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Using Meta-analysis to Inform Interpolation of Personal from Ambient Particulate Matter Exposures and Clarify Effects of Measurement Error

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Abstract:	Background: Although ambient concentrations of particulate matter ≤10μm (PM10) are often used as proxies for total personal exposure, correlation (r) between ambient and personal PM10 concentrations varies. Factors underlying this variation and its effect on health outcome-PM exposure relationships remain poorly understood. The authors therefore systematically reviewed the literature examining r and, within an accessible framework, applied the results to bias analysis. Methods: The authors conducted a random-effects meta-analysis to estimate effects of study, participant and environmental factors on r; used the estimates to impute personal from ambient PM10 concentrations among 4,012 non-smoking, diabetic Women's Health Initiative clinical trial participants; and then estimated associations of the ambient and imputed personal PM10 concentrations with electrocardiographic measures of e.g. heart rate variability. Results: Fifteen studies (1990-2009) of 342 participants in five countries were identified. The median (range) of r was 0.46 (0.13, 0.72). There was little evidence of funnel plot asymmetry, but substantial heterogeneity of r, which increased 0.05 (95% confidence interval [CI]: 0.01, 0.09) per 10 μg/m3 increase in mean ambient PM10 concentration. Substituting imputed personal for ambient PM10 concentrations shifted mean percent changes in electrocardiographic measures per 10μg/m3 increase in exposure away from the null and decreased their precision, e.g. -2.0% (-4.6%, 0.7%) versus -7.9% (-15.9%, 0.9%) for the standard deviation of normal-to-normal RR interval duration. Conclusions: Analogous distributions and heterogeneity of r in extant meta-analyses of ambient and personal PM2.5 concentrations suggest that observed shifts in mean percent change and decreases in precision may be generalizable across particle size.

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Conflicts of Interest and Sources of Funding

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(Holliday et al. 2011, 2012).

ABSTRACT

Background: Although ambient concentrations of particulate matter ≤10μm (PM_{10}) are often used as proxies for total personal exposure, correlation (*r*) between ambient and personal PM_{10} concentrations varies. Factors underlying this variation and its effect on health outcome-PM exposure relationships remain poorly understood. The authors therefore systematically reviewed the literature examining *r* and, within an accessible framework, applied the results to bias analysis. Methods: The authors conducted a random-effects meta-analysis to estimate effects of study, participant and environmental factors on *r*; used the estimates to impute personal from ambient PM_{10} concentrations among 4,012 non-smoking, diabetic Women's Health Initiative clinical trial participants; and then estimated associations of the ambient and imputed personal PM_{10} concentrations with electrocardiographic measures of e.g. heart rate variability. Results: Fifteen studies (1990-2009) of 342 participants in five countries were identified. The median (range) of *r* was 0.46 (0.13, 0.72). There was little evidence of funnel plot asymmetry, but substantial heterogeneity of *r*, which increased 0.05 (95% confidence interval [CI]: 0.01, 0.09) per 10 $\mu g/m^3$ increase in mean ambient PM_{10} concentration. Substituting imputed personal for ambient PM_{10} concentrations shifted mean percent changes in electrocardiographic measures per 10$\mu g/m^3$ increase in exposure away from the null and decreased their precision, e.g. -2.0% (-4.6%, 0.7%) versus -7.9% (-15.9%, 0.9%) for the standard deviation of normal-to-normal RR interval duration. Conclusions: Analogous distributions and heterogeneity of *r* in extant meta-analyses of ambient and personal $PM_{2.5}$ concentrations suggest that observed shifts in mean percent change and decreases in precision may be generalizable across particle size.

INTRODUCTION

Particulate matter (PM) exposure is associated with numerous adverse health outcomes, particularly those involving the cardiovascular and respiratory systems.[1] Although these health effects may be strongest for small particles[2], many studies have found that large particles have independent, adverse effects on health.[3] This fact combined with global interest in PM_{10} suggests that focus on larger size fractions is still merited when examining PM-disease associations. In studies of these associations, researchers have quantified PM exposure using ambient, micro-environmental, or personal sampling. Although personal concentrations may represent the most accurate assessment of total exposure, ambient concentrations are federally regulated by the Environmental Protection Agency under the Clean Air Act.[4] Moreover, using ambient data is often less costly for sponsors, less burdensome for participants, or the only feasible method of retrospectively characterizing PM exposure in longitudinal cohort studies. As a result, many epidemiologic studies rely on ambient concentrations of PM, which are associated with varying degrees of exposure measurement error, despite scientific interest in the effect of total personal exposure on health.

Although the variability, magnitude and determinants of such exposure measurement error have been largely unknown or ignored in analyses of PM-health outcome associations, the body of literature on this topic is growing.[5-11] Further, researchers can examine the potential effects of the measurement error provided that the relationship between ambient and personal exposures can be quantified. Fortunately, many studies have uniformly reported the correlation (r) of ambient and personal PM_{10} concentrations in a variety of geographic

locations, often with an emphasis on vulnerable populations.[12-27] However, these studies have not been systematically reviewed. The authors therefore systematically reviewed the literature examining the longitudinal, within-person, ambient-personal PM_{10} concentration correlation to identify and characterize factors influencing the observed distribution and heterogeneity of *r*. The authors illustrate how results from such a review can be used to impute personal from ambient PM concentrations and clarify effects of exposure measurement error on health outcome-PM exposure relationships in epidemiologic studies.

METHODS

Search and data abstraction strategy

The authors searched seven electronic databases using the strategy described in eAppendix 1. The authors downloaded identified articles to Endnote (EndNote X1; Thomson Reuters, New York, NY), de-duplicated and examined the list for potential omissions. The authors reviewed each article, excluding those without PM_{10} concentrations measured in ambient (central site or outside participant home) and personal environments, and an ambient-personal Pearson or Spearman correlation coefficient (*r*) or at least four paired ambient-personal concentrations. The authors then abstracted the following data from included articles: individual participant *r* (study mean or median if individual participant unavailable) or paired ambient-personal concentrations; number of paired concentrations; and selected study, participant, and environmental characteristics (eTables 1-3). Article review, exclusion, and abstraction were conducted in duplicate by two authors who resolved discrepancies by consensus, and requested additional data from primary authors as needed. The authors assigned coordinates to the cities in which studies were conducted using the

United States Geological Survey Geographic Names Information System.[28] The authors then linked additional weather variables (eTable 3) from the National Climatic Data Center[29] to the coordinates by downloading data from the three nearest monitors and calculating inverse distance-weighted means across study dates.

Meta-analysis statistical procedures

When possible, the authors calculated a study-level mean *r* (r_j) that weighted each participant's contribution by the number of that participant's paired ambient-personal PM_{10} concentrations. To do this, the authors *r*-to-z transformed participant-level measures of *r*[30] and then calculated a study-level mean z ($\bar{z_r}$) using the Hedges-Olkin and Rosenthal-Rubin method under a random-effects model.[10,11,31] In this method, $\bar{z_r}=[\sum_{i=1}^{k}(w_i)(z_{r_i})]/[\sum_{i=1}^{k} w_i]$, where k denotes the number of participants in the study, *i* identifies the participant, z_{r_i} the participant's *r*-to-z transformed correlation coefficient, and w_i the corresponding weight.[31] The weight is composed of within- and between-participant variances: $1 / (n_i - 3)$ and τ^2. It is calculated as $[(1 / (n_i - 3)) + \tau^2]^{-1}$, where n_i is the participant-level number of paired ambient-personal PM_{10} concentrations, $\tau^2 = [Q - (k - 1)] / c$, $Q=\sum_{i=1}^{k}(n_i - 3)(z_{r_i} - \bar{z_r})^2$, and $c =\sum_{i=1}^{k}(n_i - 3) - [\sum_{i=1}^{k}(n_i - 3)^2]/[\sum_{i=1}^{k}(n_i - 3)]$.[31] Negative values of τ^2 were set to zero.[31] When participant-level data were unavailable, $\bar{z_r}$ was calculated under a fixed-effects model as follows: $\bar{z_r}=[\sum_{i=1}^{k}(w_i)(z_r)]/[\sum_{i=1}^{k} w_i]$, where z_r is the study-level median *r*-to-z transformed correlation coefficient, w_i is (n - 3), and n is the study-level mean number of paired ambient-personal PM_{10} concentrations per participant.[31] The standard errors of the study-level random- and fixed-effects $\bar{z_r}$ were calculated as $SE(\bar{z_r})=(1/\sum_{i=1}^{k} w_i)^{½}$.[31]

Funnel plot asymmetry was examined by plotting the study-level $\bar{z}_r$ versus its weight (w_j = 1 / SE($\bar{z}_r$)^2), computing Begg and Egger test statistics,[32,33] and completing a trim and fill analysis.[34] The authors evaluated homogeneity of *r* using Cochran's Q[35] and explored potential sources of heterogeneity by first assembling study, participant, and environmental characteristics with putative effects on *r*, then dichotomizing interval-scale characteristics at their medians, and computing summary random-effects correlation coefficients within strata defined by the characteristics. The authors also conducted univariate, random-effects meta-regressions to examine differences in *r* among strata; estimated changes in *r* per one-unit increase in interval-scale measures;[36] and examined their sensitivity to exclusion of outlying observations identified using an extreme studentized deviate multiple-outlier procedure.[37] Potential sources of heterogeneity identified in univariate random-effects meta-regressions were dichotomized at their median values (for continuous variables) and included in bivariable random-effects meta-regressions when cross-classification cell size was ≥ 2 to examine the possibility that one variable might explain all or part of the relationship observed between *r* and the other variables.

