

Traffic-Related Outdoor Air Pollution and Respiratory Symptoms in Children

The Impact of Adjustment for Exposure Measurement Error

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Background: Outdoor concentrations of soot and nitrogen dioxide (NO₂) outside of schools have been associated with children's respiratory and eye symptoms. We assessed how adjustments for measurement error affect these associations.

Methods: Concentrations of air pollutants outside children's schools were validated by personal measurements of exposure to traffic-related air pollution. We estimated prevalence ratios of 4 health outcomes (current wheeze, conjunctivitis, phlegm, and elevated total serum immunoglobulin E) using school outdoor measurements, and then adjusted for measurement error using the personal exposure data and applying a regression calibration method. The analysis adjusting for measurement error was carried out using a main study/external validation design.

Results: Adjusting for measurement error produced effect estimates related to soot and NO₂ that were 2 to 3 times higher than in the original study. The adjusted prevalence ratio for current phlegm was 5.3 (95% confidence interval = 1.2–23) for a 9.3 µg/m³ increase in soot, and 3.8 (1.0–14), for a 17.6 µg/m³ increase in NO₂, compared with the original results of 2.2 (1.3–3.9) and 1.8 (1.1–2.8), respectively. Corrections were of similar magnitude for the prevalence of current wheeze, current conjunctivitis, and total elevated total immunoglobulin E.

Conclusions: The estimated effects of outdoor air pollution on respiratory and other health effects in children may be substantially

attenuated when based on exposure measurements outside schools instead of personal exposure.

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Adverse effects of air pollution on cardio-respiratory health are well established.¹ Pollutants of particular interest currently include particulate matter, ozone and nitrogen dioxide (NO₂).^{1,2} From a public health point of view, effects related to long-term average exposure to air pollution are of the greatest interest. In the last decade, epidemiologic studies have shown associations between small-scale variations in exposure to traffic-related air pollution and prevalence of respiratory symptoms in both children^{3,4} and adults.^{5,6} Other studies found increased cardiopulmonary mortality rates related to small-scale variations in traffic-related air pollution.^{7–9}

The requirements of personal monitoring make it difficult to measure long-term average personal exposure to traffic-related air pollution, especially particulate matter. Therefore, most studies have used surrogates of exposure such as concentrations in outdoor air measured at relevant sites (eg, the school), or dispersion or land-use regression models.¹⁰ Distance to major roads or the traffic intensity on the residential road have also been used as surrogates.¹⁰ However, outdoor surrogates have notable shortcomings. People spend a large percentage of their time indoors, they live at locations with varying traffic intensity, they live in homes that differ in indoor pollution sources and air exchange rates (affecting penetration of outdoor air into the home) and they have varying activity patterns. All these factors contribute to differences between outdoor air concentrations and personal exposure. An obvious question, therefore, is how representative these outdoor concentrations are for “true” personal exposure. Other researchers have raised concerns about the use of ambient concentrations of PM_{2.5}, elemental carbon and NO₂ as surrogates for personal exposure, since they do not always seem to reflect personal exposure.^{11–14}

We explore the effect of adjusting for exposure measurement error in a study of outdoor levels of air pollutants and chronic respiratory symptoms and other health outcomes

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in school children.³ We earlier reported associations between annual average outdoor air pollution concentrations measured at schools near major freeways of varying traffic intensity and prevalence of wheeze, conjunctivitis, phlegm and elevated total serum immunoglobulin E (IgE) in children attending those schools. Validation studies had been performed nested in the main study¹⁵ and externally.¹⁶ We used statistical methods to adjust for exposure measurement error, using the regression calibration method.^{17–19}

METHODS

Study Overview

In the measurement error analysis, we considered the school outdoor concentrations of an air pollutant to be the surrogate exposure, and the personal exposure to be the true exposure. We previously developed a regression calibration method for correcting systematic and random error in the original odds ratios (ORs) and corresponding confidence intervals (CIs) estimates using a regression model.^{17,18} This method was later generalized to estimate risk ratios (RRs) and prevalence ratios (PRs).¹⁹ The method requires a main study with data on health outcome, surrogate exposure and confounding covariates, and a validation study that assesses true exposure, surrogate exposure and confounding covariates. This paper describes the application of 2 external validation studies, 1 measuring soot and 1 measuring NO₂. The main study consists of epidemiologic data from Janssen et al.³ The NO₂ validation study consists of data including personal NO₂ measurements from Rijnders et al.¹⁵ The soot validation study consists of data with personal soot measurements from Van Roosbroeck et al.¹⁶

