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Ambient particulate air pollution and ectopy - The Environmental Epidemiology of Arrhythmogenesis in Women's Health Initiative Study, 1999-2004

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Abstract

The relationships between ambient PM_{2.5} and PM₁₀ and arrhythmia and the effect modification by cigarette smoking were investigated. Data from EPA air quality monitors and an established national-scale, log-normal kriging method were used to spatially estimate daily mean concentrations of PM at addresses of 57,422 individuals from 59 examination sites in 24 US states in 1999-2004. The acute and subacute exposures were estimated as mean, geocoded address-specific PM concentrations on the day of, 0-2 days before, and averaged over 30 days before the ECG (Lag₀; Lag₁; Lag₂; Lag₁₋₃₀). At the time of standard 12-lead resting ECG, the mean age (SD) of participants was 67.5 (6.9) years (84% non-Hispanic White; 6% current smoker; 15% with coronary heart disease; 5% with ectopy). After the identification of significant effect modifiers, two-stage random-effects models were used to calculate center-pooled odds ratios and 95% confidence intervals (OR, 95% CI) of arrhythmia per 10 µg/m³ increase in PM concentrations. Among current smokers, Lag₀ and Lag₁ PM concentrations were significantly associated ventricular ectopy (VE) - the OR (95% CI) for VE among current smokers was 2 (1.32-3.3) and 1.32 (1.07-1.65) at Lag₁ PM_{2.5} and PM₁₀, respectively. The interactions between current smoking and acute exposures (Lag₀; Lag₁; Lag₂) were significant in relationship to VE. Acute exposures were not significantly associated with supraventricular ectopy (SVE), or with VE among non-smokers. Subacute (Lag₁₋₃₀) exposures were not significantly associated with arrhythmia. Acute PM_{2.5} and PM₁₀ exposure is directly associated with the odds of VE among smokers, suggesting that they are more vulnerable to the arrhythmogenic effects of PM.

Introduction

Numerous studies have consistently found a significant association between particulate matter (PM) air pollution and the risk of cardiovascular disease (Brook et al. 2004; Craig et al.

2008). The mechanisms responsible for such association, although not fully understood, have been the focus of recent environmental health studies. Panel and population-based studies alike (Creason et al. 2001; Gold et al. 2000; Liao et al. 1999, 2004; Pope et al. 1999; Yang et al. 2004) suggested that sympathetic activation and parasympathetic suppression is one of the underlying mechanisms linking air pollution and increased risk of cardiovascular disease (CVD). It is biologically plausible that such alteration in cardiac autonomic control may decrease arrhythmia thresholds and thereby increase the risk of arrhythmia (Huikuri et al. 2001; Ultich et al. 2002). On the other hand, it is also well-documented (Engel et al. 2007; Rautaharju et al. 2006a) that ventricular ectopy (VE) and supraventricular ectopy (SVE) are the most frequent forms of arrhythmia in the general population. Ectopy, especially VE, is associated with a higher risk of incident cardiac events (Engel et al. 2007). However, only a few, typically small, single-city studies of majority-male, patient populations with implantable cardioverter-defibrillators (ICD) or Holter ECG have assessed the potential role of ventricular arrhythmogenesis in PM-mediated cardiovascular risk (Peters et al. 2000; Rich et al. 2004; 2005; 2006; Vedal et al. 2004; Dockery et al. 2005a; 2005b; Ebelt et al. 2005; Berger et al. 2006; Sarnat et al. 2006; Metzger et al. 2007).

This study was designed to investigate the relationship between exposures to ambient particulate matter $< 2.5 \mu\text{m}$ ($\text{PM}_{2.5}$) or $< 10 \mu\text{m}$ (PM_{10}) in diameter and VE and SVE as detected by a resting, standard 12-lead ECG in a relatively large and geographically diverse population of women enrolled in the Women's Health Initiative (WHI) clinical trials (WHI CT).

Methods

Population

The research objectives were addressed in *The Environmental Epidemiology of Arrhythmogenesis in WHI* (EEAWHI), an ancillary study of proarrhythmic mechanisms linking air pollution and cardiovascular disease in WHI CT participants. The clinical trials were designed to allow randomized, controlled evaluation of dietary modification, estrogen or estrogen plus progesterone, and calcium / vitamin D supplementation on risk of breast and colorectal cancer, cardiovascular disease, and bone fractures (WHI Study Group. 1998).

