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Changes in Traffic Exposure and the Risk of Incident Myocardial Infarction and All-Cause Mortality

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Abstract

Background—Traffic related exposures, such as air pollution and noise, have been associated with increased cardiovascular morbidity and mortality. Few studies, however, have been able to examine the effects of changes in exposure on changes in risk. Our objective was to explore the associations of changes in traffic exposure with changes in risk 1990–2008 in the Nurses' Health Study.

Methods—Incident myocardial infarction (MI) and all-cause mortality were prospectively identified. As a proxy for traffic exposure, we calculated residential distance to roads at all residential addresses 1986–2006, and considered addresses to be “close” or “far” based on distance and road type. To examine the effect of changes in exposure, each consecutive pair of addresses was categorized as: (1) consistently close, (2) consistently far, (3) change from close to far, and (4) change from far to close. We also examined the change in NO₂ levels between address pairs.

Results—In time-varying Cox proportional hazards models adjusted for a variety of risk factors, women living at residences consistently close to traffic were at a higher risk of an incident MI (HR= 1.11; 95% confidence interval = 1.01 – 1.22) and a higher risk of all-cause mortality (1.05; 1.00 – 1.10), compared with those consistently far. The highest risks were seen among women who moved from being far from traffic to close (incident MI: HR=1.50 (95%CI: (1.11–2.03); all-cause mortality: HR=1.17 (95%CI: 1.00–1.37)). Each 1ppb increase in NO₂ compared with the previous address was associated with a HR=1.22 for incident MI (95%CI: 0.99–1.50). 1.03 for all-cause mortality (95%CI: 0.92–1.15).

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Conclusions—Our results suggest that changes in traffic exposure (measured as roadway proximity or change in NO₂ levels) are associated with changes in risk of MI and all-cause mortality.

Exposures associated with living close to traffic, including air pollution and noise, have been associated with increases in cardiovascular disease. Long-term exposures to ambient air pollution have been associated with increased morbidity and mortality (particularly from cardiovascular disease) in a number of studies.^{1–6} In studies where multiple pollutants or size-fractions of particulate matter are available, these associations have been more strongly associated with pollutants generated mainly by traffic, including fine particulate matter (particulate matter less than 2.5 microns in diameter (PM_{2.5})) and oxides of nitrogen.^{2–4,6–10} Levels of these pollutants have been shown to decrease exponentially with distance from a roadway, and have been shown to approach background concentrations at 150 meters.¹¹ Additionally, studies of roadway noise have demonstrated pollution-independent adverse effects on cardiovascular health.^{9,12–21}

Although distance to a roadway is an imperfect and crude measure compared with direct measurements or predictions of noise or pollution levels, it has been widely used as a metric for traffic-based air pollution and noise exposures.^{22–33} Distance also has the benefit of allowing the simultaneous examination of all effects of roadway exposure. However, until recently, only a single study has examined the effect of changes in distance to roadway on changes in risk.³⁴ People in Vancouver who consistently lived in a postal code within 150m of a highway or 50m of a major road over a 4-year period had a 29% increased risk of fatal coronary heart disease (CHD) (coded as a death record with ICD-9 codes 410–414, 429.2 or ICD-10 codes I20–I25 listed), compared with those living consistently further away. Furthermore, changes in risk were observed among those who changed exposure categories.³⁴

We assessed the effects of changes in traffic exposure (measured as roadway proximity or change in NO₂ levels) with incident MI and all-cause mortality in a population of US nurses (the Nurses' Health Study (NHS)) with 20 years of detailed residential history and information on potential confounders. We have previously described increases in incident MI and all-cause mortality with increases in PM_{2.5} and PM₁₀ (particulate matter less than 10 microns in diameter) in members of this cohort living in the Northeastern and Midwestern regions of the United States.^{2,3}

Methods

Study Population

The NHS is a long-term prospective cohort study of US female nurses. The cohort was initiated in 1976 when 121,700 married female US registered nurses, 30 to 55 years old, completed a mailed questionnaire and provided informed consent. At the study inception the nurses resided in eleven states (CA, CT, FL, MA, MD, MI, NJ, NY, OH, PA, TX); however, there are now cohort members in all fifty states. Follow-up questionnaires, with response rates above 90%, are mailed every two years to update information on risk factors and the occurrence of major illnesses. This also provides updated information on residential address

biennially. Women were included in the current study if they were alive and still responding to questionnaires in 1988 (n=98,401), and if all home addresses 1988–2006 (or from 1988 to censoring) were within the continental United States and had been geocoded to the street segment level (n=93,861) and had NO₂ predictions available (n=93,807). Women were excluded if they reported coronary heart disease (n=1,077) or cancer (other than nonmelanoma skin cancer, n=8,168) prior to the start of follow-up, leaving 84,562 women available for analysis.

