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Original Contribution

Relation between Concentration of Air Pollution and Cause-Specific Mortality: Four-Year Exposures to Nitrogen Dioxide and Particulate Matter Pollutants in 470 Neighborhoods in Oslo, Norway

Øyvind Næss[1,2], Per Nafstad[1,2], Geir Aamodt[2], Bjørgulf Claussen[1], and Pål Rosland[3]

[1] Institute of General Practice and Community Medicine, University of Oslo, Oslo, Norway.
[2] National Institute of Public Health, Oslo, Norway.
[3] Norwegian Public Road Administration, Oslo, Norway.

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This study investigated the concentration-response relation between air pollution (nitrogen dioxide and particulate matter pollutants PM_{10} and $PM_{2.5}$) and cause-specific mortality. The population included all inhabitants of Oslo, Norway, aged 51–90 years on January 1, 1992 ($n = 143,842$) with follow-up of deaths from 1992 to 1998. An air dispersion model (AirQUIS; Norwegian Institute for Air Research (NILU), Oslo, Norway) was used to estimate levels of exposure in 1992–1995 in all 470 administrative neighborhoods. These data were linked to census, education, and death registries. A consistent effect on all causes of death was found for both sexes and age groups by all indicators of air pollution. The effects appeared to increase at nitrogen dioxide levels higher than 40 $\mu g/m^3$ in the youngest age group and with a linear effect in the interval 20–60 $\mu g/m^3$ for the oldest. An effect of all indicators on cardiovascular causes, lung cancer, and chronic obstructive pulmonary disease was also found in both age groups and sexes. The effects were particularly strong for chronic obstructive pulmonary disease, which appeared to have linear effects, whereas cardiovascular causes and lung cancer seemed to have threshold effects. Results show that vulnerable persons with chronic obstructive pulmonary disease and the elderly seem to be susceptible to air pollution at lower levels than the general population.

air pollution; cardiovascular diseases; cause of death; lung neoplasms; mortality; pulmonary disease, chronic obstructive

Abbreviations: COPD, chronic obstructive pulmonary disease; NO_2, nitrogen dioxide; $PM_{2.5}$, particulate matter less than 2.5 μm in aerodynamic diameter; PM_{10}, particulate matter less than 10 μm in aerodynamic diameter.

Most evidence on the potential effect of air pollution on mortality risk has been based on results from time-series analyses (1, 2), while rather few cohort studies have been conducted (3–5). These studies have mostly included exposure data at the aggregate level, where exposure is based on rather crude measurements. All participants living in the same city were assigned similar levels of exposure in the studies by Dockery et al. (3) and Pope et al. (5). Assessing air pollution exposure by using community average concentrations is likely to underestimate the elevated risk for people who live in neighborhoods with high levels (6, 7). Such misclassification may reduce the chance to identify increased risk for particularly vulnerable subgroups of the population, such as those with chronic obstructive pulmonary disease (COPD). Earlier studies have mainly pooled outcome measures into cardiopulmonary causes to obtain a sufficient sample size to detect an effect, and they have not been able to single out concentration-response associations for specific disease outcomes. Susceptibility to air pollution may differ for various causes of death and in different age groups.

Correspondence to Dr. Øyvind Næss, Institute of General Practice and Community Medicine, University of Oslo, P.O. Box 1130 Blindern, 1130 Blindern Oslo 0318, Norway (e-mail: medisin.uio.no).

This study analyzed the effect of air pollution (nitrogen dioxide (NO_2) as well as particulate matter less than 10 μm in aerodynamic diameter (PM_{10}) and particulate matter less than 2.5 μm in aerodynamic diameter ($PM_{2.5}$)) on cause-specific mortality in a population-wide sample in Oslo, Norway, based on a short-term causal model. The study aimed particularly to address the thresholds for different causes of death, and it took advantage of a large, population-wide sample to study this issue in more detail.

MATERIALS AND METHODS

Population

A cohort of all inhabitants in the age groups 51–70 and 71–90 years who lived in the municipality of Oslo in 1992 was chosen as the study population (8, 9). A total of 143,842 individuals were identified as the source population. For all of these persons, information on neighborhood code and data regarding exposure to air pollutants was available and was included in the analysis. Covariates (occupational class and education) were available for 77 percent of these persons and were treated as missing at random in the adjusted analysis. Data were obtained by linking census information from 1980 and from the education and the death registries, facilitated by the Norwegian identity code and provided by Statistics Norway.