Between 1992 and 1998, the trials enrolled 68,133 postmenopausal women aged 50 to 79 years at 59 U.S. exam sites (including satellites and remote sites). Women were not eligible if they had medical conditions predictive of survival time less than three years, if they were known to have conditions inconsistent with study participation and adherence (e.g. alcohol dependence), or if they were active participants in another randomized controlled trial. Women also were ineligible for reasons of competing risk and safety (e.g. acute myocardial infarction in the last 6 months or severe hypertension). Each intervention arm also incorporated specific eligibility criteria. Those who remained eligible and interested were invited to follow-up visits at 3, 6 and 9 years. Rigorous quality assurance programs were in place through close-out (September, 2004 - March, 2005). From the entire WHI clinical trials population ($N=68,133$), the first-recorded, resting 12-lead ECG of participants examined during 1999-2004 ($N=58,705$) were included. Those who were using an anti-arrhythmic medication, defined as prescribed Type I, I-A, I-B, I-C, III or miscellaneous anti-arrhythmic medications, at the time of ECG recording or whose ECG was of such poor quality as to prevent accurate measurement of ectopy ($N=1,283$) were also excluded. The effective sample size for this study is 57,422.

Electrocardiograms (ECG)

Centrally trained and officially certified technicians recorded standard, twelve-lead ECG at baseline and each follow-up visit (WHI Study Group 1994). They placed disposable Ag/AgCl electrodes on the precordium relative to standard anatomical landmarks using the E-V6

Halfpoint Method (Rautaharju et al. 1976), a HeartSquare (NovaHeart, Inc), and strictly standardized protocols for positioning chest electrodes in women (Rautaharju et al. 1998). They digitally recorded ECG with participants in the resting, supine position using MAC PC electrocardiographs (GE Marquette, Inc). Upon successful recording, they transmitted ECG by telephone modem to the Epidemiological Cardiology Research (EPICARE) Center for visual inspection, error / missing lead detection, quality grading, and electronic reading by the Marquette 12SL program (GE Marquette, Inc).

Ectopy identification and classification

VE and SVE beats were detected both by computer algorithms of the Minnesota code (MC) together with visual over-reads of every WHI ECG transmitted to EPICARE for “flagging” of arrhythmias. The presence or absence of either VE or SVE beats (Minnesota Codes 8.1.1 or 8.1.2) (Prineas et al. 1982) in each 10-sec recording was entered into a separate database prepared for the WHI Clinical Coordinating Center for this study. In this non-patient population, few participants had more than one VE or SVE beat in their 10-sec ECG. Therefore, outcomes were analyzed as binary variables: presence vs. absence of ectopy. For comparison, VE and SVE were also combined into a single binary outcome (any ectopy).

Addresses and Geocodes

Participant addresses were collected at each visit and updated at least biannually. All of the participant and clinical center addresses in the contiguous U.S. from baseline through follow-up were cleaned according to a standardized protocol. These addresses were submitted in bloc to a single geocoding vendor selected from 4 candidates on the basis of its accuracy (Whitsel et al. 2004; 2006). The vendor assigned coordinates (latitudes; longitudes) and unique census identifiers (U.S. Census 2000 Federal Information Processing Standards [FIPS] codes) to > 99% of the addresses. Of these addresses, 91% were street-type matches.

Air Pollutant Concentrations

All ambient criteria air pollutant concentration data recorded at monitors operating in the contiguous U.S. during the study period (1999-2004) were obtained from the U.S. Environmental Protection Agency Air Quality System (U.S. EPA AQS 2006). The data included the longitude and latitude of each monitor. The data were cleaned and then used to fit national scale, log-normal kriging with a spherical model for spatial interpolations to produce geocoded location-specific daily mean concentrations of PM_{2.5} and PM₁₀. From these daily concentration data, the daily concentrations of PM_{2.5} and PM₁₀ were calculated for each participant and exam site 0-365 days prior to the ECG measurements (Lag₀₋₃₆₅) (Liao et al, 2006, 2007). The primary focus of this study is on the acute (Lag₀ to Lag₂), subacute (Lag₁₋₃₀, calculated as 30-day average concentrations before the ECG), with secondary focus on the long-term chronic PM exposures (Lag₁₋₃₆₅, calculated as 365-day average concentrations before the ECG).