Assessment of Outcome

We assessed incident cases of myocardial infarction (MI), defined as first nonfatal or fatal MI (ICD-9 codes 410–414; ICD-10 codes I20–I25) from 1990–2008. We requested permission to review the relevant medical records from any woman who reported having a non-fatal MI on a biennial questionnaire. Physicians unaware of exposure level or self-reported risk-factor status systematically reviewed the medical records. MI was classified as confirmed if the criteria of the World Health Organization were met, specifically, symptoms and either electrocardiograph-detected changes or elevated cardiac-enzyme concentrations.³⁵ Cases of nonfatal MIs were designated as probable if an interview or letter confirming hospitalization for the infarction was obtained and medical records were unavailable. We included confirmed and probable cases in the analyses. Deaths were identified from state vital statistics records and the National Death Index or were reported by the families or the postal system. Cases of fatal MI were confirmed by hospital records or through an autopsy or if MI was listed as the cause of death on the death certificate, if it was listed as an underlying and most plausible cause of death, and if evidence of previous CHD was available.

Exposure Assessment

We calculated distance to road at each biennially assessed residential address in 1986–2000 as a proxy for traffic exposure. Distance to road (in meters) for all addresses was determined using Geographical Information System (GIS) software (ArcGIS 9.2, ESRI, Redlands, CA). Road segments from the ESRI StreetMap Pro 2007 files were selected by US Census Feature Class Code to include: A1 (primary roads, typically interstate highways, with limited access, division between the opposing directions of traffic, and defined exits), A2 (primary major, non-interstate highways and major roads without access restrictions), or A3 (smaller, secondary roads, usually with more than two lanes). For comparability with other studies, particularly the Vancouver study, we defined each address within 50 meters of an A3 road or 150 meters from an A1 or A2 road as being close to traffic, and those farther away as far from traffic.^{22,34} These cutpoints are reasonable, since as noted above, exposure studies have shown an exponential decay in exposures with increasing distance from a road, with levels equal to background concentrations at 150–200 m.^{11,22,36–38} To examine the effect of changes in distance to road, each consecutive pair of addresses was categorized using the following exposure groups: (1) consistently close, (2) consistently far, (3) change from close to far, and (4) change from far to close. Women who moved to a new address in the same exposure category as their previous address were included in category 1 or 2, as appropriate. These four exposure categories were chosen to allow us to directly compare our results to those of the previous study in Vancouver.³⁴ To examine the impact of cumulative

traffic exposure, we also calculated the total number of years of living close to a roadway in a time-varying manner.

As a secondary measure of changes in traffic exposure, we calculated the difference in ambient NO₂ between each pair of addresses. We predicted ambient NO₂ levels in 2000 at all addresses using a model incorporating spatial smoothing of USEPA monitoring information and GIS-based covariates including elevation, population density, distance to roadways, and distance and emissions of the nearest power plant.³⁹ We chose to model levels in one year only at all addresses to avoid bias due to temporal changes in traffic. We parameterized the change in NO₂ as both continuous and with indicator variables for positive and negative changes.

Additional Covariates

Information on potential confounders and effect modifiers is available every two years (every four years for diet information).⁴⁰ Therefore, when appropriate, each woman was assigned updated covariate values for each questionnaire cycle. We examined possible confounding by numerous risk factors for MI and all-cause mortality including: age (in months), race, physical activity, body mass index, alcohol consumption, hypertension, physician-diagnosed diabetes, hypercholesterolemia, and family history of MI. To control for smoking, we used lifetime smoking history to calculate pack-years (number of packs/day multiplied by number of years of cigarette smoking) and current smoking status (current/former/never). Alcohol consumption (in grams/day) was controlled for using the cumulative average consumption of all types of alcohol.