Imputation of Personal PM_{10} Concentration

The authors used the results of the meta-analysis to impute personal from ambient PM_{10} concentrations. Imputation was performed among 4,012 non-smoking, diabetic Women's Health Initiative clinical trial (WHI) participants residing in the contiguous U.S. at the time of their first resting, standard, twelve-lead electrocardiogram (ECG), from which measures of RR, PR, QRS, and QT interval durations as well as the root mean square of successive differences in and the standard deviation of normal-to-normal RR interval duration were

available.[38-40] Collectively, the measures reflect the rate of atrioventricular conduction, rate of ventricular depolarization / repolarization, and variation in heart rate.[41] Each has been recommended as a candidate outcome in studies of air pollution health effects under a mechanistic hypothesis postulating that the cardiovascular effects of air pollution depend in part on autonomic and myocardial pathophysiology.[42]

Imputation was completed in two steps. Step 1 involved estimating participant-specific correlations between ambient and personal PM concentrations using the random-effects meta-regression equation, $r = \beta_0 + \beta_1 x$ (Figure 3A, solid line), where β_0 is the intercept and x is the participant-specific ambient PM_{10} concentration, a plausible, consistently identified, and important source of between-study heterogeneity in r.[10,11] In this setting, ambient PM_{10} concentrations were geocoded address-specific daily means[43,44] averaged over the day of and two days before (lag_{0-2}) ECG recording.

Step 2 involved assuming that the distributions of the ambient and personal PM concentrations are bivariate normal (or log normal), and under this assumption, estimating the participant-specific mean personal PM_{10} concentration (p) at a given ambient PM_{10} concentration (x) using the equation, $\mu_{p|x} = \bar{y} + r \frac{s_y}{s_x} (x_i - \bar{x})$, where for each participant i, r is estimated as in Step 1; $\bar{x}$ (s_x) is the mean (standard deviation) ambient PM_{10} concentration among the WHI participants; and $\bar{y}$ (s_y) is the mean (standard deviation) personal PM_{10} concentration estimated from the distributions of the personal concentrations observed in the studies contributing to the meta-analysis. The variance of $\mu_{p|x}$ was calculated as $\sigma^2_{y/x} = (1 - r^2)s_y^2$.

Bias Analysis

The authors assessed effects of exposure measurement error by (i) iterating participant-specific estimation of $\mu_{p|x}$ as in Step 2 using y and s_y from each of the d studies contributing both pieces of information to the meta-analysis, (ii) computing the random-effects weighted mean and variance of the d estimates of $\mu_{p|x}$ for each participant, (iii) regressing each of the ECG measures on the weighted mean $\mu_{p|x}$, and then (iv) comparing the estimated associations with conventional estimates obtained by regressing the same ECG measures on x_i. In (iii), error-in-variables regression models were implemented in SAS® Proc Calis (SAS; Cary, NC) to accommodate the random-effects weighted variance of the weighted mean $\mu_{p|x}$, averaged across all participants. An identical covariable adjustment strategy similar to that in Whitsel et al.[45] was adopted in both (iii-iv). This strategy involved adjusting for the previously described sociodemographic, geographic, temporal, clinical, behavioral, and environmental variables footnoted in Table 1.

RESULTS

The electronic search strategy identified 698 articles of which 14 (2.0%) met inclusion criteria. A co-author identified an additional unpublished thesis, yielding 15 total studies. In addition, three studies provided results for varying numbers of sub-studies, totaling 21 for analysis. The studies were conducted over 20 years (1988-2007) and encompassed a large geographic area including 19 cities, 8 U.S. states, and 5 countries. The studies included 342 participants (median: 14 per sub-study) who were assessed over widely varying durations

(0.3 to 21.0 months); however, samples were collected for 24-hour periods in 19 (90% of) sub-studies (eTable 1).

The mean participant age in the studies ranged from 9 to 85 years and several sub-studies focused on populations with conditions commonly associated with increased susceptibility to PM health effects: chronic obstructive pulmonary disease (COPD, 24%), asthma (19%), and coronary artery disease (19%) (eTable 2).

As several studies spanned multiple seasons, mean weather variables should be viewed cautiously; however, the ranges of mean temperature (-4, 30°C) and wind speed (1, 7 m/s) were large. The ranges of mean personal and ambient PM_{10} concentrations also were large among studies: 11.5 to 115 $\mu g/m^3$ and 13.6 to 130.7 $\mu g/m^3$, respectively. Despite these ranges, personal concentrations were typically greater than ambient concentrations (eTable 3) and only one value was identified as an outlier: the mean ambient PM_{10} concentration in Watchalayann 2005.

The median (range) of r_j was 0.46 (0.13, 0.72) (Figure 1; eTable 3) with no outlying r values. Although the funnel plot symmetry test P-values were high (P_{Egger}=0.6, P_{Begg}=0.9), the visual impression of the plot suggested asymmetry and the trim and fill analysis imputed five hypothetically missing results, all with r_j near zero (Figure 2). In addition, there was substantial evidence of heterogeneity ($P_{Cochran's\ Q}$ <0.001). Consequently, an overall summary r was not estimated.

The magnitude and precision of stratum-specific, random-effects correlation coefficients suggested that participants without COPD (or asthma) and those exposed to higher ambient PM_{10} concentrations, higher ambient to personal concentration ratios, and lower wind speeds had more strongly correlated ambient and personal PM_{10} concentrations (Figure 3). Random-effects meta-regression results were consistent with these suggestions (Figures 3-4) as was the strengthened association between the ambient PM_{10} concentration and *r* after excluding an outlying ambient PM_{10} concentration (Figure 4). Although study location appeared to influence *r*, 76% of studies were located in the U.S., and *r* was similar among north-south and east-west dichotomization of coordinates (Figure 3). In addition, *r* was comparable among studies relying on PM_{10} measured at a central site versus outside home locations (0.54 (95% CI: 0.41, 0.65) versus 0.47 (95% CI: 0.31, 0.61)) and over the range of ambient and personal concentrations (Figure 3). Between-group differences were slightly attenuated in bivariable meta-regressions including combinations of mean ambient PM_{10} concentration, ambient to personal PM_{10} concentration ratio, and wind speed; however overall conclusions did not change (eTable 4).

The median (range) ambient PM_{10} concentration measured among WHI participants was 25.7 (7.3 -109.6) $\mu g/m^3$. Before and after excluding Watchalayaan 2005, the median (range) imputed *r* was 0.46 (0.38, 0.71) and 0.44 (0.30, 0.84), while the corresponding median (range) imputed personal PM_{10} concentration was 34.1 (23.8, 135.7) $\mu g/m^3$ and 28.6 (20.6, 152.8) $\mu g/m^3$.

The relationships between PM_{10} concentration, the root mean square of successive differences in normal-to-normal RR interval duration, and the standard deviation of normal-to-normal RR interval duration were notable in the bias analysis (Table 1). When the ambient PM_{10} concentration was used as the exposure, percent changes in the root mean square of successive differences in normal-to-normal RR interval duration and the standard deviation of normal-to-normal RR interval duration per 10 $\mu g/m^3$ increase were -1.5 (95% CI: -4.3, 1.3) and -2.0 (95% CI: -4.6, 0.7), but when the imputed personal was substituted for the ambient PM_{10} concentration, corresponding estimates shifted away from the null and their precision decreased: -6.7, (95% CI: -15.3, 2.8) and -7.9 (95% CI: -15.9, 0.9). The posterior probabilities of a positive percent change also decreased, from 0.14 to 0.08 and 0.07 to 0.04, respectively. Similar changes were observed across ECG measures in sensitivity analyses excluding 1) Watchalayann 2005, 2) child studies[14, 19, 22], and 3) both 1 and 2. For example, percent changes in the root mean square of successive differences in normal-to-normal RR interval duration and the standard deviation of normal-to-normal RR interval duration per 10 $\mu g/m^3$ increase were -5.5 (95% CI: -12.6, 2.2) and -6.5 (95% CI: -13.1, 0.7) when Watchalayann 2005 and child studies[14, 19, 22] were excluded from the bias analysis.