Weather Variables

All meteorological data recorded at stations operating in the contiguous U.S. during the study period were obtained from the National Climatic Data Center (U.S. NCDC). Data included ambient temperature and pressures, as well as station longitudes, latitudes, and altitudes. Data were cleaned and missing sea level pressures were replaced with values computed from station and altimeter pressures using the station altitude, ambient temperature, and U.S. Standard Atmosphere temperature profile (U.S. COESA 1976). For stations with ≤ 6 consecutive hr (25%) of data on temperature and sea level pressure, the station-specific daily mean temperature and sea level pressure were imputed from nearby stations. Finally, daily mean temperature (°C) and pressure (kPa) at each geocoded address from baseline to closeout were

calculated by averaging these daily means across all stations within 50 km, a distance over which their station-to-station correlations exceed 0.9 (Ito et al. 2005). In 2000, for example, such calculations were based on an average across 4.2 stations. To the 2% of addresses ≥ 50 km (on average, 63 km) away from the nearest temperature station, the daily mean of that station was assigned. Thereafter, acute, subacute, and chronic meteorological exposure measures were calculated for each participant as described above.

Other Participant-Level Characteristics

Self-reported socioeconomic characteristics (education; total family income in the preceding year), health history (see below) and a variety of other attributes were determined at each visit by standardized participant interview and examination. Interim health events also were identified via standardized medical record review and physician adjudication. Medications taken at least twice per week for the two-week period before the ECG recording were therapeutically classified according to the Medispan Master Drug Database (MDDDB). Anti-arrhythmic medications specifically included those with Type I, I-A, I-B, I-C, III or miscellaneous anti-arrhythmic activity. The definition for anti-arrhythmic medication excluded the beta-antagonists (i.e. β -blockers), diuretics, and cardiac glycosides (e.g. digitalis). These latter categories were included in the study's definitions of hypertension and congestive heart failure, respectively. Diabetes was defined by anti-diabetic medication use or history; hypertension by anti-hypertensive medication use, systolic blood pressure ≥ 140 mmHg, or diastolic blood pressure ≥ 90 mm Hg, or history; body mass index as the ratio of weight to height squared (BMI, kg/m²); smoking as current, former, or never; chronic lung disease by history of asthma, emphysema or lung cancer; coronary heart disease (CHD) by anti-anginal medication use, history of angina or myocardial infarction and medical record review / adjudication; revascularization by history of coronary artery angioplasty, stent or bypass and medical record review / adjudication; and congestive heart failure (CHF) by cardiac glycoside / diuretic use, history and medical record review / adjudication.

Statistical Analysis

All analyses were conducted among the effective sample of 57,422 participants. A three-stage analysis was performed. The first two stages were performed using SAS Version 9.01, and the third stage using Stata Version 9.0. At the first stage, logistic regression models were used that allowed PM effects to vary randomly across exam sites to test, individually, the *a priori* hypothesized interactions between PM exposures and current smoking status, age, ethnicity, treatment arm, history of CVD (i.e. CHD, stroke, hypertension, or diabetes), and chronic lung disease. Our objective here was to identify any potential PM effect modifiers. The second and third stage forms traditional "two-stage random-effects models". Specifically, at the second stage, center-specific, individual-level covariable-adjusted logistic regression analysis was performed to obtain center-specific PM regression coefficients and their corresponding standard errors (SE). At this stage, if an effect modifier was identified in first stage of analysis (e.g., smoking), then, a center-specific multivariable logistic regression was performed to obtain PM regression coefficients (SE) for each level of the effect modifier. At the third stage, the random-effects meta-analysis model was performed, averaging across the inverse-variance-weighted, center-specific regression coefficients, to obtain pooled odds ratios and their 95% CI at each level of the effect modifier (Berkey et al., 2005). The OR) and their 95% CI are therefore center-variance weighted overall estimates of the association between PM exposures and the occurrence of ectopy on the 12-lead ECG. In addition to reporting the results by effect modifier status, the overall OR for all participants was also presented. The effect modifier was treated as a covariate in the second stage of the multivariate logistic regression analysis as mentioned above. As a result, each center only had one regression coefficient, which was then pooled together in meta-analysis to yield the final OR for the entire cohort. All results are expressed as per 10 $\mu\text{g}/\text{m}^3$ increase in PM₁₀ or PM_{2.5}.