Diet was controlled for using a summary score based on the Alternate Healthy Eating Index.⁴¹ As previously used in this cohort, the score included eight components of the Index: higher intakes of vegetables, fruit, nuts, soy and cereal fiber, high ratios of chicken plus fish to red meat and polyunsaturated to saturated fat, low intake of trans fat and multivitamin use of 5 years. As a general indicator of overall mental health status, we adjusted for the 5-item Mental Health Index subscale of the Short-Form 36 Health Status Survey designed to identify psychological distress as compared with well-being, with lower score indicating more severe symptoms.^{42,43}

To control for individual level socioeconomic status, we included several variables including nurses' educational level, occupation of both parents, time-varying marital and employment status, and if applicable, husband's education. To control for area-level socioeconomic status (SES), we included area level information from the 2000 Census on tract level median income and house value for each residence. To control for the potential impact of differences in area-level SES between addresses, we also calculated the difference in the area-level SES between each subsequent pair of addresses.

To determine potential confounding, each variable (or set of indicator variables) was added separately to a model including age and race. Variables with p-values <0.05 as predictors of risk in univariate models were included in the final multivariable model. To assess the potential for effect modification, we also examined models stratified by diet score (at the median), physical activity (at the median), outdoor (walking, jogging, running, biking)

physical activity (at the median), BMI (underweight/normal, overweight, obese), and ever/never smoking status, based on our previous analyses in this cohort.^{2,44,45}

Statistical Analysis

Since exposure was updated every 2 years, we used prospective time-varying Cox proportional hazards models to assess the relationship of incident MI or all-cause mortality with exposure to traffic at the address at the time of the questionnaire mailing, and with changes in exposure. Person-months of follow-up time were calculated from 1 July 1990 until censoring, date of death, or the end of follow-up (30 June 2008). All models were based on a biennial time scale and were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs). The dataset was converted to an Anderson-Gill data structure with a record for each 2-year time period, including all information on person-time during that interval, the exposure during that time period, whether the person was censored during the interval, and covariate information. To tightly control for age and calendar year, we estimated separate baseline hazards for age in months and calendar year in the Cox models. The proportional hazards assumptions were checked and verified using interaction terms between the time metric and exposure variables. In sensitivity analyses, we also performed analyses without excluding women who were diagnosed with cancer before baseline (n=91,107). Statistical analyses were performed in SAS version 9.2 (SAS Institute, Cary, NC).

Results

We identified 2,948 incident MI cases and 11,502 non-accidental deaths over the follow-up period. The distribution of subject characteristics by exposure group is presented in Table 1, and each nurse may have been in more than one exposure group during the period of follow-up. Women were on average 64 years of age, primarily white, and had a registered nursing degree. Few were current smokers or consumed more than 15 grams of alcohol per day. There was little difference in the distribution of potential confounders by exposure category. The majority of the cohort (and their person-years) were consistently at addresses located more than 50 meters from an A3 road or more than 150 meters from an A1 or A2 road. Fifty percent of person-time was spent at addresses more than 250m from an A1–A3 road, and 25% was at addresses more than 450m. The median (interquartile range (IQR), range) levels of NO₂ was 13.9ppb (7.5, 0.0–80.4), and the median (IQR) change in levels between address pairs was 0.00 (0.00), with a range of –56.1 to 49.3, indicating that while most women did not move, there were equal numbers of women moving to areas with more or less NO₂ than their previous address.

In age-, race-, and calendar-year-adjusted models that include distance for each address at the time of each questionnaire mailing, women close to a roadway had an increased risk of an incident MI (HR= 1.14; 95%CI= 1.04 – 1.25) and an increased risk of all-cause mortality (1.10; 1.05 – 1.15), compared with women far from a roadway. There was little change in fully adjusted models additionally controlling for BMI, physical activity, healthy-diet score, alcohol consumption, hypercholesterolemia, high blood pressure, diabetes, family history of MI, smoking status and pack-years, overall mental health status, and socioeconomic status

(MI HR= 1.11, 95%CI: 1.01 – 1.21; all-cause HR= 1.05, 95%CI= 1.00 – 1.10). In fully adjusted models, every additional two years at an address close to a roadway was associated with an HR=1.01 (95%CI: 1.00,1.02) for all-cause mortality and an HR=1.02 (95%CI: 1.00,1.04) for incident MI. We could not examine periods shorter than 2 years due to the biennial administration of the questionnaire. Penalized splines were used to determine that this association was not statistically significantly different from linear ($p=0.60$ for incident MI and $p=0.21$ for all-cause mortality). An interquartile range increase (8 ppb) in NO₂ levels at the address at the time of the questionnaire mailing was not associated with risk of incident MI (HR= 0.98; 95%CI= 0.94 – 1.03), but was associated with a small increase in the risk of all-cause mortality (HR= 1.02; 95%CI= 1.00 – 1.05), in fully adjusted models.