Background of the Studies

The main study is an epidemiologic study that examined respiratory health of 2083 children from 24 schools located within 400 m of freeways in the Netherlands.³ Respiratory symptoms were collected by a questionnaire designed by the International Study of Asthma and Allergies in Childhood. Details are described elsewhere.²⁰ Data included traffic-related characteristics such as traffic intensities and distance to a major road. Outdoor measurements of soot and NO₂ were conducted at all 24 schools between April 1997 and July 1998. Annual average concentrations of soot and NO₂ outside all schools were calculated as described in detail by Janssen et al.²¹

The first validation study was nested in the main study, with personal and school outdoor NO₂ concentrations measured in 110 schoolchildren from 3 of the 24 schools.¹⁵ The average personal NO₂ concentration was based on from one to four 1-week measurements in each of the 4 seasons. The average outdoor concentrations were measured in the same weeks. All measurements were performed using Palmes diffusion tubes that could either be attached to the back side of

a home (using a specially-designed device for the outdoor measurement) or be attached to a badge worn between breast and head for personal measurements. Details on the sampling methods are described elsewhere.¹⁵ Since participants were also in the main study, the same health outcome and confounder information was available.

The second validation study was conducted 6 years later. We collected personal soot measurements in Dutch school children using flow-controlled battery-operated pumps in a made-to-fit backpack.¹⁶ From March to June 2003, personal monitoring of soot was performed during four 48-hour periods in 54 school children aged 10 to 12 years. The children were recruited from 4 schools in Utrecht with varying proximity to busy roads. Outdoor measurements at the school location were performed concurrently with the personal measurements using the same sampling device. All pollutant concentrations from the original exposure study were averaged per child and then standardized for background concentrations according to Janssen's method.²¹ Further details on the sampling methods are described elsewhere.²²

Both validation studies reported absolute differences in personal exposure between children classified as high and low exposed according to outdoor characteristics. For the purpose of this paper, we calculated the correlation between individual average personal and outdoor exposures.

Data Analysis

In the main study, the sample sizes vary by health outcome. Information on respiratory symptoms was collected by a parent-completed questionnaire for 2083 schoolchildren. Total IgE was determined for a subgroup of 881 school children. Some information on covariates and health outcomes were missing and could therefore not be included in the measurement error analysis. This again resulted in a smaller study population than the original study. Sample sizes for current wheeze, current conjunctivitis, and current phlegm were 1862, 1871, and 1843, respectively. Sample size was 774 for total IgE.

In the validation studies, only those children with 3 or 4 repeated measurements and no missing data on the confounding covariate information were included in the analysis, leaving 67 participants in the NO₂ validation study and 45 in the soot validation study. Since the group of children selected for the personal NO₂ measurements was drawn from the 2083 children and not from the 881, some information on covariates and health outcomes were missing in the validation dataset. Thus, sample size was smaller when looking at total elevated IgE in the NO₂ validation study ($n = 43$).

Rosner et al's¹⁸ regression calibration method uses a 3-step procedure to adjust point and interval estimates for bias due to exposure measurement error. First, the unadjusted point estimates and their variances are obtained by fitting the standard regression model in the main study (here, a log-binomial model). We used log-binomial models to directly

estimate the PR rather than the prevalence OR, which fails as an approximation of the parameter of interest when the disease is not rare.^{23,24} The log-binomial model has the form $\Pr(D = 1 | E, \mathbf{C}) = e^{\beta_0 + \beta_1 E + \beta_2' \mathbf{C}}$, where, for example, when the outcome of interest is wheeze and the exposure of interest is NO₂, $D = 1$ if the child reported wheeze and 0 otherwise, E = personal exposure to NO₂ ($\mu\text{g}/\text{m}^3$), $\mathbf{C}$ is the vector of confounders: parental smoking, gas cooking, presence of an unvented water heater, sex, age (years), and current pet possession, and

$\Pr(D = 1 | E + \Delta, \mathbf{C}) = e^{\beta_1 \Delta}$, where Δ is a scientifically meaningful increment in the exposure of interest. For example, when E equals personal exposure to NO₂ ($\mu\text{g}/\text{m}^3$), then Δ equals 17.6 $\mu\text{g}/\text{m}^3$, corresponding to the difference between the highest and lowest exposed schools.³ Similarly, a contrast of 9.3 $\mu\text{g}/\text{m}^3$ was used for black smoke.