Causes of death

Deaths were recorded in the period 1992–1998. All death certificates are registered with Statistics Norway, with no missing cases. They were coded according to *International Classification of Diseases*, Ninth Revision (ICD-9) until 1996 and *International Statistical Classification of Diseases and Related Health Problems* (ICD-10) onward (codes in ascending order), as follows: lung cancer (ICD-9: 162, ICD-10: C34), chronic obstructive pulmonary disease/COPD (ICD-9: 490–496, ICD-10: J40–J47), and cardiovascular causes (ICD-9: 390–459, ICD-10: I00–I119).

Exposure assessment

The Norwegian Institute for Air Research (NILU) has calculated concentrations (in micrograms per meter cubed) of air pollutants such as NO_2 and PM_{10} and $PM_{2.5}$ with the AirQUIS air dispersion model system (NILU, Oslo, Norway (www.nilu.no/airquis)) in 470 neighborhoods in the city of Oslo for 1992–1995 (10–12). Concentrations were calculated hourly by using hourly emissions and meteorologic data for the period. In Oslo, the major sources of air pollution from the above-mentioned compounds during the period were car traffic, road dust, wood burning, and long-range transport by trucks (mainly for $PM_{2.5}$ and PM_{10}).

The hourly averaged concentration values for each neighborhood were calculated as a weighted average of the concentration values determined for the building points within the neighborhood, using the number of inhabitants in each building as the weights. The resulting person-averaged concentration thus describes the expected level of air pollution to which a person in the neighborhood is potentially exposed.

The ability of the model to predict long-term levels has been evaluated and was found to be reliable in epidemiologic studies, giving somewhat better prediction for NO_2 and $PM_{2.5}$ than for PM_{10} (13). Daily average exposure values for each individual residing in any of the neighborhoods were calculated over the 4-year period 1992–1995 and were categorized into quartiles for each air pollutant. The mean value for NO_2 was 39 $\mu g/m^3$ (range, 2–73), for PM_{10} was 19 $\mu g/m^3$ (range, 7–30), and for $PM_{2.5}$ was 15 $\mu g/m^3$ (range, 7–22).

Covariates

Education was defined as the highest level of education obtained in 1990 derived from the education register of Statistics Norway. Length of education was ordered into two groups: primary school only or more than primary school. Occupational class was recorded in the 1980 census and was dichotomized into manual or nonmanual. Ordering education and occupational class in five categories produced similar results.

Statistical analysis

Cox proportional hazards regression models were used to evaluate the association of mortality from all causes, cardiovascular causes, COPD, and lung cancer with the indicators of air pollution in the statistical package Stata 8.0 (14). The models were age adjusted in 5-year age bands. Covariates were then added to the model and were treated as missing at random. To model the relation between air pollutants and mortality, we used the "generalized additive model," which estimates smooth and nonparametric functions rather than parametric associations (figure 1 and Appendix) (15). Neighborhood-level variances were estimated in a random-effects models by using MLwiN software (figure 2) (16). The variance, σ^2_μ, is on the log-odds scale and is calculated from the neighborhood-level residual μ_j, where individual i resides in neighborhood j. The proportion of explained variance is calculated by the percentage change in variance from the models with and without a given covariate (17).

RESULTS

Correlations between the averaged air pollutants were high, between 0.88 and 0.95. They were poorly correlated with education and occupation (less than 0.05). The percentages of the population with a primary education only were 61 in the youngest age group and 74 in the oldest. Respective values for manual occupational class were 20 percent and 27 percent. Age-adjusted mortality was similar for neighborhoods with different numbers of inhabitants. Number of neighborhoods was fairly equally distributed for each quartile of air pollutants, with somewhat more neighborhoods in the highest exposure quartiles (table 1).

Hazard ratios for all causes of death across quartiles of $PM_{2.5}$ showed an increasing effect for men and women in both age groups: ages 51–70 and 71–90 years (table 2). For the youngest age group, effect estimates were larger. In the oldest age group of women, the effect was comparatively