To examine change in exposure comparing the address at the time of each questionnaire mailing to the address at the previous questionnaire mailing, women who consistently lived at addresses close to a roadway were compared with those who were consistently far. Women consistently close to a roadway were at a higher risk of an incident MI (HR=1.15; 1.04 – 1.26) adjusting for age, race, and calendar year. Women moving from close to far had an increased risk of MI (HR=1.12; 1.02 – 1.23), while those moving from far to close had a larger increased risk (HR=1.56; 1.17 – 2.08) (Table 2). Additional adjustment for BMI, physical activity, healthy-diet score, alcohol consumption, hypercholesterolemia, high blood pressure, diabetes, family history of MI, smoking status and pack-years, and overall mental health status slightly attenuated the results. In fully adjusted models, there was little evidence of additional confounding by the individual- or area-level socioeconomic status variables (census-tract median income, parent's occupation, marital status, husband's education, or nurses' education level). There was little evidence of effect modification by smoking status, physical activity, diet or BMI (Supplemental Figure 1).

For all-cause mortality, in age-, race-, and calendar-year-adjusted models, compared with women who consistently lived far from a roadway, women consistently living close were at higher risk (HR=1.07; 1.02 – 1.13) (Table 3). Women moving from close to far had no apparent change in risk (HR=1.02; 0.98 – 1.07), while those moving from far to close had an increased risk (HR=1.44; 1.24 – 1.67). After multivariate adjustment, results were slightly attenuated. Again, there was no evidence of confounding by individual or area-level socioeconomic status, or effect modification by smoking status, physical activity, diet, or BMI (Supplemental Figure 2). In sensitivity analyses, inclusion of women with prior cancer did not change the results (data not shown).

In models examining the effect of changes in NO₂ concentrations between each pair of residences (Table 4), there was little immediate benefit to those women moving to areas with lower levels of NO₂, but a suggestion of increased risks of incident MI and all-cause mortality for those women moving to areas with higher levels of NO₂. For example, in fully adjusted models, for each 1ppb increase in NO₂ levels compared to the previous address, women were at 3% (95%CI: –8%, 15%) and 22% (95%CI: –1%, 50%) increased risk of all-cause mortality and incident MI, respectively.

Discussion

In our study of older US women, living close to an A1–A3 roadway was associated with a modest increased risk of incident MI and all-cause mortality. There was a suggestion that changes in exposure (measured as either distance to roadway or changes in NO₂ concentrations) were associated with changes in incident MI and all-cause mortality risk. Although the number of cases was relatively small, the risks were most pronounced in women who had moved from a residence far from an A1–A3 roadway to one close, or who had moved to residences with a higher level of ambient NO₂. The observed associations with cumulative exposure as well as with short-term changes imply both short- and long-term effects of near-roadway exposures on MI and all-cause mortality risk.

These results are similar to those from a recent study from Vancouver.³⁴ Using the provincial universal health-insurance database, the authors identified all individuals in metropolitan Vancouver aged 45–85 without a prior diagnosis of CHD. Individuals were included who changed traffic-exposure category one time or less during the exposure period (1/1994–12/1998) and did not change exposure during the follow-up period (1/1999–12/2002). Deaths from CHD during the follow-up period were identified using the provincial death register and hospital records. Among the 414,793 individuals in the study, adjusting for age, sex, neighborhood SES, and comorbidities, those consistently living in postal codes exposed to traffic (centroid 150m from a highway or 50 meters from a major road) were at an increased risk of CHD mortality (RR=1.29; 95%CI: 1.18,1.41) compared with those consistently unexposed. Similar to our results, changes in exposure were associated with changes in risk. Those moving from an unexposed to an exposed postal code were at a higher risk (RR=1.20; 95%CI: 1.00,1.43), and those moving from an exposed to an unexposed postal code had a 14% increased risk (95%CI: –5%, 37%), compared with those in consistently unexposed postal codes.