DISCUSSION

The use of ambient PM_{10} concentrations in health association studies remains common. Although potentially important sources of measurement error in this surrogate of true personal exposure have been suggested by many investigators, [5-11] no systematic review or application of results from studies examining the correlation between ambient and personal PM_{10} concentrations has been completed to date. The authors therefore summarized these

studies, characterized factors influencing the among-study heterogeneity of *r*, then described an accessible framework for using quantitative information about the sources of heterogeneity to impute personal from ambient PM concentrations and clarify the effects of exposure measurement error on health outcome-PM exposure relationships.

The summary included a funnel plot suggesting that the historically high costs and burdens associated with personal PM monitoring may have resulted in more studies of *r* enrolling few participants (scattered near the bottom of the plot) and less enrolling many participants (near the top). The results imputed by the accompanying trim and fill analysis could represent those that remain unpublished for a variety of reasons, such as implausibility (correlations near or below zero) or discordance with the extant literature. Were such low correlations actually withheld from publication, the observed among-study heterogeneity of *r* would have been even greater. Despite this possibility, the tests of funnel plot asymmetry support the ability of the included studies to represent the literature and their suitability for meta-analysis.

Because the meta-analysis provided substantial evidence of among-study heterogeneity of *r*, presentation of an overall fixed- or random-effects summary correlation coefficient was not warranted. Instead, the authors characterized the potential sources of heterogeneity. As *r* changed little with the range of the study-specific ambient or personal PM_{10} concentration, its association with other variables was anticipated. That expectation was substantiated by the observed increase in the ambient-personal PM_{10} concentration correlation with increasing ambient PM_{10} concentration, increasing ambient to personal PM_{10} concentration ratio, and

decreasing wind speed. Additionally, the authors observed higher correlations in participants without versus with COPD (or asthma).

There are a variety of plausible explanations for the observed patterns. In areas where ambient concentrations or ambient to personal concentration ratios are high, ambient PM may contribute more to total personal exposure than in areas where they are low. Direct increases in exposure to ambient concentrations, changes in ventilation, or altered activity patterns may account for this observation. Wind speed also may influence the ambient-personal PM_{10} concentration correlation as it affects the distribution of PM in the environment. Lower wind speed impedes dispersion of PM_{10} from its sources, thus allowing central site monitors to better predict an individual participant's exposure to ambient PM.[46] Individuals with and without COPD (or asthma) also may have different activity patterns, such as time spent outdoors,[47] which could influence the relationship between their personal and ambient concentrations of PM.

Bivariable meta-regression models were used to address the possibility that one of the aforementioned factors could explain part or all of the association of another with *r* (eTable 4). However, too few studies included participants with COPD, thereby preventing examination of this characteristic in bivariable meta-regression. Estimates of *r* did not differ substantially among the uni- and bi-variable meta-regression models, suggesting that meta-confounding of the univariable association of *r* with ambient PM_{10} concentration, ambient to personal PM_{10} concentration ratio, and wind speed may be less of a concern in this context.

Nevertheless, all bivariable meta-regressions should be interpreted cautiously given sample size constraints.

The pattern of the ambient-personal PM_{10} correlation coefficients observed in this setting ($r > 0$; low median; high range) is similar to those observed in meta-analyses of $PM_{2.5}$.[10,11] Further, the meta-analyses of both PM_{10} and $PM_{2.5}$ suggest that ambient PM concentrations are an important source of heterogeneity in r.[10,11] Although $PM_{2.5}$ concentrations comprise a large portion of PM_{10} concentrations, the extent of the similarity was unexpected given the differing distributive properties of the two size fractions,[48] which suggested that r would be somewhat higher for $PM_{2.5}$ than PM_{10}. While the ambient-personal PM_{10} correlation may have been driven by $PM_{2.5}$, data availability and methodological constraints limit ability of the present study to determine the extent to which this is true. Nonetheless, the similarity reinforces the idea that there is a variable and non-negligible degree of measurement error incurred when using ambient PM concentrations as proxies for personal exposures in studies of PM-health associations, regardless of particle size.

The direction of PM effects on heart rate variability observed in this setting is consistent with that described by a recent review of the topic concluding that ambient PM is inversely associated with the root mean square of successive differences in and the standard deviation of normal-to-normal RR interval duration, overall and among a variety of sub-groups.[49] However, the review did not address the error inherent in substituting ambient for personal exposures, which has several components.[8] In the present study, we addressed the component most likely to produce bias (the difference between average personal and true

ambient exposure), because the remaining components are largely Berksonian and therefore less likely to do so. The results suggest that this non-Berksonian component behaves like classical exposure measurement error to the extent that it biases PM_{10} health effects estimates toward the null when *r* depends on the ambient PM_{10} concentration as in the current meta-analysis. This observation may well generalize across particle size given the analogous dependence of *r* on centrally and proximally measured ambient $PM_{2.5}$ concentrations in prior meta-analyses.[10,11] As such, the magnitude of PM effects on heart rate variability may be larger than that previously anticipated by Pieters et al.

Controlling for the effects of PM measurement error as described herein has some general disadvantages when compared with error correction methods like regression calibration and hierarchical Bayesian analyses. One is its dependence on relatively small, technically complex, and in some cases, incompletely documented studies of potentially low-level exposures measured with behavior-altering personal monitors. Another is that bias and precision may vary among populations with ambient or personal PM concentrations unlike those observed in WHI or the meta-analyses, and perhaps unpredictably so among populations that smoke. Simultaneously evaluating multiple sources of heterogeneity in the ambient-personal PM_{10} correlation within a meta-analysis of 21 studies is an additional challenge. The study's frequentist methods also assume bivariate normality of ambient and personal PM concentrations, which may be unrealistic. Nevertheless, the range of ambient PM concentrations is wide in both the WHI[44,45, 50-52] and these meta-analyses[10,11]; four of five U.S. adults aged $\geq$ 18 years do not smoke[53]; and robustness to modest departure from normality is well-known. Moreover, error-in-variables regression and quantitative bias

assessments are familiar to epidemiologists[54] and readily accessible to a wide variety of users. In this case, they are illustrative of the meta-analytic foundation on which more comprehensive and rigorous (e.g. hierarchical Bayesian) approaches to improving estimation of air pollution effects could be built and applied in settings where only ambient PM concentration data are available.[55]

Such application may well benefit from reliance of the present data collection effort on a systematic review encompassing a wide variety of settings and allowing for broad examination of study, participant, and environmental effects on the ambient-personal PM_{10} correlation. By focusing on total personal PM_{10} exposure instead of personal exposure to PM_{10} of ambient origin, the data collection effort also avoided complications associated with the potentially unrealistic assumption that personal exposure is best assessed by relying on a distinctly smaller and less accessible group of microenvironmentally homogenous, single marker (e.g. sulfate) studies. In contrast, the data that were collected, quality controlled, and tabulated in eTables 1-3, readily facilitate sensitivity analyses at the discretion of future users, an option infrequently available with regression calibration factors published in isolation.

Other powerful methods for improving estimation of ambient exposures at geocoded participant addresses have been proposed.[44, 56-61] The dual benefit of improving estimation of total personal exposure to PM—a particular interest in etiologic studies—and clarifying the downstream effects of the measurement error with which it is associated, helps distinguish the meta-analytically informed interpolation method illustrated here from those alternatives.

Although total personal exposure to PM is not regulated under the Clean Air Act, the effect of aggregate PM exposure on health is of no less scientific interest. The current and published meta-analyses[10,11] provide the necessary data and an accessible statistical framework for estimating such exposure and conducting participant-level analysis of bias in ambient PM concentration-health association studies related to the exclusive focus on ambient PM concentrations. In combination, the data and framework detailed here can be leveraged to increase understanding of the true, but often masked relationships underlying such associations.

REFERENCES

1. United States Environmental Protection Agency. *Integrated Science Assessment for Particulate Matter (Final Report).* United States Environmental Protection Agency, Washington, DC, EPA/600/R-08/139F, 2009.

2. Peng RD, Chang HH, Bell ML, et al. Coarse particulate matter air pollution and hospital admissions for cardiovascular and respiratory diseases among Medicare patients. *JAMA.* 2008; 299(18): 2172-2179.

3. Brunekreef B and Forsberg B. Epidemiological evidence of effects of coarse airborne particles on health. *Eur Respir J.* 2005; 26(2): 309-318.

4. Clean Air Act 1990. Public Law 101-549. 42 U.S.C. §7401-7671q, 104 Stat. 2399.

5. Shy CM, Kleinbaum DG, and Morgenstern H. The effect of misclassification of exposure status in epidemiological studies of air pollution health effects. *Bull N Y Acad Med.* 1978; 54(11): 1155-1165.