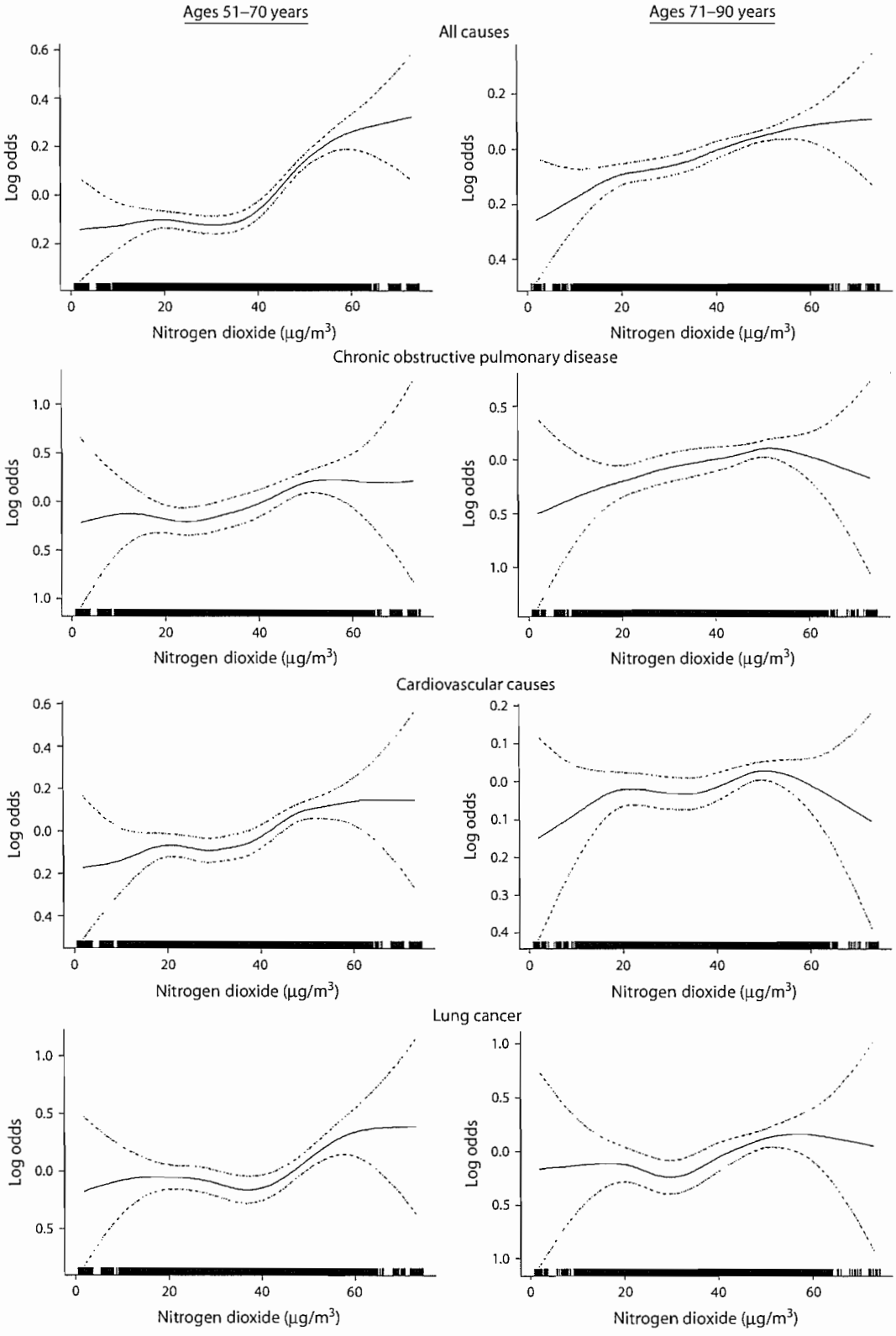

FIGURE 1. Age-adjusted, nonparametric, smoothed relation between nitrogen dioxide and mortality from all causes, chronic obstructive pulmonary disease, cardiovascular causes, and lung cancer in Oslo, Norway, 1992–1995. 95% confidence intervals depict the relation between nitrogen dioxide and mortality. Nitrogen dioxide values ($\mu g/m^3$) on the *x*-axes range from 1.94 $\mu g/m^3$ to 73.16 $\mu g/m^3$.