Several other studies have examined the association of distance to road with cardiovascular outcomes, with mixed results. In a long-term study of 4,800 older German women, living within 50m of a major road was associated with a 70% (95%CI: 2%–181%) increased risk of cardiopulmonary mortality.⁴⁶ Living within 300m of a major road was associated with a 12% increased risk of fatal and non-fatal CHD in a population of over 13,000 middle-aged men and women in the ARIC study, with stronger risks for those living near roads with higher traffic density.²⁷ However, in over 117,000 members of a Dutch cohort study, there was no evidence of an increased risk of cardiovascular mortality among those living near a major road (RR=1.05, 95%CI: 0.93–1.18), although there was some evidence of increased risk with traffic intensity and traffic-related pollutants (black smoke, NO₂, PM_{2.5}).⁹ In a case-control study in Massachusetts, each interquartile-range increase in traffic density was associated with a 4% (95%CI: 2–7%) increased risk of acute MI.²⁸ Other studies have demonstrated associations between exposures related to traffic exposure (including NO₂, NO_x, and black carbon) and cardiovascular mortality.^{32,33,47} Unlike many of these studies, we did not find evidence of an association between NO₂ levels measured at the current home address and an increased risk of incident MI or all-cause mortality. However, the majority of cohort studies examined longer exposure intervals, which may account for the discrepant findings.

Recent studies have assessed the mechanism responsible for the association of CHD and mortality with traffic-related exposures.⁴⁸ Traffic-exposures may specifically adversely affect future CHD by accelerating systemic atherosclerosis (and presumably coronary atherosclerosis),^{25,49} assessed by quantity of aortic calcification,²⁶ increases in pulse-wave velocity⁵⁰ and carotid intima-media thickness,^{51,52} or effects on blood pressure^{53–58}. Findings in experimental animal models also support the potential for fine-particulate air pollution (and specifically traffic-related particles) to contribute to the progression of atherosclerosis.^{59–61}

This study has several important limitations. Members of this cohort are middle-aged and older women who tend to have stable residential histories. Therefore, the number of cases who changed exposure categories (unexposed to exposed, exposed to unexposed) was small, limiting our ability to detect associations. The results from this cohort are not necessarily generalizable to other racial groups, to men, or to people with frequent changes in residence. Women also had to remain alive through 1988 and continue to respond to questionnaires to be included in this analysis. These restrictions may further limit generalizability as these cohort members are likely younger and healthier than members of the cohort who died before the beginning of follow-up or refused additional questionnaires. It is also an important limitation that for non-fatal MI, we are relying on an initial self report of MI. As this cohort is composed of nurses, we are assuming that they would be knowledgeable about their health diagnoses, but any bias in their initial reporting of disease (if also associated with changes in roadway proximity) could lead to a positive bias in our results.

Our primary measure of exposure in this study is a binary variable (living close or far from a roadway), not direct measures of traffic-related pollution or traffic noise. The use of a binary cutpoint does not take into account the gradual changes in exposures with increasing distance from a road. However, in secondary analyses examining changes in NO₂ levels between address pairs (a measure that does not align with our traffic exposure categories), we also observed suggestions of increases in risk with increases in ambient NO₂. Additionally, distance to a roadway may be related to other non-traffic related exposures such as walkability, availability of green space, etc, which may also be related to risk of CHD and mortality. We were able to include adjustment for area-level SES and changes in SES in our models. Still, there may be residual confounding by other uncontrolled neighborhood factors. Lastly, we used road data from 2007 to generate distance-to-road measures in each year. It is possible that the 2007 roads do not accurately represent the US roadway system in earlier years. However, the most likely scenario is that new roads have been built and that existing roads have gotten larger. If this is the case, some of the earlier addresses considered close to roadways may have in fact not been close. This misclassification would bias the results towards the null.