Results

The demographic and cardiovascular disease risk profiles of the study population are presented in Table 1. The mean age at the time of ECG recording was 67.5 years, with 84% non-Hispanic white. The proportion of participants who reported being current cigarette smokers was only about 6%, which is lower than the national average. Other levels of cardiovascular disease risk factors / co-morbidity in this population were similar to that of national samples. Overall, the prevalence of 12-lead ECG detected VE, SVE, and both ectopy was 1.68%, 2.88%, and 0.12%, respectively, resulting in any ectopy rate of 4.68%. Both estimated PM_{2.5} and PM₁₀ in this study population were normally distributed, with the inter-quartile values close to 2-times the standard deviations of PM_{2.5} and PM₁₀.

Of the interactions examined at the first stage, only acute PM_{2.5} and PM₁₀ interactions with current smoking status were significant when VE was the outcome of interest. Subsequent analyses of VE were therefore stratified by current smoking status. At the second stage, the center-specific PM-VE regression coefficients (SE) were adjusted for age, race, center, education, history of CVD and chronic lung disease, relative humidity, temperature and 365-day average PM concentration. Those for SVE and any ectopy also were adjusted for current smoking. Results of the random-effects meta-regression analysis of these center-specific regression coefficients (SE) are presented in Table 2. In summary, among current smokers, Lag₀ and Lag₁ PM concentrations were significantly associated VE. For example, the OR (95% CI) for VE among current smokers was 2 (1.32-3.3) at Lag₁ PM_{2.5} and 1.32 (1.07-1.65) at Lag₁ PM₁₀, respectively. For non-current smokers, the OR (95% CI) was 1.05 (0.94-1.17) and 1.01 (0.94-1.07), respectively. The Lag₂ concentrations also were associated with VE, but the associations were not significant. Acute PM exposures were not significantly associated with SVE. Additional adjusting treatment arm, day-of-week, and seasonal indicator variables did not change the pattern of association (data not shown).

PM as subacute exposure (Lag₃₀), as well as chronic exposure (Lag₃₆₅), was also analyzed and none of them was significantly associated with ectopy (data not shown). It may be possible that the lack of association with subacute and chronic exposures may be explained by the lower variation in the longer-term exposure levels, especially between participants within centers.

As a sensitivity analysis, Lag₀, Lag₁, and Lag₂ were also forced together in to one model, and the pattern of associations with both VE and SVE was similar to that presented in Table 2 (data not shown). It is worth noting that our GIS-based PM estimates relied solely on the measured PM concentrations near the geocoded participants' addresses. As such, for some very remote locations on the days when no nearby air quality monitors reported PM concentration data, the errors of estimated PM, judged from the prediction error from the kriging model, tended to be larger. This was especially the case when there were no measured PM data within a 100 mile radius of a geocoded address. Sensitivity analysis was thus performed by excluding participants from the final models when their Lag₀ PM prediction errors were greater than two times their estimated PM concentrations. As anticipated, such an approach yielded similar OR, with narrower 95% CI (data not shown). The OR and their 95% CI reported here are based on the more inclusive, but also more conservative, models.

