMI and PM2.5 exposure. However, this study is not without limitations, and therefore these findings should be interpreted with caution. Because our exposure varied spatially, we included other spatially varying covariates that also predicted AMI, such as percent of households living in poverty, distance to large supermarkets, and distance to recreation areas, in our models. However, these measures do not perfectly account for individual-level AMI risk factors (e.g., smoking, dietary patterns, physical activity) that also vary spatially, and therefore could be a source of unmeasured confounding in our models. We attempted to account for this by running models that included an exchangeable correlation structure within census block groups and census tracts, which did not change results substantially. Nonetheless, some residual confounding by socioeconomic and lifestyle factors is likely. Associations varied, somewhat, by section of the study area, which may be a function of varying exposure and residual confounding. Our PM2.5 prediction models have a relatively coarse spatial resolution (10 × 10 km), which may have led to some error in characterizing area-level exposure. Although estimation conducted at a finer spatial resolution is preferable, the ability to capture background area PM2.5 and still account for local PM2.5 by the separate covariate was an advantage of this study. Models used to predict exposures were also limited by a lack of data on the exact composition of AOD particles. In addition, our model predicted ambient PM2.5 exposure at a subject’s residential location, without accounting for the amount of time spent in other locations, indoors versus outdoors, or the length of residence at the current address. Finally, our area PM2.5 exposure metric was approximated from the year 2000 annual exposure for the study area. This year was selected based on AOD data availability and because it was within the study period of case accrual. Because our cases were accrued before and after this date, we do not expect differential exposure error in the cases, but it is possible that there is some differential exposure misclassification with respect to residential history for the controls. When we stratified by study time period, the OR for the area PM2.5 estimate was greater during the later time period. Because controls were sampled by proxy from resident lists in 2003 to represent the study base over the entire study period, exposure estimates for controls in the earlier time periods may have been higher than the actual exposure for these subjects, leading to a downward bias of our results.

Conclusions

After accounting for local pollution exposure, long-term exposure to area PM2.5 was associated with the occurrence of AMI in this population-based study. The association between total PM2.5 and AMI occurrence was weak, but this metric of combined spatial scales may provide a better estimate of total PM2.5 exposure at an individual’s residence. This study adds to the growing body of literature on long-term regional particulate pollution and cardiovascular morbidity, and highlights the importance of examining pollutant variability within a single metropolitan area, rather than solely focusing on comparisons across large spatial scales.

References

Adar SD, Klein R, Klein BE, Zipiria AA, Cotch MF, Wong TV, et al. 2010. Air pollution and the microvascular: a cross-sectional assessment of in vivo retinal images in the population-based Multi-Racial Study of Atherosclerosis (MESA). PLos Med 7(11):e1000372. doi:10.1371/journal.pmed.1000372 (Online 30 November 2010).

Allen RW, Cruqu MH, Diez Roux AV, Allison M, Shea S, Detrano R, et al. 2006. Fine particle pollution, proximity to traffic, and aortic atherosclerosis. Epidemiology 2002(1):284–294.

Bauer M, Moebius S, Mihlenkamp S, Drago N, Nonnenmacher M, Fuchsburger M, et al. 2010. Urban particulate matter air pollution distribution with subclinical atherosclerosis results from the HINE (Heinz Niederkof Recall) study. J Am Coll Cardiol 56(22):1802–1808.

Bhaskaran K, Hajat S, Haines A, Wilkinson P, Soobader MJ. 2010. Effects of air pollution on the incidence of myocardial infarction. Heart 95(21):1746–1759.

Brochu PJ, Yanosky JD, Paciorek CJ, Schwartz J, Chen JT, Herrick RF, et al. 2011. Particulate air pollution and socioeconomic position in rural and urban areas of the northeastern United States. Am J Public Health 101(suppl 1):S224–S230.

Brownson RC, Baker EA, Housemann RA, Brennan LK, Bacak SJ. 2011. Environmental and policy determinants of physical activity in the United States. Am J Public Health 91(12):1995–2005.

Chen LC, Nadziejko C. 2005. Effects of subchronic exposure to concentrated ambient particles (ICAPs) in mice. V. ICAPs exacerbate aortic plaque development in hyperlipidemic mice. Inhal Toxicol 17(4):217–224.

Diez Roux AV, Aucinloss AH, Franklin TG, Raghunathan T, Barr RG, Kaufman J, et al. 2008. Long-term exposure to ambient particulate matter and prevalence of subclinical atherosclerosis in the multi-ethnic study of atherosclerosis. Am J Epidemiol 167(8):687–695.