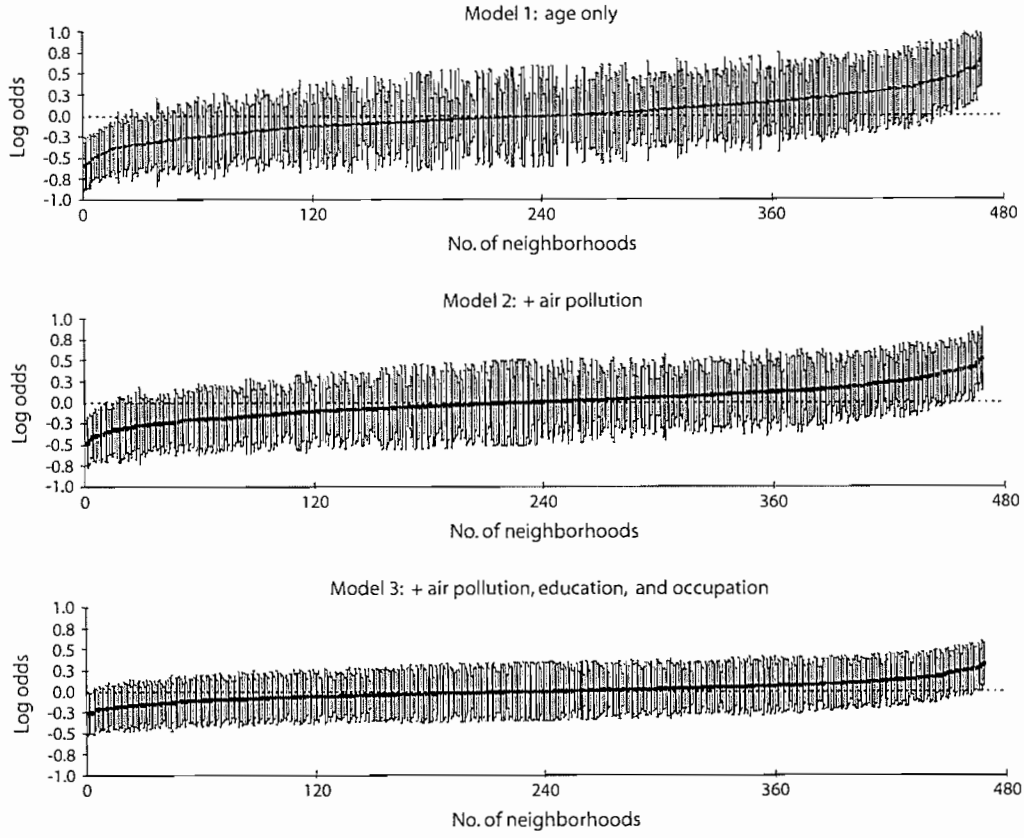

FIGURE 2. Caterpillar plot with departure in the 470 neighborhoods in Oslo, Norway, 1992–1995, from overall probability of death (residuals) after adjusting for age (model 1), air pollutants (model 2), and social variables (model 3). Caterpillar plots show the log odds of mortality associated with living in each neighborhood relative to a neighborhood with average effect. Uncertainty around this estimate is illustrated by 95% confidence intervals. Each plot is ranked from the lowest on the left to the highest on the right.

small. There appeared to be no effect of $PM_{2.5}$ in the two lowest quartile levels below 14 $\mu g/m^3$. For NO_2 and PM_{10}, there was the most evidence of effects in the two highest quartiles above 42 $\mu g/m^3$ for NO_2 and 19 $\mu g/m^3$ for PM_{10} (not tabulated). Even here, the effect size for the old age group of women was small. There was some attenuation in effects in the adjusted model, but the estimates remained significant.

In the cause-specific analysis, the estimates differed by cause of death (tables 3 and 4). For cardiovascular causes, the effects were rather large in the young age group of women, whereas old age in women had no apparent effect. In the adjusted models, the effects were attenuated to only a small degree and remained significant except in the old age group of women. Large effects were seen particularly regarding COPD in both age groups and for both sexes. The effects were attenuated somewhat in the adjusted model. The strong effect for this outcome was seen most clearly among men. The effects for lung cancer were small in the young age group of men and moderate to large in the old age group. Women had particularly large effects for lung cancer in the young age group, somewhat less so for the old. Several of the cause-specific results were borderline significant when analyzed separately for each sex. When both sexes were analyzed together, these results were highly significant ($p < 0.001$) or significant ($p < 0.05$) for all causes and exposures in the adjusted model except COPD and cardiovascular causes in the oldest age group.

Figure 1 displays the age-adjusted, nonparametric, smoothed relation between NO_2 and mortality for both age groups separately and both sexes combined. It shows the log-odds departure from the average effect as a function of the exposure variable. In the youngest age group, risk of death from all causes started to increase at the level of 40 $\mu g/m^3$. In the oldest age group, this increase in risk was linear in the interval 20–60 $\mu g/m^3$. For COPD, a linear effect was seen for both age groups. For cardiovascular causes of death, risk appeared to start increasing at the level of 40 $\mu g/m^3$. The same appeared to be true for lung cancer in the youngest age group, whereas, in the oldest, it started at 40 $\mu g/m^3$. We investigated this nonparametric model for $PM_{2.5}$ and PM_{10} and found similar thresholds with a linear effect for all causes of death in the old age group and COPD in both age groups. We investigated this association for men and women separately, and we found similar patterns.