Discussion

A large number of epidemiologic studies showed an association between short-term exposure to increased particulate air pollution and CVD morbidity and mortality (Brook et al. 2004; Craig et al. 2008). However, the mechanisms responsible for such an association have not been fully identified. Previous studies suggested several promising underlying mechanisms, including cardiac autonomic impairment as measured by lower heart rate variability (Creason

et al. 2001; Gold et al. 2000, Liao et al. 1999, 2004; Pope et al. 1999). Other studies indicated that impaired cardiac autonomic control may lower the threshold for arrhythmia (Huikuri et al. 2001), and that ECG-detected ectopy, especially that of ventricular origin, may predict cardiovascular disease mortality (Engel et al, 2007; Rautaharju et al, 2006a). Because many publications repeatedly reported an association between acute PM exposure and lower HRV, it was postulated that an acute increase in ambient PM concentration may imbalance sympathetic and parasympathetic nervous control of the heart and thereby decrease threshold for ectopy. Through such PM-mediated decreases, short-term acute PM exposure may thereby trigger the onset of clinical cardiac events. In our study, data on the PM exposures, the HRV measures, and ectopy measures were presented. However, since ectopy is an exclusion criterion for our HRV measures, it was not possible to assess this hypothesis directly in this population. Instead, the associations of PM exposure with ectopy (this paper) and HRV (to be published else where), were assessed, respectively.

Among the post-menopausal women participating in the WHI clinical trials, a significant, direct association was found between acute exposure to ambient PM_{2.5} and PM₁₀ and ventricular ectopy among current smokers that gives some credence to this hypothesis. This study, however, did not find significant associations between acute PM exposure and ventricular ectopy among non-smokers, acute PM exposure and supraventricular ectopy, or chronic PM exposure and ectopy.

This is the first study to demonstrate such an association in a large, non-patient, geographically diverse, female population not selected on the basis of having an ICD (Table 3). The study thereby broadens the scope of the extant literature in the area, which to date, has been based on a handful of small, overlapping, single-city studies of majority-male, patient populations with ICD or Holter ECG assessed potential role of ventricular arrhythmogenesis in PM-mediated cardiovascular risk (Peters et al 2000; Rich et al. 2004;2005;2006; Vedal et al. 2004; Dockery et al. 2005a;2005b; Ebelt et al. 2005; Berger et al. 2006; Sarnat et al. 2006; Metzger et al. 2007). Our findings are nonetheless consistent with those previously described in several of these populations, although as a group, the WHI CT participants were clearly much less vulnerable to ventricular tachyarrhythmia than those in Table 3. If our findings are confirmed by others, the confirmation would provide support for the hypothesized role of autonomic imbalance and ventricular arrhythmogenesis in PM-mediated cardiovascular risk.

It should be noted that this study has several limitations that may affect interpretation of its findings. First, it is an ancillary study of participants in the WHI clinical trial. As such, women in it were randomized to estrogen ± progestin treatment, calcium / vitamin D supplementation, and / or dietary modification. Although randomized, these exposures may have affected measures of both ectopy and smoking status. However, it is of interest that adjustment of treatment arm did not change the pattern of association in our data. Similarly, the participants selected to participate in the WHI clinical trials may not be representative of the general female population. This is evidenced by lower current smoking rate in this population (6%) as compared to the US female population (about 18%).

Second, ectopy was measured from resting, standard 12-lead ECG which were only 10 sec in duration. The presence and temporal distribution of ectopy are highly variable and dependent on circadian rhythms, physical activity, as well as on other environmental and clinical conditions. Clinically, the standard duration used to evaluate ectopy is 24 hr, which was not feasible in this large-scale, population-based study. However, it is important to note that a standard 12-lead ECG only captures an extremely small window of cardiac rhythm, and is insensitive for detecting ectopy among relatively healthy populations especially when its frequency is low or varies diurnally. Despite such insensitivity, it has been argued that when

the purpose is to identify participants at risk with relatively high specificity, short ECG recordings serve this epidemiologic objective reliably. Indeed, ectopy frequent enough to be captured by short recordings may carry more prognostic significance than ectopy infrequent enough to require long recordings to capture it (Abdalla et al. 1987; Evenson et al. 2000; Ruberman et al. 1981;1981b). The insensitivity of the ECG may have nevertheless biased the observed association between acute PM exposure and ventricular ectopy towards the null. It is also possible that the frequency of ectopy among smokers is higher than that among non-smokers, which may lead to even lower sensitivity of detection among non-smokers. This may help explain why an association between PM and ectopy among non-smokers was not found.