In the validation study, the measurement-error-model parameters are estimated by regressing the true exposure on the surrogate exposure and all other covariates included in the primary regression model, following the standard linear model $E = \gamma_0 + \gamma_1 X + \gamma_2' \mathbf{C} + \varepsilon$, where X_i is the validation study subject's surrogate exposure value and ε is a random error term. In our study, both E and X are arithmetic means of all available measurements within validation study participant. Finally, the estimates are adjusted for measurement error by combining these 2 sets of estimates and their variance-covariances. In order for this method to be valid, we need to verify that the assumptions associated with it are applicable to the data at hand. These assumptions include^{18,25}: (1) the measurement error model is linear and homoscedastic; (2) the main study model is linear on the assumed scale (here, the log scale); (3) measurement error is not severe; and (4) the surrogate exposure contains no further information about the distribution of disease once data on the true exposure are available.

To assess the validity of the first assumption concerning the linearity of measurement error model (here, the linear relationship between personal exposure to soot and NO₂, with their corresponding surrogates) we fit stepwise restricted cubic splines.²⁶ We use an SAS macro²⁷ developed for this purpose. This macro compares the linear measurement error models to models with a step-wise 17-knot restricted cubic spline function to flexibly assess any nonlinearity in the relationship. There was no evidence for nonlinearity in either measurement error model.²⁸

Homoscedasticity of the measurement error models was assessed by computing the correlation between the predicted values and the absolute values of residuals of the linear measurement error models. For soot, the Pearson correlation coefficient was 0.09, indicating no violation of this assumption. For NO₂, the correlation was 0.34, which suggested some heteroscedasticity. However, there is evidence suggesting that the standard linear regression calibration gives a good

approximation, nevertheless.^{29–31} Although there was evidence of some heteroscedasticity of the measurement error model for NO₂, it is unlikely to detract appreciably from the validity of the adjusted results.

To assess the validity of the second assumption, concerning the (natural log) linearity of the relationship between the exposures (soot and NO₂) and the 4 outcomes, we again fit large stepwise restriction cubic-spline models; none of the 8 models showed nonlinearity. The third assumption can be satisfied by a small measurement-error approximation, that is, if $\beta^2 \sigma^2$ is small (where β is the log relative risk for exposure obtained from the primary regression model in the main study, and σ^2 is the residual variance of the measurement error model fit in the validation study). For all the health outcomes, $\beta^2 \sigma^2$ was very small (ranging from 0.000005 to 0.0002), thus satisfying the assumption. The last assumption can be empirically verified only when the validation study includes outcome data with a sufficient number of cases. There were some outcome data in the NO₂ validation study only, although too few to verify the assumption. We note, however, that this assumption is biologically plausible in that ambient exposure (as measured by area monitoring) would not be expected to have any health effect once personal exposure is fully accounted for.

The validity of the regression-calibration method requires only that the measurements taken as the “true exposure” be an unbiased estimate of the truth, and that errors in the “true exposure” are uncorrelated with the errors in the surrogate.^{32–34} In nutritional epidemiology, the “true exposure” and the surrogate are both assessed by self-report, which raises doubts as to whether the errors can be assumed to be noncorrelated. In environmental health however, where the “true exposure” is an objective measure (and often, as here, so is the surrogate), the uncorrelated errors assumption is likely to be reasonable. We therefore accept this assumption as reasonable in the present application.

For this and most other methods for correction of measurement-error bias to be valid, we must assume that the form and relevant parameters of the measurement error model that generated the validation study are identical to those that generated the main study data. This can be ensured by an internal validation study design, as was the case for the validation of NO₂. The soot validation study was external to the main study—conducted 6 years later and in different schools. Since the exposure-assessment methods were the same as in the main study, there is no obvious reason to question the validation of the transportability assumption. However, this assumption cannot be empirically verified.