TABLE 1. Number of neighborhoods and individuals in the study population by levels of NO_2,* $PM_{2.5}$,* and PM_{10}* ($\mu g/m^3$), Oslo, Norway, 1992–1995

	Neighborhoods	Individuals
NO_2		
1.94–27.32	102	36,224
27.33–42.06	86	36,153
42.07–49.07	128	35,544
49.08–73.16	154	35,921
$PM_{2.5}$		
6.56–11.45	99	36,848
11.46–14.25	88	35,561
14.26–18.43	116	35,664
18.44–22.34	167	35,769
PM_{10}		
6.57–13.33	98	36,113
13.34–19.18	84	36,238
19.19–23.74	123	35,694
23.75–30.13	165	35,797
Total	470	143,842

* NO_2, nitrogen dioxide; $PM_{2.5}$, particulate matter less than 2.5 μm in aerodynamic diameter; PM_{10}, particulate matter less than 10 μm in aerodynamic diameter.

TABLE 2. Hazard ratios with 95% confidence intervals for death (1992–1998) from all causes in the study population according to 4-year exposure to particulate matter less than 2.5 μm in aerodynamic diameter ($\mu g/m^3$, quartiles) at participants' home addresses in 1992–1995, Oslo, Norway

	Crude		Adjusted*	
	HR†	95% CI†	HR	95% CI
Men				
Ages 51–70 years (n = 37,797)				
6.56–11.45	1.00		1.00	
11.46–14.25	0.96	0.89, 1.04	0.97	0.89, 1.06
14.26–18.43	1.12	1.03, 1.22	1.13	1.03, 1.23
18.44–22.34	1.48	1.36, 1.60	1.44	1.32, 1.58
p trend	<0.001		<0.001	
Ages 71–90 years (n = 19,072)				
6.56–11.45	1.00		1.00	
11.46–14.25	0.99	0.93, 1.06	0.99	0.93, 1.06
14.26–18.43	1.10	1.03, 1.17	1.04	0.97, 1.11
18.44–22.34	1.19	1.12, 1.27	1.18	1.10, 1.26
p trend	<0.001		<0.001	
Women				
Ages 51–70 years (n = 44,094)				
6.56–11.45	1.00		1.00	
11.46–14.25	0.96	0.87, 1.07	1.00	0.90, 1.11
14.26–18.43	1.08	0.98, 1.20	1.06	0.95, 1.18
18.44–22.34	1.44	1.30, 1.59	1.41	1.27, 1.57
p trend	<0.001		<0.001	
Ages 71–90 years (n = 38,014)				
6.56–11.45	1.00		1.00	
11.46–14.25	1.03	0.97, 1.09	1.03	0.97, 1.09
14.26–18.43	1.07	1.01, 1.12	1.05	0.99, 1.11
18.44–22.34	1.11	1.05, 1.16	1.11	1.05, 1.17
p trend	<0.001		<0.001	

* Adjusted for occupational class and length of education.
† HR, hazard ratio; CI, confidence interval.

A random-effects model was used to assess the proportion of the variability in mortality between neighborhoods explained by air pollution (18) (refer to the Appendix). Some part of the neighborhood variance in mortality from all causes could be explained by each indicator of air pollution. For $PM_{2.5}$ in the young age group, this variance dropped from 0.093 with adjustment for only age to 0.078 after including air pollutants. By further including the individual-level covariates education and occupation in the model, neighborhood variances dropped to insignificant levels except in the old age group of women. Neighborhood-level departures from average mortality risk (neighborhood residuals) are shown in figure 2 in a caterpillar plot, demonstrating that the estimated air pollutants explain probability of death across neighborhoods and that, by adding individual-level indicators of socioeconomic position, differences between neighborhood in risk of death were reduced even further.

DISCUSSION

We investigated the effect of estimated air pollutants (NO_2, PM_{10}, and $PM_{2.5}$) in 470 neighborhoods on all-cause and cause-specific mortality in a cohort of 143,842 individuals aged 51–70 and 71–90 years. We found a consistent effect on all causes of death in both age groups for men and women by all indicators of air pollution. The effects appeared to increase at NO_2 levels above 40 $\mu g/m^3$. This threshold was confirmed in a nonparametric model. In the cause-specific analysis, we found an effect of all indicators for cardiovascular causes, lung cancer, and COPD in both age groups and for both sexes. The effects were particularly strong for COPD. For this disease, there appeared to be no threshold value, in contrast with the other causes. After adjustment for indicators of socioeconomic position, the effects for all causes of death were reduced only partially.