Third, PM₁₀ was not directly measured in the personal breathing space of participants. Instead, it was spatially interpolated at each participant's geocoded address, raising questions about its validity as a surrogate of personal exposure or biological exposure. To overcome this particular limitation, the reliability and accuracy of address geocoding (Whitsel 2004;2006), and spatial interpolations (Liao et al. 2006;2007) was carefully established. The advantages of our spatial correlation based PM estimation over traditional area averages was previously discussed (Liao et al. 2006). Finally, data on the chemical components of the ambient particles were not available. Therefore, one can only implicate the involvement of both PM₁₀ and PM_{2.5} concentrations, but can not elucidate the specific chemical components responsible for their adverse effects.

In this study, a significant effect modification by current smoking status in the acute PM exposure-ventricular ectopy relationship was shown. Our finding is consistent with that from the American Cancer Society-Cancer Prevention II (ACS-CPII) study, which also found that PM exposures were more strongly associated with mortality from dysrhythmias and cardiac arrest among current than former or never smokers (Pope et al. 2004). Such effect modification is biologically relevant, for several reasons. It is well-known that smoking increases vulnerability to various adverse health conditions, as illustrated by e.g. ACS-CPII. Our data are suggestive of a higher vulnerability to PM effects among smokers. It is also likely that current smoking is related to higher frequency of ectopy, and by extension, higher chance of detection by the standard 12-lead ECG. These arguments provide plausible explanations as to why observed associations between acute PM exposures and ventricular ectopy in non-smokers lacked significance in this context, if not others.

The present data show that the subacute exposures (Lag₃₀) and chronic exposures (Lag₃₆₅) are not significantly associated with ectopy. Moreover, when simultaneously controlled for subacute and chronic exposures into the analyses, the association between acute exposures (Lag₀; Lag₁; Lag₂) and ectopy remained similar. Such a lack of chronic effects, similar to our previous findings (Liao et al. 2006; 1999), support our hypothesis that PM effects on cardiac autonomic control are in general acute. Studies are needed to examine the actual time course of PM effects.

Finally, multiple statistical models were utilized in our analyses. Given the biological plausibility, our *a priori* hypothesized short-term acute effect (e.g. Lag₀ and Lag₁ effects), data were not adjusted for multiple testing in our main findings. As such, it was not possible to fully exclude the possibility of significant findings by chance. However, it is very unlikely that "the chance findings" just occurred among those to be most vulnerable and on the exposure windows that are believed to be the most important time period for PM action. For the interested readers, Bonferroni correction was performed on OR of PM_{2.5} effect on ventricular ectopy among current smokers (OR=2, 95% CI 1.32, 3.03, Table 2). After correction for 30 tests performed in Table 2, the Bonferroni-corrected OR remained significant (OR=1.36, 95% 1.03 to 3.89). It can be argued that this application of Bonferroni correction is over-conservative; that is, various studies showed that PM exerted more adverse health effects at lag₁ and lag₀ than at

other lags. Therefore, the number of tests need to be adjusted for need to be smaller than 30 used in the above example. For all of the above reasons it was decided to present the main results without adjusting for multiple testing.

In summary, *acute* exposure to ambient PM_{2.5} and PM₁₀ is directly associated with higher odds of ventricular ectopy among smokers, suggesting that they are more vulnerable to the arrhythmogenic effects of PM. These and other published data support the proposed role of autonomic imbalance and ventricular arrhythmogenesis in PM-mediated cardiovascular risk.

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Table 1

The demographic and cardiovascular disease risk profiles (mean [SD] or proportion) of the study population on the date of ECG examination

	ALL (N=57,422)	Any Ectopy	
		NO (N=54,732)	YES (N=2,690)
Age at ECG date (years)	67.5 (6.9)	67.3 (6.8)	70.5 (6.8)
Race (%, White)	83.52	83.47	84.57
Education (%, <= HS)	24.05	24.02	24.54
Current smoking (%)	5.85	5.83	6.31
Diabetes (%)	8.63	8.55	10.30
Hypertension (%)	51.97	51.57	60.15
Chronic lung disease (%)	10.33	10.25	11.86
CHD (%)	7.59	7.46	10.30
Ventricular ectopy (%)	1.68	--	--
Supraventricular ectopy (%)	2.88	--	--
Lag ₁ PM _{2.5} (µg/m ³)			
- Mean (SD)	13.8 (7.9)	13.8 (7.9)	13.8 (7.6)
- 5 th / 95 th Percentile	5 / 29.1	5 / 29.2	5.06 / 28.5
Lag ₁ PM ₁₀ (µg/m ³)			
- Mean (SD)	27.5 (12.1)	27.5 (12.1)	27.5 (11.9)
- 5 th / 95 th Percentile	12.2 / 48.9	12.3 / 48.8	11.8 / 49.3
Lag-1 relative humidity (%)	68 (15)	68 (15)	67 (16)
Lag-1 temperature (°C)	13.9 (9.1)	13.9 (9.1)	14 (8.7)