It is also possible that the associations we are observing are in some way a reflection of the general overall stress of moving to a new location. However, in analyses restricted to women who moved (including those staying in the same exposure categories), results were similar to those from the whole study, although with much wider confidence intervals (data not shown). Another limitation is that we have no information on the proportion of the day each woman spent at her home, or on the characteristics of the home (age, ventilation rate,

soundproofing, orientation to prevailing winds, etc.) that would influence the actual levels of ambient pollution exposure experienced inside the home. Nor do we have information on work exposures to pollution or other factors at work that may or may not be associated with distance to roadway. Finally, we do not have information on why each nurse moved. Although we were able to control for changes in marital and employment status and changes in area-level SES, we are unable to adjust for all possible reasons for moving that may be independently related to risk of MI and mortality.

This large nationwide prospective cohort of women also provided several important strengths. We had 20 years of detailed residential address history and included only residential addresses with a street segment level geocoding match. Unlike many studies, we were able to examine the impacts of changes in exposure on incident MI, not only fatal MI. The use of only street-segment-level matches likely reduced exposure misclassification. Another strength of this study was the large amount of time-varying data available on a wide range of individual-level potential confounders. Although the associations did not appear to be confounded by personal-or area-level markers of socioeconomic status, we did see evidence of confounding, particularly by lifestyle characteristics (including diet and alcohol consumption), comorbid conditions, and family history of MI.

Overall, our results are consistent with a growing body of literature that indicate an association between adverse health effects and living close to roadways. Similar to a recent study in Canada, our results also suggest that these risks can change with changes in exposure, and that those moving to areas of higher exposure may be at greater risk.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1
Age Standardized Characteristics of the Cohort Over the Full Period of Follow-up by Change in Distance to Road Exposure Category

Characteristic	Traffic Exposure Category ^d			
	Consistently far	Consistently close	Far to close	Close to far
Age (in years); mean (SD)	63.8 (8.6)	64.4 (8.7)	64.0 (9.1)	64.3 (8.6)
Pack-years of smoking; mean (SD) ^b	24.3 (21.2)	25.4 (21.4)	26.1 (22.2)	25.6 (21.6)
White race; %	94	93	94	92
BMI; %				
Underweight/Normal	43	41	44	43
Overweight	32	33	32	32
Obese	20	22	21	22
Smoking status; %				
Current	11	12	13	12
Former	42	42	46	43
Never	44	44	40	43
Physical activity (MET-hours/week); %				
<3	18	19	20	19
3–<9	19	19	19	20
9–<18	17	17	17	17
18–<27	11	10	10	11
27	18	17	17	17
Alcohol consumption (g/day); %				
0	27	29	27	28
0.1–4.9	20	21	19	21
5.0–14.9	12	12	14	13
15.0–29.9	4	4	5	4
>30.0	3	3	3	3
Healthy Diet Score; mean (SD)	114 (75)	112 (72)	115 (73)	113 (72)
Family history of MI; %	33	34	34	34
Hypercholesterolemia; %	53	52	55	54
Diabetes; %	8	8	9	9

Characteristic	Traffic Exposure Category ^a			
	Consistently far	Consistently close	Far to close	Close to far
High blood pressure; %	44	45	45	46
Father's occupation; %				
Professional/Manager	26	25	27	25
Other Job	74	75	73	75
Mother's occupation; %				
Housewife	64	63	63	64
Other Job	36	37	37	36
RN Degree; %	73	75	73	75
Retired; %	37	36	38	36
Currently Married; %	65	63	56	64
Husband's Education; %				
Less than high school	3	5	3	4
High school	25	28	23	26
Greater than high school	38	33	35	36
Missing or Not Applicable	34	34	39	34
Median census tract family income; mean (SD)	\$67,000 (25,000)	\$65,000 (27,000)	\$64,000 (26,000)	\$65,000 (26,000)
Median census tract household value; mean (SD)	\$178,000 (126,000)	\$181,000 (146,000)	\$187,000 (143,000)	\$186,000 (144,000)

^aNote: Addresses are considered "close" to traffic if they are within 50 meters of an A3 road or 150 meters from an A1 or A2 road. Individuals may be in multiple exposure categories over time.

^b Among ever smokers

Hazard Ratios and 95% Confidence Intervals from Cox Proportional Hazards Models for Incident CHD with Categories of Change in Distance to Road.