Diagnostics and statistical analyses were performed using S-plus (Insightful Corporation Seattle, WA) and SAS (Version 9; SAS Institute Inc., Cary, NC). The SAS macro for adjusting for measurement error used in this paper is publicly available and can be downloaded.²⁷ It is also available in an

electronic appendix that is available with electronic version of the article.

RESULTS

Table 1 presents traffic characteristics, air pollution concentrations of soot and NO₂, the prevalence of current wheeze, current conjunctivitis, current phlegm, and elevated total IgE, and other characteristics of main and validation-study participants. The prevalences of the 4 health outcomes were very similar in the NO₂ validation and main study. Traffic characteristics and covariate information were also comparable. The levels of outdoor NO₂ were similar in the main and validation studies. The levels of soot, however, were higher in the validation study. Spiegelman et al³⁵ show that the only compatibility assumption needed for validity of the regression-calibration method is that the measurement error model estimate be reasonably assured to be the one observed in the main study, had true exposure measurements been available.

Figure 1 shows the scatterplot of personal soot levels versus outdoor concentrations in the validation study. The correlation coefficient between the true and the surrogate exposure was 0.53. After adding all confounding covariates

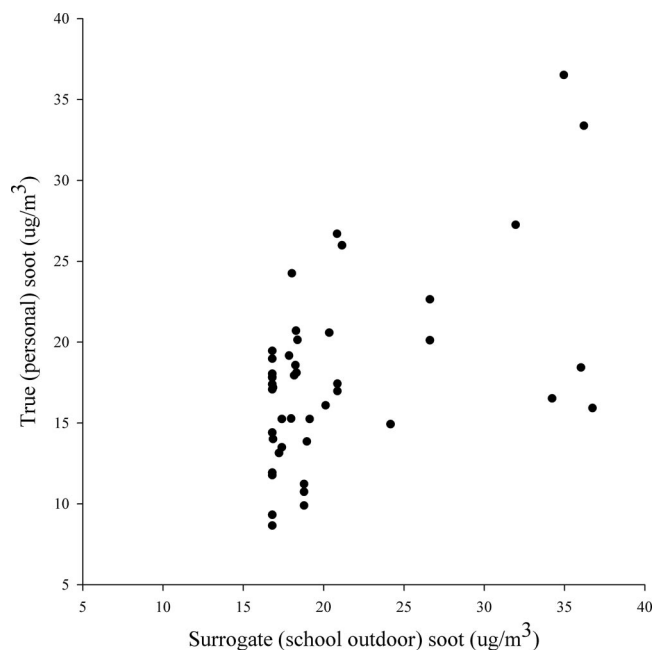


FIGURE 1. Scatter plot of average outdoor school soot versus personal soot exposure in the validation study ($n = 45$); $r = 0.53$.

TABLE 1. Basic Characteristics of the Main and Validation Study Participants

	Soot Validation Study ($n = 45$)	NO ₂ Validation Study ($n = 67$)	Main Study ($n = 1871$)
Traffic characteristics; mean (SD)			
Car traffic intensity near school (cars/24 h)	47,016 (26,598)	76,623 (38,065)	90,406 (34,457)
Truck traffic intensity near school (trucks/24 h)	3,948 (4,438)	12,852 (7,605)	12,806 (4,618)
Total traffic intensity near school (vehicles/24 h)	50,067 (30,936)	89,474 (45,387)	103,212 (35,995)
Distance from school to busy road (m)	193 (113)	202 (139)	221 (103)
Air pollution concentrations (ug/m ³) ^a ; mean (SD)			
Average school outdoor soot	20.8 (6.1)	NA	10.2 (2.1)
Average personal soot	17.8 (5.7)	NA	NA
Average school outdoor NO ₂	NA	37.4 (7.0)	34.5 (5.1)
Average personal NO ₂	NA	23.7 (9.3)	NA
Health outcomes; no. (%)			
Current wheeze	NA	6 (9)	176 (9)
Current conjunctivitis	NA	9 (14)	133 (7)
Current phlegm, no cold	NA	5 (8)	175 (9)
Elevated total IgE ^b	NA	12 (28)	315 (41)
Other characteristics			
Parental smoking in the home (yes); no. (%)	16 (36)	39 (58)	1080 (58)
Gas cooking (yes); no. (%)	25 (56)	52 (78)	1574 (84)
Unvented water heater in kitchen (yes); no. (%)	1 (2)	5 (7)	165 (9)
Sex (male); no. (%)	21 (47)	35 (52)	914 (49)
Age (yrs); mean (SD)	11 (0.8)	10 (0.9)	9 (1.6)
Current pet possession (yes); no. (%)	26 (58)	41 (61)	1113 (59)

^aAir pollution concentrations were standardized for background concentrations (following Janssen et al²¹). The average school outdoor concentrations for the main study are the average of 24 annual average school concentrations.