6. United States Environmental Protection Agency. *Human exposure to particulate matter: relations to ambient and indoor concentrations. In: United States Environmental Protection Agency. Air quality criteria for particulate matter*. United States Environmental Protection Agency, Washington DC, EPA/600/P-95/001aF-cF, 1996. http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=2832#Download.

7. Wallace L. Correlations of personal exposure to particles with outdoor air measurements: a review of recent studies. *Aerosol Science and Technology*. 2000; 32(1):15-25.

8. Zeger SL, Thomas D, Dominici F, et al. Exposure measurement error in time-series studies of air pollution: concepts and consequences. *Environ Health Perspect.* 2000; 108(5): 419-426.

9. Dominici F and Zeger SL. A measurement error model for time-series studies of air pollution and mortality. *Biostatistics.* 2000; 1(2): 157-175.

10. Avery CL, Mills KT, Williams R, et al. Estimating error in using ambient PM2.5 concentrations as proxies for personal exposures: a review. *Epidemiology*. 2010; 21(2): 215-223.

11. Avery CL, Mills KT, Williams R, et al. Estimating error in using residential outdoor $PM_{2.5}$ concentrations as proxies for personal exposures: a meta-analysis. *Environ Health Perspect.* 2010; 118(5): 673-678.

12. Lioy PJ, Waldman JM, Buckley T, et al. The personal, indoor and outdoor concentrations of PM-10 measured in an industrial community during the winter. *Atmospheric Environment*. 1990; 24(1): 57-66.

13. Wallace L. Indoor particles: a review. *J Air Waste Manag Assoc.* 1996; 46(2): 98-126.

14. Janssen NAH, Hoek G, Harssema H, et al. Childhood exposure to PM10: relation between personal, classroom, and outdoor concentrations. *Occup Environ Med*. 1997; 54(12): 888-894.

15. Janssen NAH, Hoek G, Brunekreef B, et al. Personal sampling of particles in adults: relation among personal, indoor, and outdoor air concentrations. *Am J Epidemiol.* 1998; 147(6): 537-547.

16. Linn WS, Gong H Jr, Clark KW, et al. Day-to-day particulate exposures and health changes in Los Angeles area residents with severe lung disease. *J Air Waste Manag Assoc*. 1999; 49(9 Spec No): 108-115.

17. Rojas-Bracho L, Suh HH, and Koutrakis P. Relationships among personal, indoor, and outdoor fine and coarse particle concentrations for individuals with COPD. *J Expo Anal Environ Epidemiol.* 2000; 10(3): 294-306.

18. Sarnat JA, Koutrakis P, and Suh HH. Assessing the relationship between personal particulate and gaseous exposures of senior citizens living in Baltimore, MD. *J Air Waste Manag Assoc.* 2000; 50(7): 1184-1198.

19. Wheeler AJ, Williams I, Beaumont RA, et al. Characterisation of particulate matter sampled during a study of children's personal exposure to airborne particulate matter in a UK urban environment. *Environ Monit Assess*. 2000; 65(1-2): 69-77.

20. Rodes CE, Lawless PA, Evans GF, et al. The relationships between personal PM exposures for elderly populations and indoor and outdoor concentrations for three retirement center scenarios. *J Expo Anal Environ Epidemiol.* 2001; 11(2): 103-15.

21. Evans GF, Highsmith RV, Sheldon LS, et al. The 1999 Fresno particulate matter exposure studies: comparison of community, outdoor, and residential PM mass measurements. *J Air Waste Manag Assoc.* 2000; 50(11): 1887-1896.

22. Yip FY, Keeler GJ, Dvonch JT, et al. Personal exposures to particulate matter among children with asthma in Detroit, Michigan. *Atmospheric Environment.* 2004; 38(31): 5227-5236.

23. Watchalayann P, Srisatit T, Watts D, et al. Exposure to PM-10 of shop house dwellers in Bangkok, Thailand. *Science Asia.* 2005; 31(4): 359-367.

24. Williams R, Case M, Yeatts K, et al. Personal coarse particulate matter exposures in an adult cohort. *Atmospheric Environment*. 2008; 42(28): 6743-6748.

25. Arhami M, Polidori A, Delfino RJ, et al. Associations between personal, indoor, and residential outdoor pollutant concentrations: implications for exposure assessment to size-fractionated particulate matter. *J Air Waste Manag Assoc*. 2009; 59(4): 392-404.

26. Scapellato ML, Canova C, de Simone A, et al. Personal PM10 exposure in asthmatic adults in Padova, Italy: seasonal variability and factors affecting individual concentrations of particulate matter. *Int J Hyg Environ Health*. 2009; 212(6): 626-636.

27. Hsu S. *Characterization of Exposures to Urban Particulate Matter (PM) and its Components in COPD Patients in New York City and Seattle* [dissertation]. New York, NY: New York University; 2009.

28. United States National Geological Survey. Geographic Names Information System. Available: http://geonames.usgs.gov/pls/gnispublic/f?p=154:1:559715803173776 Accessed February 2010.

29. National Climatic Data Center. Weather/Climate Events. Available: http://www.ncdc.noaa.gov/oa/climateresearch.html Accessed February 2010.

30. Fisher RA. *Statistical Methods for Research Workers*. Edinburgh: Oliver and Boyd; 1925.

31. Field AP. Meta-analysis of correlation coefficients: a Monte Carlo comparison of fixed- and random-effects methods. *Psychol Methods*. 2001; 6(2):161–180.

32. Egger M, Davey Smith G, Schneider M, et al. Bias in meta-analysis detected by a simple, graphical test. *BMJ*. 1997; 315:629–634.

33. Begg CB, Mazumdar M. Operating characteristics of a rank correlation test for publication bias. *Biometrics*. 1994; 50(4):1088 –1101.

34. Duval S, Tweedie R. Trim and fill: A simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. *Biometrics*. 2000; 56(2):455– 463.

35. Cochran WG. The combination of estimates from different experiments. *Biometrics*. 1954; 10(1):101-129.

36. Berkey CS, Hoaglin DC, Mosteller F, et al. A random-effects regression model for meta-analysis. *Stat Med*. 1995; 14(4):395– 411.

37. Rosner B. Percentage points for a generalized ESD many-outlier procedure. *Technometrics*. 1983; 25:165-172.

38. The Women's Health Initiative Study Group. Design of the Women's Health Initiative clinical trial and observational study. *Control Clin Trials.* 1998; 19(1):61-109.

39. Heart rate variability. Standards of measurement, physiological interpretation, and clinical use. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Circulation. 1996; 93(5): 1043–1065.

40. Schroeder EB, Whitsel EA, Evans GW, et al. Repeatability of heart rate variability measures. *J Electrocardiol*. 2004; 37(3):163–172.

41. Prineas, RJ, Crow RS, Zhang, Z. *The Minnesota Code Manual of Electrocardiographic Findings*. 2nd ed. London: Springer-Verlag London Limited; 2010.

42. Zareba W, Nomura A, Couderc JP. Cardiovascular effects of air pollution: what to measure in ECG? *Environ Health Perspect*. 2001; 109 Suppl 4:533-538.

43. Whitsel EA, Quibrera PM, Smith RL, et al. Accuracy of commercial geocoding: assessment and implications. Epidemiol Perspect Innov 2006; 3(1):8.

44. Liao D, Peuquet DJ, Duan Y, et al. GIS approaches for the estimation of residential-level ambient PM concentrations. Environ Health Perspect 2006; 114(9):1374-1380.

45. Whitsel EA, Quibrera PM, Christ SL, et al. Heart rate variability, ambient particulate matter air pollution, and glucose homeostasis: the environmental epidemiology of arrhythmogenesis in the Women's Health Initiative. *Am J Epidemiol*. 2009; 169(6): 693-703.

46. Marcazzan GM, Vaccaro S, Valli G, et al. Characterization of PM10 and PM2.5 particulate matter in the ambient air of Milan (Italy). *Atmospheric Environment.* 2001; 35(27):4639-4650.

47. Liu LJS, Box M, Kalman D, et al. Exposure assessment of particulate matter for susceptible populations in Seattle. *Environ Health Perspect.* 2003; 111(7): 909-918.

48. Godoy SM, Mores PL, Santa Cruz ASM, et al. Assessment of impact distances for particulate matter dispersion: a stochastic approach. *Reliability Engineering and System Safety.* 2009; 94(10): 1658-1665.

49. Pieters N, Plusquin M, Cox B, et al. An epidemiological appraisal of the association between heart rate variability and particulate air pollution: a meta-analysis. *Heart*. 2012; 98(15): 1127-1135.

50. Miller KA, Siscovick DS, Sheppard L et al. Long-term exposure to air pollution and incidence of cardiovascular events in women. *N Engl J Med.* 2007; 356(5):447-58.