Table 2

Traffic Exposure Group ^a	Cases	Person-years	Basic Model ^b		Multivariate Adjusted Model ^c		Fully Adjusted Model ^d	
			HR	HR (95%CI)	HR	HR (95%CI)	HR	HR (95%CI)
Consistently far	2,841	1,256,346	1.00	(reference)	1.00	(reference)	1.00	(reference)
Consistently close	539	207,551	1.15	(1.04–1.26)	1.13	(1.02–1.24)	1.11	(1.01–1.22)
Far to close	48	13,585	1.56	(1.17–2.08)	1.48	(1.11–1.97)	1.50	(1.10–2.03)
Close to far	603	228,746	1.12	(1.02–1.23)	1.08	(0.99–1.19)	1.08	(0.98–1.18)

^a Addresses are considered “close” to traffic if they are within 50 meters of an A3 road or 150 meters from an A1 or A2 road. Individuals may be in multiple exposure categories over time, therefore the number of cases sums to more than 2,927.

^b Adjusted for age, race, and calendar year

^c Additionally adjusted for BMI, physical activity, healthy diet score, alcohol consumption, hypercholesterolemia, high blood pressure, diabetes, family history of MI, smoking status and pack-years, and overall mental health status

^d Additionally adjusted for mother and father’s occupations, marital status, husband’s education, nurses’ education level, employment status, and Census tract median income and median home value (at current address and difference from previous address)

Hazard Ratios and 95% Confidence Intervals from Cox Proportional Hazards Models for All Cause Mortality with Categories of Change in Distance to Road

Table 3

Traffic Exposure Group ^a	Cases	Person-years	Basic Model ^b		Multivariate Adjusted Model ^c		Fully Adjusted Model ^d	
			HR	(95%CI)	HR	(95%CI)	HR	(95%CI)
Consistently far	11,095	1,258,062	1.00	(reference)	1.00	(reference)	1.00	(reference)
Consistently close	2,063	207,857	1.07	(1.02–1.13)	1.06	(1.01–1.11)	1.05	(1.00–1.10)
Far to close	181	13,888	1.44	(1.24–1.67)	1.29	(1.12–1.50)	1.17	(1.00–1.37)
Close to far	2,156	234,347	1.02	(0.98–1.07)	1.00	(0.95–1.04)	0.98	(0.94–1.03)

^a Addresses are considered “close” to traffic if they are within 50 meters of an A3 road or 150 meters from an A1 or A2 road. Individuals may be in multiple exposure categories over time, therefore the number of cases sums to more than 11,502.

^b Adjusted for age, race, and calendar year

^c Additionally adjusted for BMI, physical activity, healthy diet score, alcohol consumption, hypercholesterolemia, high blood pressure, diabetes, family history of MI, smoking status and pack-years, and overall mental health status

^d Additionally adjusted for mother and father’s occupations, marital status, husband’s education, nurses’ education level, employment status, and Census tract median income and median home value (at current address and difference from previous address)

Hazard Ratios and 95% Confidence Intervals from Cox Proportional Hazards Models for Incident MI and All-cause Mortality for each 1 ppb Increase in NO₂ Concentrations from the Previous Questionnaire Cycle

Table 4

Change in NO ₂	Cases	Person-years	Basic Model ^a		Multivariate Adjusted Model ^b		Fully Adjusted Model ^c	
			HR	(95%CI)	HR	(95%CI)	HR	(95%CI)
Incident MI								
Negative change	141	63,851	0.98	(0.83–1.16)		1.02 (0.86–1.21)		1.01 (0.85–1.20)
Zero	2,690	1,189,559	Reference			Reference		Reference
Positive change	96	37,714	1.24	(1.01–1.52)		1.25 (1.02–1.53)		1.22 (0.99–1.50)
All Cause Mortality								
Negative change	532	63,925	0.95	(0.87–1.04)		1.03 (0.94–1.12)		1.01 (0.93–1.10)
Zero	10,660	1,191,162	Reference			Reference		Reference
Positive change	310	37,785	1.04	(0.93–1.17)		1.08 (0.96–1.21)		1.03 (0.92–1.15)

^a Adjusted for age, race, and calendar year

^b Additionally adjusted for BMI, physical activity, healthy diet score, alcohol consumption, hypercholesterolemia, high blood pressure, diabetes, family history of MI, smoking status and pack-years, and overall mental health status

^c Additionally adjusted for mother and father's occupations, marital status, husband's education, nurses' education level, employment status, and Census tract median income and median home value (at current address and difference from previous address)