^bSample size for NO₂ validation and main study are 43 and 774, respectively, when looking at elevated total IgE as a health outcome.

NA indicates not available.

TABLE 2. Measurement Error Model for Average Personal Exposure to Soot ($\mu\text{g}/\text{m}^3$) ($n = 45$)

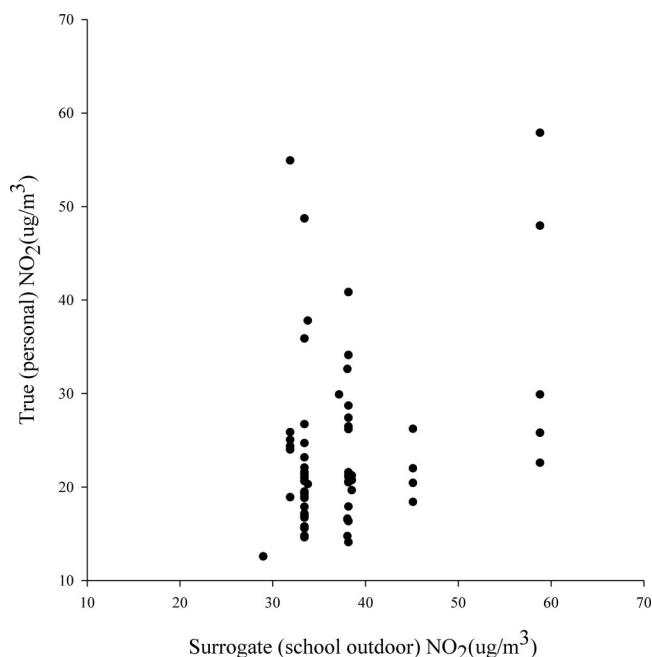
	$\hat{\gamma}$	$SE(\hat{\gamma})$	P
Intercept	13.16	12.48	0.30
Variable			
School outdoor soot ($\mu\text{g}/\text{m}^3$)	0.48	0.13	<0.001
Exposure to ETS (yes/no)	5.72	1.80	<0.01
Exposure to gas cooking (yes/no)	2.55	1.76	0.16
Presence of unvented water heater in the kitchen (yes/no)	-1.84	4.81	0.70
Sex (boy/girl)	0.19	1.42	0.89
Age (yr)	-0.80	1.01	0.43
Current pet possession (yes/no)	1.62	1.37	0.25

$\hat{\gamma}$ indicates regression slope; $SE(\hat{\gamma})$, standard error. For all categorical variables yes is coded as "1" and no as "0."

TABLE 3. Measurement Error Model for Personal Exposure to NO_2 ($\mu\text{g}/\text{m}^3$) ($n = 67$)

	$\hat{\gamma}$	$SE(\hat{\gamma})$	P
Intercept	6.67	8.95	0.46
Variable			
School outdoor NO_2 ($\mu\text{g}/\text{m}^3$)	0.42	0.11	<0.001
Exposure to ETS (yes/no)	1.94	1.69	0.26
Exposure to gas cooking (yes/no)	2.53	1.85	0.18
Presence of unvented water heater in the kitchen (yes/no)	24.89	3.17	<0.0001
Sex (boy/girl)	-2.41	1.60	0.14
Age (yr)	-0.13	0.86	0.88
Current pet possession (yes/no)	-1.92	1.63	0.24

$\hat{\gamma}$ indicates regression slope; $SE(\hat{\gamma})$, standard error. For all categorical variables yes is coded as "1" and no as "0."