51. Zhang ZM, Whitsel EA, Quibrera PM et al. Ambient fine particulate matter exposure and myocardial ischemia in The Environmental Epidemiology of Arrhythmogenesis in the Women's Health Initiative (EEAWHI). *Environ Health Perspect.* 2009; 117(5):751-756.

52. Liao D, Whitsel EA, Duan Y, et al. Ambient particulate air pollution and ectopy – The Environmental Epidemiology of Arrhythmogenesis in WHI (EEAWHI), 1999-2004. *J Toxicol Environ Health A.* 2009; 72(1):30-38.

53. Centers for Disease Control and Prevention (CDC). Vital signs: current cigarette smoking among adults aged 18 years—United States, 2005–2010. *MMWR Morb Mortal Wkly Rep* 2011; 60:1207–1212.

54. Lash T, Fox P, and Fink A. Applying Quantitative Bias Analysis to Epidemiologic Data. New York, NY: Springer Science+Business Media; 2009.

55. McBride SJ, Williams RW, and Creason J. Bayesian hierarchical modeling of personal exposure to particulate matter. *Atmospheric Envionrment*. 2007; 41: 6143-6155.

56. Raghunathan TE, Diez-Roux A, Chen W. Predicting cumulative particulate matter exposure using space-time models and historical monitor data. *Epidemiol*. 2006; 17(6S):S250.

57. Yanosky JD, Paciorek CP, Schwartz J, et al. Spatio-temporal modeling of chronic PM10 exposure for the Nurses' Health Study. *Atmos Environ.* 2008; 42:4047-4062.

58. Paciorek CJ, Yanosky JD, Suh HH. Practical large-scale modeling of particulate matter. *Ann Appl Stat.* 2009; 3:370-397.

59. Szpiro AA, Sheppard L, and Lumley T. Efficient measurement error correction with spatially misaligned data. *Biostatistics.* 2011; 12(4): 610-623.

60. Yanosky JD. Paciorek CJ, and Suh HH. Predicting chronic fine and coarse particulate exposures using spatiotemporal models for the Northeastern and Midwestern United States. *Environ Health Perspect*. 2009; 117(4): 522-529.

61. Christakos G, Serre ML. BME analysis of spatiotemporal particulate matter distributions in North Carolina. *Atmospheric Environment*. 2000; 34: 3393-3406.

Figure Legends

Figure 1. Forest plot of 21 estimates of r_j (95% confidence interval) from twenty-one sub-studies of the within-participant correlation between ambient and personal PM_{10} concentration (eTable 3).

Figure 2. Funnel plot of 21 reported (•) and five imputed (°) estimates of the z-transformed r_j from twenty-one sub-studies of the within-participant correlation coefficient between ambient and personal PM_{10} concentrations, where w_j is the inverse variance of the z-transformed r_j.

Figure 3. Summary Random-Effects Correlation Coefficients and Meta-Regression Differences by Study, Participant, and Environment Characteristics. Summary *r* computed within strata of each characteristic. Difference in *r* from meta-regression analyses predicting *r* from the characteristics. Abbreviations: CI, confidence interval; n, number of studies.

Figure 4. Plot of 21 estimates of r_j (95% confidence interval) from twenty-one sub-studies of the within-participant correlation between ambient and personal PM_{10} concentrations versus (A) mean ambient PM_{10} concentration ($\mu g/m^3$), (B) mean ambient to personal concentration ratio, and (C) mean wind speed (m/s). Univariate random-effects regression lines (−). Excluding the outlying 130.7 $\mu g/m^3$ ambient PM_{10} concentration from Watchalayann 2005 (---).

Table

Table 1. Percent Change in Electrocardiographic Measures per 10μg/m^3 Increase in PM_{10} Concentration Among 4,012 Non-smoking, Diabetic Women's Health Initiative Clinical Trial Participants, United States, 1993-2004.

ECG Measure	Ambient PM_{10}		Imputed Personal PM_{10}	
	% (95% CI)[a]	P (%>0)	% (95% CI)[a]	P (%>0)
Root mean square of successive differences in normal-to-normal RR interval duration	-1.5 (-4.3, 1.3)	0.14	-6.7 (-15.3, 2.8)	0.08
Standard deviation of normal-to-normal RR interval duration	-2.0 (-4.6, 0.7)	0.07	-7.9 (-15.9, 0.9)	0.04
RR interval duration	-0.2 (-0.8, 0.4)	0.25	-1.0 (-2.9, 0.9)	0.15
PR interval duration	-0.2 (-0.7, 0.3)	0.21	-0.5 (-2.2, 1.3)	0.30
QRS interval duration	0.1 (-0.4, 0.6)	0.66	0.2 (-1.5, 1.9)	0.59
QT interval duration	0.0 (-0.3, 0.3)	0.50	-0.2 (-1.2, 0.8)	0.34

Abbreviations: CI, confidence interval; P, posterior probability

[a] Fully Adjusted (age, race/ethnicity, education, region, time of day (minutes), day of week, season, body mass index (kg/m^2), hypertension, systolic blood pressure (mm Hg), anti-arrhythmia medication use, total energy expenditure (kcal/kg*week), chronic lung disease, hypercholesterolemia, coronary heart disease, revascularization, congestive heart failure, lag_{0-1} temperature (ºC), dew point (ºC), and barometric pressure (kPa))

Figure 1.