This study has several strengths. Compared with investigators in other cohort studies, we were able to examine the effects of air pollutants estimated hourly over a period of 4 years in a whole range of all 470 neighborhoods in the city of Oslo with half a million inhabitants. This fine level provided detailed exposure contrasts, which made it possible to consider threshold effects. The response levels seen between different causes and age groups appeared consistent for both

TABLE 3. Hazard ratios with 95% confidence intervals for death (1992–1998) from cardiovascular causes (CVD†), COPD†, and lung cancer in men according to NO_2,† PM_{10},† and $PM_{2.5}$† exposure (quartile increase) at participants' home addresses in 1992–1995‡ among men and women aged 51–70 years in Oslo, Norway

	Crude		Adjusted§	
	HR†	95% CI†	HR	95% CI
Men				
CVD (2,007 deaths)				
NO_2	1.08**	1.04, 1.13	1.08*	1.04, 1.13
PM_{10}	1.10**	1.06, 1.15	1.09**	1.04, 1.15
$PM_{2.5}$	1.11**	1.06, 1.16	1.10**	1.05, 1.16
COPD (233 deaths)				
NO_2	1.28**	1.13, 1.44	1.21*	1.05, 1.39
PM_{10}	1.33**	1.17, 1.50	1.29**	1.12, 1.48
$PM_{2.5}$	1.32**	1.17, 1.49	1.27**	1.11, 1.47
Lung cancer (449 deaths)				
NO_2	1.08	0.99, 1.18	1.07	0.97, 1.18
PM_{10}	1.07	0.98, 1.17	1.07	0.97, 1.18
$PM_{2.5}$	1.07	0.98, 1.17	1.07	0.97, 1.18
Women				
CVD (946 deaths)				
NO_2	1.11**	1.04, 1.18	1.07*	1.00, 1.14
PM_{10}	1.14**	1.07, 1.21	1.11*	1.04, 1.19
$PM_{2.5}$	1.16**	1.09, 1.24	1.14**	1.06, 1.21
COPD (203 deaths)				
NO_2	1.13*	1.00, 1.29	1.06	0.92, 1.21
PM_{10}	1.16*	1.02, 1.32	1.06	0.92, 1.22
$PM_{2.5}$	1.18*	1.03, 1.34	1.09	0.94, 1.25
Lung cancer (295 deaths)				
NO_2	1.19*	1.07, 1.33	1.23*	1.10, 1.38
PM_{10}	1.22**	1.10, 1.37	1.27**	1.13, 1.43
$PM_{2.5}$	1.23**	1.10, 1.37	1.27**	1.13, 1.43

* p for trend < 0.005; ** p for trend < 0.001.

† CVD, cardiovascular disease; COPD, chronic obstructive pulmonary disease; NO_2, nitrogen dioxide; PM_{10}, particulate matter less than 10 μm in aerodynamic diameter; $PM_{2.5}$, particulate matter less than 2.5 μm in aerodynamic diameter; HR, hazard ratio; CI, confidence interval.

‡ Average exposure values for the period 1992–1995 were assigned to all participants.

§ Adjusted for occupational class and length of education.

TABLE 4. Hazard ratios with 95% confidence intervals for death (1992–1998) from cardiovascular causes (CVD†), COPD,† and lung cancer in men according to NO_2,† PM_{10},† and $PM_{2.5}$† exposure (quartile increase) at participants' home addresses in 1992–1995‡ among men and women aged 71–90 years in Oslo, Norway

	Crude		Adjusted§	
	HR†	95% CI†	HR	95% CI
Men				
CVD (4,531 deaths)				
NO_2	1.04**	1.01, 1.07	1.02	0.99, 1.05
PM_{10}	1.05**	1.02, 1.08	1.04*	1.01, 1.08
$PM_{2.5}$	1.06**	1.03, 1.09	1.05*	1.01, 1.08
COPD (503 deaths)				
NO_2	1.08	0.99, 1.18	1.04	0.95, 1.14
PM_{10}	1.13*	1.04, 1.24	1.08	0.98, 1.18
$PM_{2.5}$	1.14*	1.04, 1.24	1.10*	1.00, 1.21
Lung cancer (424 deaths)				
NO_2	1.11*	1.01, 1.22	1.09	0.98, 1.20
PM_{10}	1.10*	1.00, 1.21	1.08	0.98, 1.20
$PM_{2.5}$	1.08	0.98, 1.19	1.07	0.97, 1.18
Women				
CVD (7,480 deaths)				
NO_2	1.01	0.99, 1.04	1.01	0.99, 1.04
PM_{10}	1.01	0.99, 1.04	1.01	0.99, 1.04
$PM_{2.5}$	1.02*	1.00, 1.05	1.03*	1.00, 1.05
COPD (516 deaths)				
NO_2	1.09	0.99, 1.18	1.07	0.97, 1.17
PM_{10}	1.11*	1.01, 1.21	1.08	0.98, 1.19
$PM_{2.5}$	1.09*	1.00, 1.18	1.05	0.96, 1.16
Lung cancer (285 deaths)				
NO_2	1.13*	1.01, 1.27	1.12	0.98, 1.27
PM_{10}	1.18*	1.04, 1.33	1.17*	1.03, 1.33
$PM_{2.5}$	1.16*	1.03, 1.31	1.16*	1.02, 1.32

* p for trend < 0.005; ** p for trend < 0.001.