**FIGURE 2.** Scatter plot of average outdoor school NO_2 versus personal NO_2 exposure in the validation study ($n = 67$); $r = 0.35$.

in the main study regression model (exposure to parental smoking, gas cooking, presence of an unvented water heater in the kitchen, sex, age, and current pet possession) to the measurement error model, the multiple correlation coefficient increased to 0.71 (Table 2). This suggests that school outdoor concentration provides a reasonably accurate estimate of personal exposure to soot when we include covariate information on lifestyle and possible indoor sources. The correlation coefficient of the true-versus-surrogate exposure was considerably lower for NO_2 (0.35) (Fig. 2). However, including the main-study-model covariates in the measurement error model increased the multiple correlation coefficient to 0.77 (Table 3).

This indicates the important contribution of indoor sources in the home to the total personal NO_2 exposure.

PRs for the associations between soot exposure and various health outcomes are shown before and after adjustment for measurement error (Table 4). The PR for current wheeze was 1.45 before adjustment (95% CI = 0.80–2.61), and 2.15 after adjustment (0.59–7.74). Effects of adjustment were somewhat larger for current conjunctivitis, current phlegm and elevated total IgE (Table 4). The larger CIs reflect the small sample size of the validation study, as well as the increased estimate of uncertainty due to the magnitude of the measurement error observed.

Table 5 presents the results of error adjustment for NO_2 exposure. The adjusted PRs expressed for a $17.6 \mu\text{g}/\text{m}^3$ difference in NO_2 , were about double the unadjusted PR for wheeze, phlegm and total elevated IgE (Table 5). For conjunctivitis, adjustment increased the prevalence 3-fold for a $17.6 \mu\text{g}/\text{m}^3$ -increment in NO_2 .

It was not possible to adjust for the same confounders, as in Janssen et al.'s³ original analysis. First, not all covariates were available in the validation studies. Second, because the number of observations is much smaller in both validation studies, not as many variables can be included in regression models. In regression calibration, covariates in the primary regression model are supposed to be included in the measurement error model unless uncorrelated with both the true exposure and the measurement error. This is because the estimated effects of these perfectly-measured covariates pick up some of the effect of the true exposure in the primary regression model on the surrogate.^{18,36} However, the ORs, adjusted for the more limited set of confounders given in the footnotes to Tables 4 and 5, corresponded well with the ORs from the original analysis.³

Since the NO_2 validation study was nested in the original validation study, full health outcome data was available for the validation study participants and, as a result, these

TABLE 4. Association Between Exposure to Soot ($\mu\text{g}/\text{m}^3$) and Selected Health Outcomes

	Current Wheeze PR (95% CI)	Current Conjunctivitis PR (95% CI)	Current Phlegm PR (95% CI)	Elevated Total IgE PR (95% CI)
Unadjusted	1.45 (0.80–2.61)	2.18 (1.13–4.21)	2.24 (1.27–3.93)	1.69 (1.21–2.36)
Adjusted	2.15 (0.59–7.74)	5.06 (1.02–24.96)	5.29 (1.24–22.62)	2.98 (1.22–7.26)

Prevalence ratios are calculated for the main study/external validation study design and expressed for a $9.3 \mu\text{g}/\text{m}^3$ difference, the difference between the highest and lowest exposed schools in the original study.³ Adjusted for exposure to parental smoking, gas cooking, presence of an unvented water heater in the kitchen, sex, age, and current pet possession.

TABLE 5. Association Between Exposure to NO_2 ($\mu\text{g}/\text{m}^3$) and Selected Health Outcomes

	Current Wheeze PR (95% CI)	Current Conjunctivitis PR (95% CI)	Current Phlegm PR (95% CI)	Elevated Total IgE PR (95% CI)
Unadjusted	1.58 (0.99–2.51)	2.22 (1.31–3.76)	1.76 (1.10–2.81)	1.83 (1.39–2.42)
Adjusted	2.94 (0.85–10.18)	6.60 (1.33–32.77)	3.82 (1.03–14.21)	4.20 (1.54–11.48)

Prevalence ratios are calculated for the main study/external validation study design and expressed for a $17.6 \mu\text{g}/\text{m}^3$ difference, the difference between the highest and lowest exposed schools in the original study.³ Adjusted for exposure to parental smoking, gas cooking, presence of an unvented water heater in the kitchen, sex, age, and current pet possession.

data could be employed in an internal validation study following methods developed by Spiegelman et al.³⁵ However, the validation study was too small to provide reliable estimates of PRs for the 4 health outcomes. In view of the technical complexities of obtaining long-term measures of personal exposures, the possibilities for adequately-powered internal validation studies likely will remain limited.