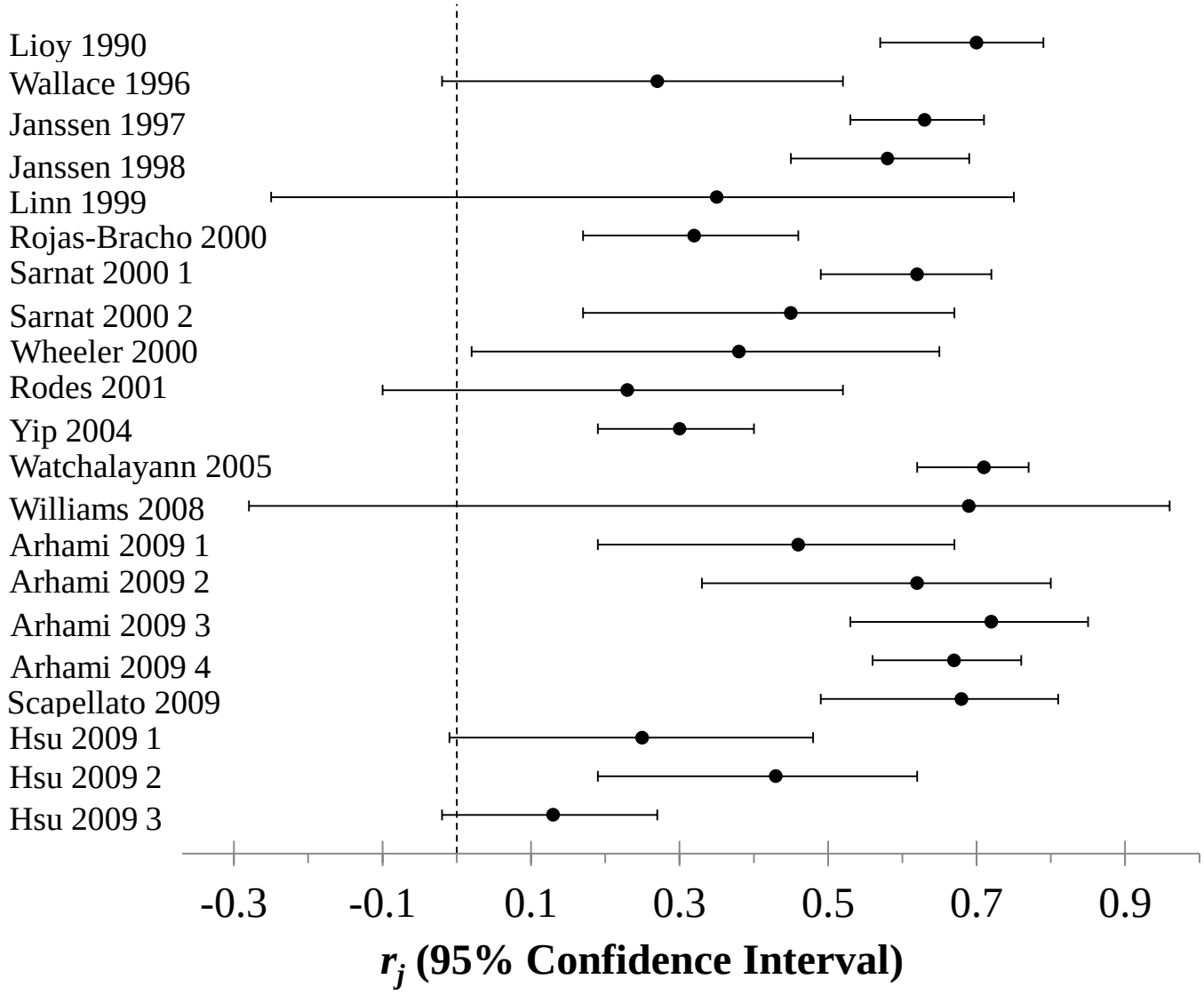
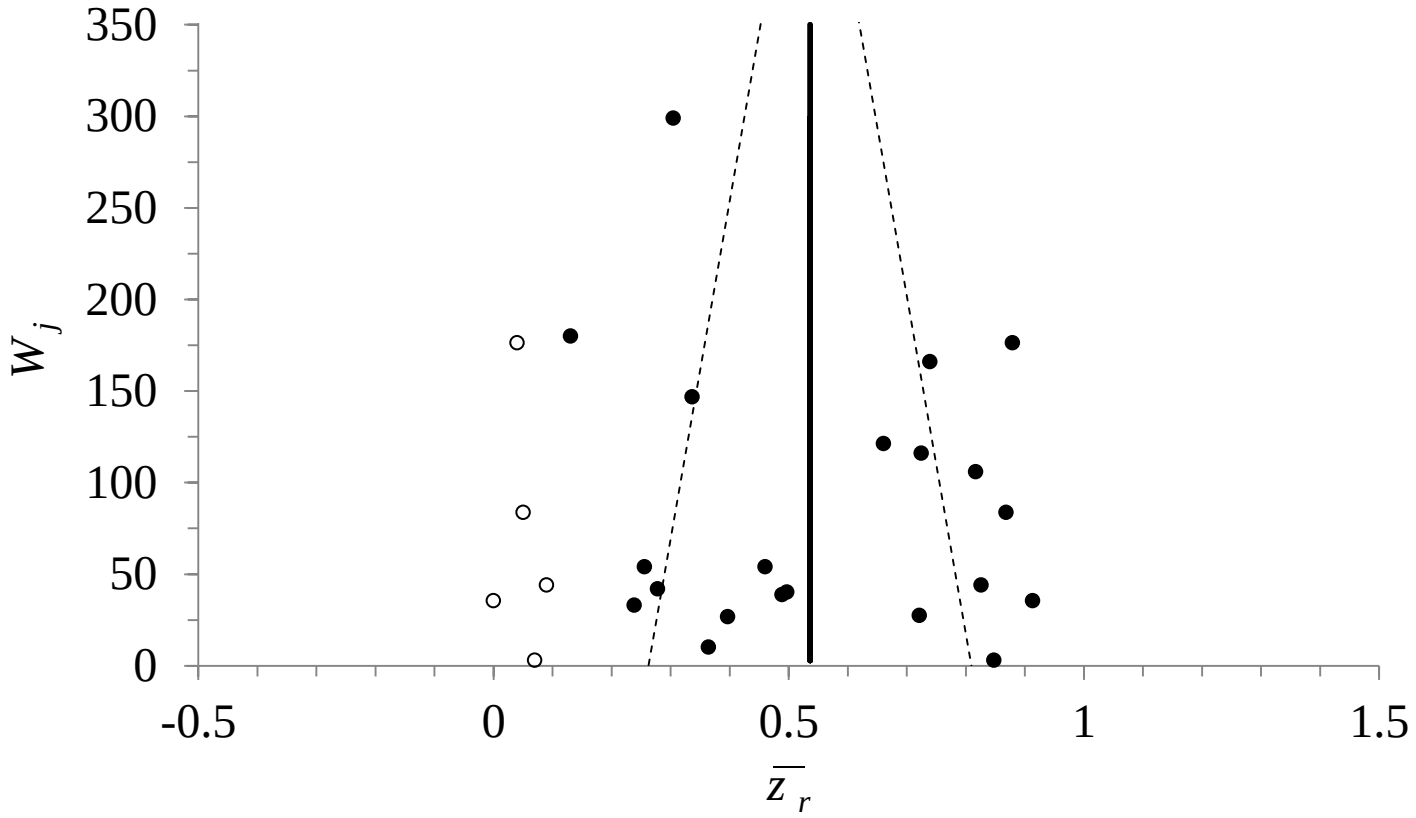
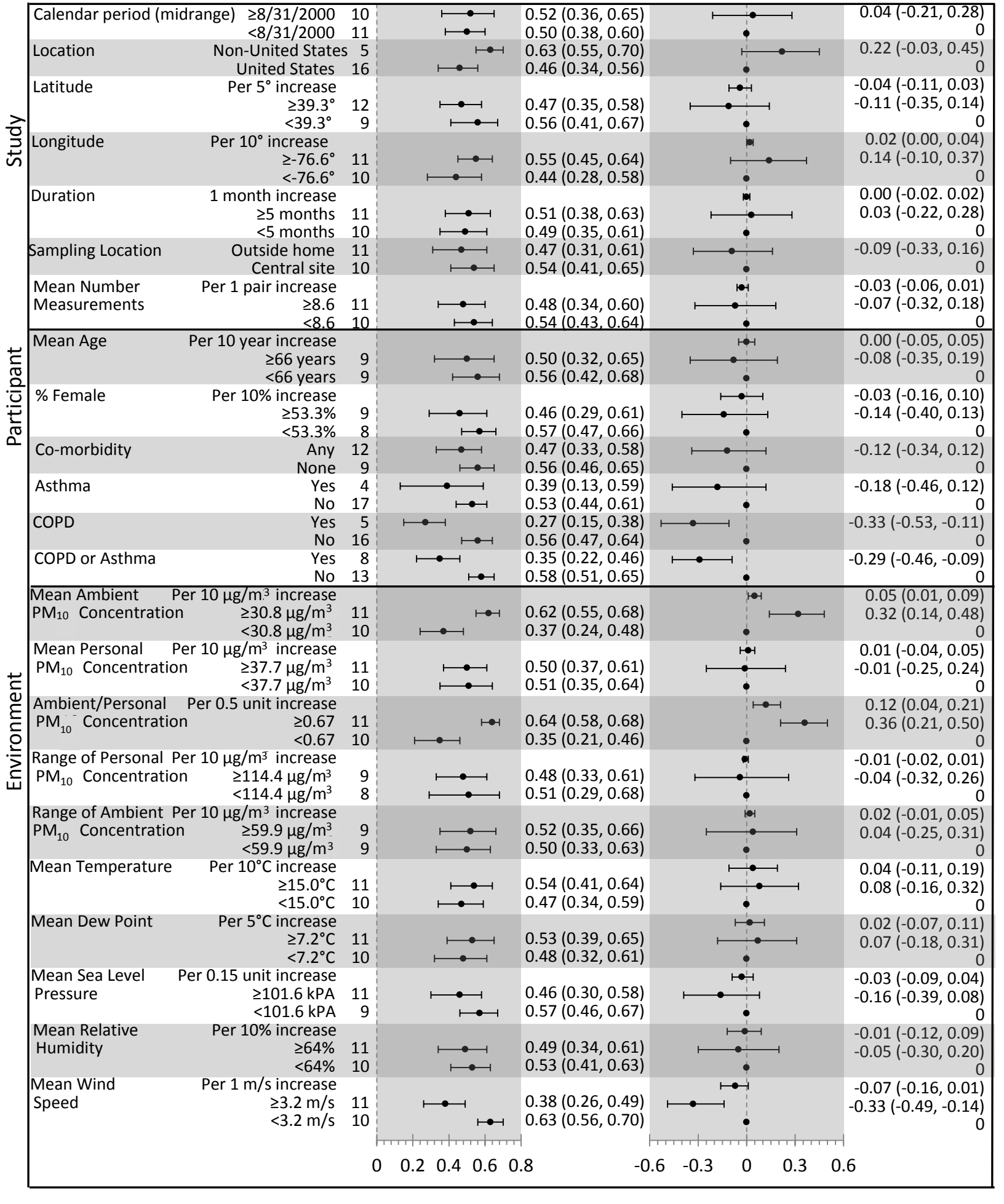

Lioy 1990
Wallace 1996
Janssen 1997
Janssen 1998
Linn 1999
Rojas-Bracho 2000
Sarnat 2000 1
Sarnat 2000 2
Wheeler 2000
Rodes 2001
Yip 2004
Watchalayann 2005
Williams 2008
Arhami 2009 1
Arhami 2009 2
Arhami 2009 3
Arhami 2009 4
Scapellato 2009
Hsu 2009 1
Hsu 2009 2
Hsu 2009 3
-0.3
-0.1
0.1
0.3
0.5
0.7
0.9
r_j (95% Confidence Interval)

Figure 2.