† CVD, cardiovascular disease; COPD, chronic obstructive pulmonary disease; NO_2, nitrogen dioxide; PM_{10}, particulate matter less than 10 μm in aerodynamic diameter; $PM_{2.5}$, particulate matter less than 2.5 μm in aerodynamic diameter; HR, hazard ratio; CI, confidence interval.

‡ Average exposure values for the period 1992–1995 were assigned to all participants.

§ Adjusted for occupational class and length of education.

sexes. The study also included the whole population in the age groups of interest.

This study was based on register data for the whole population without information on smoking history, and the potential impact of smoking as a confounder was assessed in several ways. First, on the basis of a health survey sampled from the same population and age group, we investigated whether smokers were more likely to live in polluted neighborhoods (19). The correlation between daily smoking and NO_2 was 0.06, and the percentage of smokers was rather similar in all quartiles of NO_2 (14–24 percent). This low correlation suggests that smokers, to only a small degree, reside in areas with high levels of air pollution and that omitting smoking from our analysis may not have seriously affected the results. Second, we know from other studies that smoking exhibits a social pattern in Oslo, and, given

the accumulated evidence on the effect of air pollution after adjusting for smoking in other studies, this finding suggests that potential confounding from smoking will to some extent be taken into account by adjusting for occupational class and education (20).

Third, in another cohort study of air pollution and lung cancer from Oslo among the same age group (4), there was no attenuation in effect after adjusting for smoking. Fourth, recent years of epidemiologic research have documented the importance of exposures acting across the life course for a number of chronic diseases in adulthood (21). This finding is particularly well demonstrated for COPD and coronary heart disease, where socially mediated exposures from infancy onward increase the risk of developing disease (8). Smoking is strongly linked to developing COPD. In this sense, smoking is an important confounder in studies looking at development of the disease. However, in this study, where we looked at exposure over a relatively short period of the life course, we consider it unlikely that individuals with COPD who smoke are more likely than individuals with COPD who have given up smoking to live in highly polluted neighborhoods.

We know from previous research that risk of air pollution is associated with deprivation at the neighborhood level (Øyvind Næss, University of Oslo, unpublished manuscript). Health-damaging and -promoting factors might be located at the ecologic level, such as access to public health infrastructure and recreational facilities (17). Health and social care are administratively provided at a much higher level than in neighborhoods. In addition, some of the most polluted neighborhoods are located close to "green," recreational areas. We intend to investigate this issue in future research.

In a previous study of the same population, those living in polluted areas had an increased risk of mortality with 27 years of follow-up of deaths (4). This finding could have several interpretations. People who lived in polluted areas in the past still lived in such areas during follow-up of death, or there might be a genuine long-term effect. To disentangle this issue, one would need to follow the residential and exposure history of a cohort, which we intend to do later. Our main intention in this study was to look at the concentration-response relation with a short-term causal model in mind because we consider this issue to be separate from the long-term effect of air pollution. Of persons in the cohort, 20 percent migrated out of their neighborhood during the period of follow-up. Of those who did move to another neighborhood in the city, only 2 percent migrated to one in another exposure quartile. We tested the robustness of our findings by investigating the results for those who had stayed in the same neighborhood during the period of exposure to air pollution; doing so had little impact on the size of effects and the cause-specific pattern except for COPD in men in the youngest age group, where evidence of linear effect was not significant.

The World Health Organization meta-analysis of time series showed a risk of 1.006 (95 percent confidence interval: 1.004, 1.008) for cause-specific mortality for each 10-$\mu g/m^3$ increase in PM_{10} in urban air the same or next few days (22). For respiratory mortality, the same figures were 1.013 (95 percent confidence interval: 1.005, 1.020); for cardiovascular disease, they were 1.009 (95 percent confidence interval: 1.005, 1.013). The results compare with those from other cohort studies in terms of size of effect for different causes of death. In a six US cities study, Dockery et al. (3) found the effect greatest for lung cancer and cardiopulmonary disease between the least and most polluted cities. Pope et al. (23) found increased long-term effects on cardiopulmonary mortality and lung cancer in a 17-year follow-up. In a Dutch study, Hoek et al. (24) found particularly strong effects for NO_2 on cardiopulmonary mortality. Nafstad et al. (4) found an increased effect of NO_2 for lung cancer and cardiopulmonary disease.