Dockery DW, Pope CA III, Xu X, Spengler JD, Ware JH, Fay ME, et al. 1993. Association between air pollution and mortality in six U.S. cities. N Engl J Med 329(18):1753–1759.

Floyd KC, Zarebski J, Spencer FA, Lessard D, Dalen JE, Alpert JS, et al. 2009. A 30-year perspective (1975–2005) into the changing landscape of patients hospitalized with initial acute myocardial infarction: The Worcester Heart Attack Study. Circ Cardiovasc Qual Outcomes 2(2):89–95.

Goldberg RJ, Gore JM, Alpert JS, Dalen JE. 1988. Incidence and case fatality rates of acute myocardial infarction (1975–1984): the Worcester Heart Attack Study. Am Heart J 116(4):761–787.

Goldberg RJ, Zarebski J, Lessard D, Gore JM. 1999. A two-decades (1975 to 1995) long experience in the incidence, inhospital and long-term case-fatality rates of acute myocar- dial infarction: a community-wide study. J Am Coll Cardiol 33(16):1533–1539.

Hoek G, Brunekree B, Goldbohm S, Fischer P, van den Brandt PA. 2002. Association between mortality and indicators of traffic- related air pollution in the Netherlands: a cohort study. Lancet 360(9310):1203–1209.

Jerrrett M, Burnett RT, Ma R, Pope CA III, Krewski D, Neveild KB, et al. 2005. Spatial analysis of air pollution and mortality in Los Angeles. Epidemiology 16(6):727–738.

Kloog I, Kouratrix P, Couil BA, Lee HJ, Schwartz J. 2011. Assessing temporally and spatially resolved PM2.5 exposures for epidemiological studies using satellite aerosol optical depth measurements. Ann Epidemiol 21(2):67–75.

Krewski D, Jerrrett M, Burnett RT, Ma R, Hughes E, Shi Y, et al. 2009. Extended follow-up and spatial analysis of the American Cancer Society study linking particulate air pollution and mortality. Respiration. MassGIS. 2012. MassGIS Data—Protected and Recreational Open Space. Available: https://www.mass.gov/mgis/ [accessed 2 March 2012].

Michimi A, Wimberly MC. 2010. Associations of supermarket accessibility with obesity and fruit and vegetable consumption in the conterminous United States. Int J Health Geogr 9:48. doi:10.1186/1476-072X-9-48 (Online 8 October 2010).

Miller KA, Siscovick DS, Sheppard L, Shephard K, Sullivan JH, Anderson GL, et al. 2007. Long-term exposure to air pollution and incidence of cardiovascular events in women. N Engl J Med 356(14):478–488.

Pope CA III, Burnett RT, Thurston GD, Thun MJ, Calle EE, Krewski D, et al. 2004. Cardiovascular mortality and long-term exposure to particulate air pollution: epidemiological evidence of general pathophysiological pathways of disease. Circulation 109(1):71–77.

Puetz RC, Hart JE, Yanosky JD, Paciorek C, Schwartz J, Suh H, et al. 2009. Chronic fine and coarse particulate exposure, mortality, and coronary heart disease in the Nurses’ Health Study. Environ Health Perspect 117:1687–1701.

Soares SR, Carvalho-Oliveira R, Ramos-Sanchez E, Catanoso S, da Silva LF, Mauad T, et al. 2009. Air pollution and antibodies against modified lipoproteins are associated with atherosclerosis and vascular remodeling in hyperlipidemic mice. Atherosclerosis 207(2):368–373.

Tonne C, Melly S, Mittleman M, Coull B, Goldberg R, Schwartz J. 2007. A case–control analysis of exposure to traffic and acute myocardial infarction. Environ Health Perspect 115:53–57.

Tonne C, Yanosky J, Gryparis A, Melly S, Mittleman M, Goldberg R, et al. 2009. Traffic particles and occurrence of acute myocardial infarction: a case-control analysis. Occup Environ Med 66(11):797–801.

U.S. Census Bureau. 2000a. Cartographic Boundary Files. Available: https://www.census.gov/geo/www/cob/cbg_/metadata.html [accessed 20 December 2012].

U.S. Census Bureau. 2000b. American FactFinder. Available: http://factfinder2.census.gov/faces/nav/jsf/pages/index.xhtml [accessed 18 December 2012].

U.S. Environmental Protection Agency. 2009. Integrated Science Assessment for Particulate Matter (Final Report). EPA/600/R-08/139F. Research Triangle Park, NC:U.S. EPA. Available: http://cfpub.epa.gov/ncea/CFM/renderdisplay.cfm?fi=216546 [accessed 18 December 2012].