Multivariable adjusted* odds ratios and 95% CI of ectopy associated with 10 µg/m³ increases of residence-level PM₁₀ and PM_{2.5} concentrations—Results from random-effects meta-analysis of center-specific logistic regression coefficients to adjust for ECG centers

Outcome	PM _{2.5} (10 µg/m ³)			PM ₁₀ (10 µg/m ³)		
	Lag 0	Lag 1	Lag 2	Lag 0	Lag 1	Lag 2
Ventricular Ectopy**						
All Participants	1.01 (0.91, 1.13)	1.07 (0.96, 1.20)	1.09 (0.98, 1.21)	1.01 (0.95, 1.07)	1.02 (0.96, 1.09)	0.99 (0.93, 1.06)
Current Smoker	1.52 (1.04, 2.24)	2 (1.32, 3.03)	1.59 (0.99, 2.55)	1.21 (0.96, 1.53)	1.32 (1.07, 1.65)	1.22 (0.95, 1.56)
Nonsmoker	0.99 (0.89, 1.11)	1.05 (0.94, 1.17)	1.08 (0.97, 1.21)	1 (0.93, 1.06)	1.01 (0.94, 1.07)	0.98 (0.92, 1.05)
Supraventricular ectopy						
All Participants	1.04 (0.96, 1.13)	1.01 (0.93, 1.10)	0.96 (0.87, 1.05)	1 (0.95, 1.06)	1 (0.95, 1.05)	0.99 (0.94, 1.04)
Ventricular Ectopy or Supraventricular ectopy						
All Participants	1.03 (0.96, 1.11)	1.04 (0.97, 1.11)	1 (0.94, 1.07)	1 (0.95, 1.04)	1 (0.96, 1.04)	0.98 (0.94, 1.02)

* Adjusted for age, race, center, education, history of CVD and chronic lung disease, relative humidity, temperature, 365-day average PM concentration, and current smoking when the models used all participants (when not stratified by current smoking).

** Current smoking and PM₁₀ and PM_{2.5} interaction terms were significant at p < 0.05 in relationship to ventricular ectopy.

Table 3
Human studies of the PM-ventricular arrhythmia association

Authors	Year	n	Setting	Female	Outcome	Method of Detection
Peters et al.	2000	100	Boston, MA	21%	DC	ICD
Vedat et al.	2004	50	Vancouver, BC	18%	DC	ICD
Rich et al.	2004	34	Vancouver, BC	20%	DC	ICD
Dockery et al.	2005a	195	Boston, MA	26%	VT	ICD
Dockery et al.	2005b	203	Boston, MA	25%	VT	ICD
Rich et al.	2005	203	Boston, MA	21%	VT	ICD
Ebel et al.	2005	16	Vancouver, Canada	56%	SVE	Holler
Rich et al.	2006	56	St. Louis, MO	NR	VT	ICD
Sarnat et al.	2006	30	Steubenville, OH	93%	SVE & VE	Holler
Berger et al.	2006	57	Efurt, Germany	0%	SVT & VT	Holler
Metzger et al.	2007	884	Atlanta, GA *	22%	VT	ICD
Current study	2008	57,422	59 Exam Sites	100%	SVE & VE	ECG

* In the contiguous U.S. DC = defibrillator discharge. ECG = resting, supine, standard twelve-lead electrocardiogram. ICD = implantable cardioverter-defibrillator. NR = not reported. SVT = supraventricular tachyarrhythmia. VT = ventricular tachyarrhythmia. SVE = supraventricular ectopy. VE = ventricular ectopy.