Compared with previous studies providing evidence on threshold effects and possible lack of such, this is the first cohort study known to look at this issue and has several implications. Schwartz and Marcus (2) reported a lack of threshold effect on daily mortality in London, United Kingdom. This finding has been reproduced in other studies with a multicenter design (25). Such studies have used average concentrations in large cities, making them prone to heterogeneity and misclassification (26). This study used neighborhood concentrations in a city with a topography that provides a range of local contrasts between neighborhoods with low to high levels of air pollution. Also important was study power, which made it possible to investigate threshold effects in more detail. Limited evidence on threshold effects among vulnerable groups defined by age or cause of death has evolved from time-series studies (27).

The size of the effects and the cause-specific pattern indicate that some subpopulations may be more susceptible than the general population to lower levels of air pollution. This study provides some evidence for this notion among patients with COPD and the oldest age group. The linear effect seen in the oldest age group regarding all causes of death suggests that they have no clear threshold value because comorbidity makes them susceptible independent of the cause of death recorded on the death certificate and because they may include subgroups with different thresholds, which, in sum, produces a linear effect. COPD is biologically more closely linked to air pollution, making the increased effect size and the linear effect seen in both age groups more plausible. Evidence of particular short-term vulnerability of patients with severe asthma is shown elsewhere (28, 29). Because age seemed to be important in specifying vulnerable groups, we investigated this possibility by slightly increasing the age band of the youngest and the oldest groups. By adding 1 or 2 extra years to the youngest group, the overall pattern seemed to be even more pronounced, with a linear effect of COPD at younger ages as compared with the other causes. The impact of air pollution at lower levels than current recommendations of thresholds must be evaluated based on the share of the population being particularly vulnerable. Further evidence on linear effects in vulnerable subgroups in contrast with the general population should be provided by future cohort studies with both short- and long-term follow-up of deaths.

This study investigated the concentration-response relation between indicators of air pollution in a range of neighborhoods in Oslo and found a linear effect among the oldest and those with COPD in both age groups. For those younger and dying of other causes, there appeared

to be evidence of a threshold. More research is needed to provide robust evidence on subgroups. The study did not have information on smoking and other lifestyle factors; thus, we were not able to fully judge the contribution of these factors to the effect estimates. Policies directed at reducing levels of air pollution need to consider the impact that this may have on the health of such different subgroups in the population. Results from this study suggest that the elderly and patients with COPD may have an increased risk at lower levels compared with the general population.

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Sam Erik Walker at the Norwegian Institute for Air Research developed the AirQUIS model and calculated concentration values of NO_2, $PM_{2.5}$, and PM_{10} in each neighborhood. Statistics Norway linked census data with the death registry.

Conflict of interest: none declared.

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APPENDIX

The random-effects model was fitted by using multilevel logistic regression with data for individuals (level 1) nested within neighborhoods (level 2). The dependent variable was a dichotomous outcome (death), and the model was binomial (logistic regression):

$$Y_{ij} \sim \mathrm{Bin}(1, \pi_{ij})$$
$$\mathrm{logit}(\pi_{ij}) = X\beta + \mu_j$$
$$\mu_j \sim N(0, \sigma_u^2),$$

where $X\beta$ is the age term (fixed part) and μ_j is the neighborhood-level residual that gives rise to the neighborhood-level variance σ_u^2 (random part) (model 1). Variations between neighborhoods in the outcome of interest (the random part) can be explained by the fixed effects of indicators of air pollution (model 2) and individual-level socioeconomic position (model 3). Parameters were estimated by using the second-order, penalized, quasi-likelihood method (16). To illustrate these random effects, caterpillar plots were fitted. These plots show the log odds of mortality associated with living in each neighborhood relative to a neighborhood with an average effect. Uncertainty around these estimates is illustrated by 95 percent confidence intervals. Each plot is ranked from the lowest on the left to the highest on the right (18).

We used the GAM function in S-PLUS software (Insightful Corporation, Seattle, Washington) to fit a generalized additive model and produced Web Appendix figure 1. (This figure is posted on the *Journal*'s website (http://aje.oupjournals.org/).). The syntax associated with this figure is as follows:

$$\text{gam}([\text{Death}] \sim s(NO_2) + \text{Age} + \text{Sex},$$
$$\text{data=mydata, family=binomial}).$$

With [Death], we substituted the four different causes: all causes, lung cancer, COPD, and cardiovascular causes. The plotted figures show smooth functions of the effect of NO_2 on logit of different causes of death. Each function is centralized around zero and shows any deviation from this value. The estimated smooth functions are depicted with their corresponding 95 percent confidence intervals.