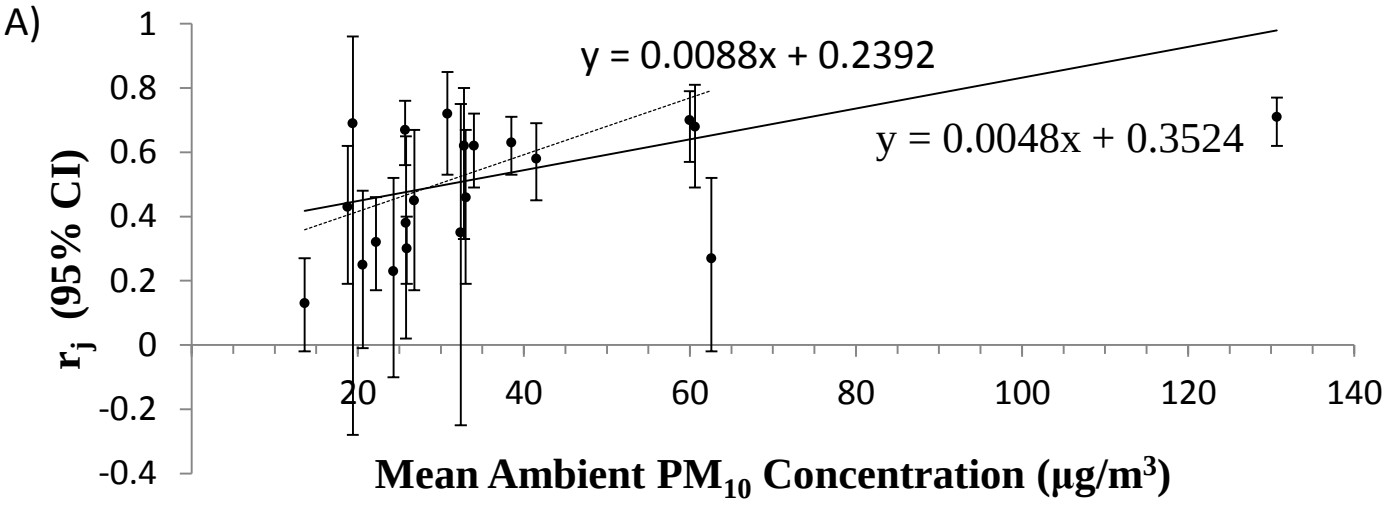
Figure

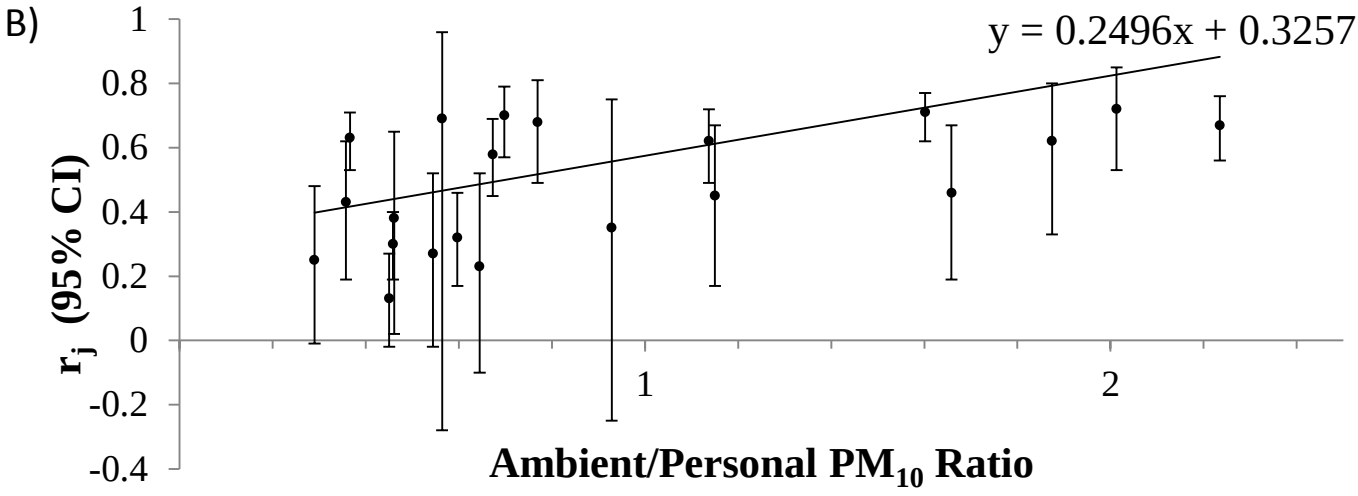
Figure 3.

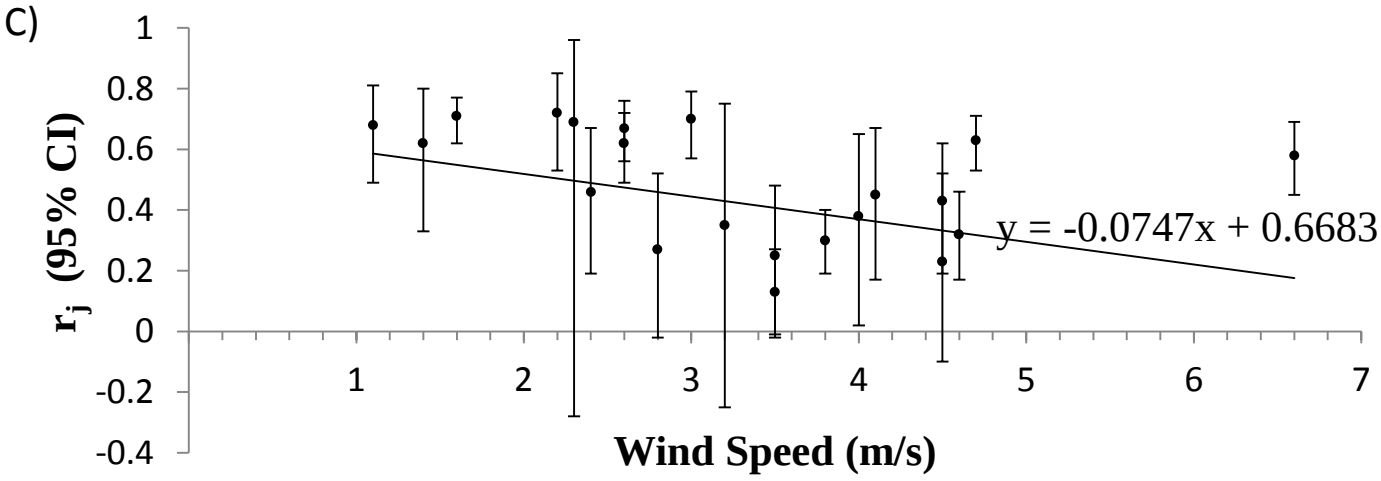


Figure

Figure 4.







Supplemental Material

Title: Using Meta-analysis to Inform Interpolation of Personal from Ambient Particulate Matter Exposures and Clarify Effects of Measurement Error

Authors: Katelyn M Holliday, Christy L Avery, Charles Poole, Kathleen McGraw, Ronald Williams, Duanping Liao, Richard L Smith, and Eric A Whitsel

Table of Contents

eAppendix 1.

Databases
PubMed (1950 to October 2009)
Web of Science (1955 to October 2009 via ISI Web of Knowledge)
BIOSIS Previews (1969 to October 2009 via ISI Web of Knowledge)
EMBASE (1988 to 2009 Week 43 via OvidSP)
Environmental Sciences and Pollution Management (1967 to October 2009 via CSA Illumina)
Toxline (1965 to October 2009 via TOXNET)
Dissertations and Theses (1861 to October 2009 via Proquest)