DISCUSSION

We used the regression-calibration method to explore the impact of adjustment for errors in the measurement of outdoor air pollution, when using outdoor measurements as a surrogate for personal exposure. The effects of air pollution on health and points, adjusted for measurement error, were substantially higher than previously reported. This shows the attenuation of risk when using school outdoor concentrations instead of personal exposure measurements.

This analysis uses health outcome data from over 2000 children from the main study (in which personal exposure had not been directly measured) to obtain a single quantitative estimate of the effect of personal exposure to soot and NO_2 on health outcomes. There is some loss of power in the adjusted analysis (as evident in the broader CIs). From a statistical point of view, the adjusted CIs reflect the true power in the study for an approximately unbiased result, in contrast to the original analysis, which gives a biased CI around a biased point estimate.

Information on potential confounders was not the same in the full study as in the external validation study. However, recalculation of ORs in the main study with the more limited set of confounders available in the external validation study

produced nearly identical results. In our tables, comparisons are always between effect estimates calculated using exactly the same set of potential confounders.

This is the first application of a measurement-error adjustment in a study on the health effects of soot or NO_2 using measurements of personal exposure. Li et al³⁷ presented a measurement-error-corrected estimate for the effect of indoor NO_2 exposure on respiratory symptoms in subjects where exposure was not directly measured but information on NO_2 sources and residential characteristics was available. The measurement-error-corrected estimate (OR = 1.60; 95% CI = 1.10–2.32) was similar to that from the validation study (1.41; 1.13–1.75) which included direct measurements of indoor NO_2 and health outcome information. Horick et al¹⁹ applied the same measurement-error adjustment method to measures of airborne and house-dust endotoxin showing a large impact on the point estimate of effect (adjusted RR = 5.56; 95% CI = 1.19–26.03) compared with unadjusted RR = 1.45 (1.20–1.76). CIs increased substantially, as in the current study. Correlations between personal and outdoor measurements in the present study were higher than correlations between living-room airborne and living-room floor dust endotoxin in the Horick study, leading to smaller corrections in our study.

The impact of adjustment for measurement error was approximately the same for NO_2 and soot. A critical assumption in the adjustments is that personal-exposure measurements reflect the true biologically relevant exposure. This is probably less true for NO_2 than for soot. First, NO_2 is generally not considered to be an important causal component of traffic-related air pollution, but rather a convenient indi-

cator of traffic pollutants. In contrast, soot probably represents a causal agent in diesel exhaust.^{38–40} Second, indoor sources make important contributions to personal NO₂ exposure. Although we adjusted for indoor sources in the measurement error model, it is not possible to estimate these separate effects in an unbiased manner without additional measurements that separate indoor sources from outdoor.¹⁸ Indoor sources are less important for soot, as evidenced by the smaller change in the multiple correlation after adding indoor source indicators to the surrogate exposure in the measurement error model. Third, the personal NO₂ concentrations were considerably lower than ambient concentrations in the NO₂ validation study. This is because NO₂ is reactive; indoor concentrations are lower because the NO₂ dissipates rapidly even when indoor sources are present. In contrast, soot penetrates easily into indoor environments and has only limited sinks, resulting in indoor concentrations that are typically 60%–70% of the outdoor concentration in the absence of indoor sources. We argue that the unadjusted risk estimates were underestimated; however, it is also likely that our adjustments for NO₂ measurement error were overestimated.

Clearly, correlations between personal and school outdoor measurements depended on the design of the study, which sought to maximize exposure contrasts. Results can therefore not be extrapolated to situations with different exposure contrasts.

In contrast to the endotoxin study reported by Horick et al¹⁹ and the NO₂ study reported by Li et al,³⁷ the exposure estimations in the current study are likely to be subject to both Berkson and classic measurement error. In the endotoxin and NO₂ studies, as well as in the current analysis, error of the classic type was introduced because the measured exposure, repeated or not, was likely to vary around the true exposure. In addition, in the current analysis, a school's average was assigned to each participating child attending that school and, accordingly, error of the Berkson type was introduced. This latter error creates little bias in risk estimates compared with the classic error, which was found to have more serious consequences.⁴¹ The regression method used in the current work handles both types of error separately or in combination.^{42(pp52–57,67)}

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