Search Strategy
((coarse[tw] OR respirable[tw] OR inhalable[tw] OR thoracic[tw]) AND
(particle* OR particulate* OR dust[tw]) OR pm 10[tw] OR pm10[tw]) AND
(ambient[tw] OR outdoor[tw] OR outdoors[tw] OR outside[tw] OR exterior[tw] OR external[tw] OR background[tw] OR fixed site*) AND
(longitudinal[tw] OR individual[tw] OR within person[tw] OR within persons[tw] OR personal[tw]) AND
(correlat* OR associat* OR relat* OR compar* OR pearson[tw] OR spearman[tw]))

eTable 1. Study Characteristics

Author, Year	Sub-Study	Location		Date		Duration (months)
		City	State/ Country	Start	End	
Lioy 1990		Phillipsburg	New Jersey	1/8/1988	1/22/1988	0.5
Wallace 1996		Azusa	California	3/6/1989	3/13/1989	0.3
Janssen 1997		Wageningen and Amsterdam	Netherlands	2/16/1994	5/18/1995	15.0
Janssen 1998		Amsterdam	Netherlands	1/17/1994	12/23/1994	11.2
Linn 1999		Los Angeles	California	10/24/1996	2/17/1997	3.8
Rojas-Bracho 2000		Boston	Massachusetts	2/5/1996	2/22/1997	12.6
Sarnat 2000	1	Baltimore	Maryland	6/29/1998	8/7/1998	1.3
	2	Baltimore	Maryland	2/2/1999	3/13/1999	1.3
Wheeler 2000		London	England	1/1997	9/1997	9.0
Rodes 2001		Fresno	California	4/18/1999	5/15/1999	0.9
Yip 2004		Detroit	Michigan	2/12/2000	10/6/2001	19.8
Watchalayann 2005		Bangkok	Thailand	12/2002	8/2003	9.0
Williams 2008		central	North Carolina	4/2004	6/2004	3.0
Arhami 2009	1	San Gabriel Valley	California	7/6/2005	12/10/2005	5.2
	2	San Gabriel Valley	California	8/24/2005	2/18/2006	5.9
	3	San Gabriel Valley	California	7/5/2006	12/1/2006	4.9
	4	Riverside	California	8/23/2006	2/16/2007	5.8
Scapellato 2009		Padova	Italy	6/21/2004	3/20/2006	21.0
Hsu 2009	1	New York	New York	07/2000	10/2000	4.0
	2	New York	New York	11/2000	1/2001	3.0
	3	Seattle	Washington	11/2002	03/2003	5.0
1990-2009[a]	21	19	12	1988-2007		5

[a]Summary statistics: ranges (year, date), counts (sub-study, location), median (duration)

eTable 2. Participant Characteristics

Author	Sub-Study	n	Mean Age	%Female	Co-Morbidity
Lioy 1990		14	46.5	57.1	N
Wallace 1996		10	34.1	30	N
Janssen 1997		45	10	53.3	N
Janssen 1998		37	62	51.4	N
Linn 1999[14]		14	70[d]	53.3	P
Rojas-Bracho 2000		17	NR	NR	P
Sarnat 2000 [a]	1	14	75	60	N
	2	14	75	60	N
Wheeler 2000		10	10	30	N
Rodes 2001		14	85	68	N
Yip 2004		20	9[d]	68	A
Watchalayann 2005		28	47.5[d]	NR	N
Williams 2008		3	41	67	A
Arhami 2009	1	17	84	41	C
	2	14	84	41	C
	3	17	84	41	C
	4	18	84	41	C
Scapellato 2009		21	29[e]	48.4	A
Hsu 2009[c]	1	9	Elderly	NC	P
	2	9	Elderly	NC	P
	3	15	75.5	53.3	P, A
1990-2009[f]	21	342[g]	66 (9-85)	53.3	43% N, 24% P, 19% A, 19% C

Abbreviations: n, number of participants; NR, not reported; NC, not collected; N, none; P, chronic obstructive pulmonary disease; A, asthma; C, coronary artery disease

[a] Includes 9 overlapping participants in the two sub-studies, [b] Includes 4 sub-studies of independent participants, [c] Includes 9 overlapping participants in the two NY sub-studies, [d] Median of range, [e] Median of inclusion criteria age range, [f] Summary Statistics: range (year, age), counts (sub-studies), totals (n), median (age, percent female), percent of studies (co-morbidities), [g] Number of independent participants

eTable 3. Environmental Characteristics

Author	Sub-Study	T (°C)	DP (°C)	SLP (kPa)	RH (%)	WS (m/s)	n	PM_{10} µg/m^3 Mean (SD)		r_j (95% CI)
								Personal	Ambient[a]	
Lioy 1990		-3.8	-9.6	102.3	64.0	3.0	12.9	86	60[a]	0.70 (0.57, 0.79)[c]
Wallace 1996		16.6	4.9	.	45.9	2.8	7.2	115	62.6 (3.5)	0.27 (-0.02, 0.52)
Janssen 1997		6.7	3.6	101.2	80.6	4.7	6.7	105.2 (28.7)	38.5 (5.6)[a]	0.63 (0.53, 0.71)[c]
Janssen 1998		6.7	4.4	101.5	85.3	6.6	7.1	61.7 (18.3)	41.5 (4.3)[a]	0.58 (0.45, 0.69)[c]
Linn 1999		15.0	7.2	101.8	59.6	3.2	4.0	34.9 (15.1)	32.4 (12.9)[a]	0.35 (-0.25, 0.75)[c]
Rojas-Bracho 2000		13.6	7.8	101.5	68.0	4.6	12.8	37.2 (22.8)	22.2 (18.7)	0.32 (0.17, 0.46)
Sarnat 2000	1	25.1	17.5	101.6	62.8	2.6	11.3	29.9(10.8)	34.0(12.8)[a]	0.62 (0.49, 0.72)
	2	3.4	-3.9	101.8	58.8	4.1	11.3	23.3(15.1)	26.8 (12.0)[a]	0.45 (0.17, 0.67)
Wheeler 2000		13.0	6.9	101.8	66.5	4.0	8.1	56.0 (31.8)	25.8 (20.9)	0.38 (0.02, 0.65)[c]
Rodes 2001[18, 19]		17.6	5.1	101.4	43.7	4.5	6.6	37.7 (14.7)	24.3 (5.9)[a]	0.23 (-0.10, 0.52)[c]
Yip 2004		13.2	7.4	101.8	67.9	3.8	18.0	56.5 (38.2)	25.9 (13.4)[a]	0.30 (0.19, 0.40)[c]
Watchalayann 2005		29.5	23.7	100.9	71.1	1.6	9.3	81.6 (14.3)	130.7(39.0)	0.71 (0.62, 0.77)[b]
Williams 2008		18.3	11.0	101.6	62.5	2.3	4.0	34.4 (7.5)	19.4 (8.0)[a]	0.69 (-0.28, 0.96)[c]
Arhami 2009	1	19.7	10.0	101.5	53.6	2.4	8.6	19.9 (15.6)	33.0 (11.0)	0.46 (0.19, 0.67)[c]
	2	17.1	7.3	101.5	52.5	1.4	8.0	17.5 (8.3)	32.8 (12.2)	0.62 (0.33, 0.80)[c]
	3	20.9	9.6	101.5	48.4	2.2	7.6	15.3 (6.7)	30.8 (13.2)	0.72 (0.53, 0.85)[c]
	4	18.7	5.9	101.5	43.1	2.6	8.9	11.5 (6.5)	25.7 (13.8)	0.67 (0.56, 0.76)[c]
Scapellato 2009		12.9	7.4	101.7	69.2	1.1	5.1	78.8	60.6[a]	0.68 (0.49, 0.81)[b]
Hsu 2009	1	18.5	13.2	101.7	71.3	3.5	12.0	71.1	20.6	0.25 (-0.01, 0.48)[b]
	2	1.9	-3.7	101.7	66.4	4.5	12.0	52.6	18.8	0.43 (0.19, 0.62)[b]
	3	7.9	4.7	101.7	80.2	3.5	12.0	30.2	13.6	0.13 (-0.02, 0.27)[b]
15 Studies, 1990-2009[d]	21	15.0	7.2	101.6	64.0	3.2	8.6	37.7	30.8	0.46

Abbreviations: T, mean temperature; DP, mean dew point; SLP, mean sea level pressure; RH, mean relative humidity; WS, mean wind speed; n, mean number of paired ambient-personal measurements per participant; SD, standard deviation; r, random-effects meta-analyzed summary correlation coefficient weighting individual correlation coefficients by number of measurements; CI, confidence interval

[a] Indicates ambient; otherwise outdoor

[b] Individual level data unavailable for random-effects meta-analysis; reported median used for r and fixed-effects used for SD

[c] Authors contacted for primary data; additional data for Lioy 1990 published in Wallace 1996 Table 12[13]

[d] Summary statistics: medians

eTable 4. Bivariable Meta-Regressions of the Relationship Between *r* and Selected Environment Characteristics

			r difference (95% CI)
Regression 1	Mean Ambient PM_{10}	≥30.8 μg/m^3 (n=11)	0.18 (-0.02, 0.37)
		<30.8 μg/m^3 (n=10)	0
	Ambient/Personal PM_{10}	≥0.67 (n=11)	0.28 (0.09, 0.37)
		<0.67 (n=10)	0
Regression 2	Mean Ambient PM_{10}	≥30.8 μg/m^3 (n=11)	0.21 (-0.01, 0.42)
		<30.8 μg/m^3 (n=10)	0
	Wind Speed	≥3.2 m/s (n=11)	-0.22 (-0.43, -0.003)
		<3.2 m/s (n=10)	0
Regression 3	Ambient/Personal PM_{10}	≥0.67 (n=11)	0.28 (0.04, 0.52)
		<0.67 (n=10)	0
	Wind Speed	≥3.2 m/s (n=11)	-0.15 (-0.39, 0.09)
		<3.2 m/s (n=10)	0