Supplemental Material

Study Population

The NAS is an ongoing longitudinal study of aging established in 1963 by the Veterans Administration (Bell et al. 1972) Briefly, 2,280 community-dwelling men free from known chronic medical conditions living in the Greater Boston area were enrolled between 1963 and 1968. Every three to five years, participants visited the clinic after an overnight fast and abstention from smoking for a thorough examination, including extensive physical examination, laboratory tests, blood collection, and a self-administered questionnaire on alcohol consumption, food intake, medical history, medication usage, smoking history, and other factors that could affect health.

ECG Measurement and Analysis

The ECG was recorded for five to ten minutes between 0530 and 1400 hours with a two-channel (five lead) ECG monitor (Trillium 3000, Forest Medical, East Syracuse, NY) using a sampling rate of 256 Hz per channel. A detailed description of the protocol is provided elsewhere (Park et al. 2005; Pope et al. 2001). The ECG digital recordings were processed using commercial PC-based software (Trillium Platinum™ Holter Analysis Software for MS Windows; Forest Medical, NY). Each file was processed for QT interval (QT) and heart rate - corrected QT interval (QTc) values using the Bazett's formula (Bednar et al. 2001). QT interval was measured from the QRS onset to the end of the T-wave only on Normal or Supraventricular beats. The QT interval was not calculated if the T wave did not have sufficient amplitude. For each participant at each visit, we calculated the mean QTc.

Air Pollution and Meteorology

Ambient BC and $PM_{2.5}$ concentrations were continuously measured at the Harvard University Countway Library stationary ambient monitoring site which is located <1 km from the clinical laboratory where subjects were examined. BC was measured continuously using an Aethalometer (model AE-14, Magee Scientific, Inc., Berkeley, CA), and $PM_{2.5}$ was measured using a tapered element oscillating microbalance (TEOM model 1400A, Rupprecht and Pataschnick Co, East Greenbush, NY). For $PM_{2.5}$ measurements, a season-specific correction was used to compensate for the loss of semi-volatile mass that occurs when the TEOM sample filters are heated to 50°C (Allen et al. 1997). Occasional missing values of BC and $PM_{2.5}$ were estimated using an imputation linear regression method. Hourly ambient CO, O_3, NO_2, and SO_2 concentrations were obtained from local monitoring sites of the Massachusetts Department of Environmental Protection. All gaseous concentrations were measured using US Environmental Protection Agency (EPA) reference methods (U.S. EPA 2008). Roxbury, Bremen, Kenmore Square, and Northend of Boston MA, Lynn MA, and Waltham MA sites were used to calculate the mean concentrations of the gases. The distance of the sites from the clinical laboratory varied from <2 km to <20 km. Temperature data were obtained from the first order weather station at Boston Logan airport.

Genotyping

DNA from white blood cells was extracted with commercially available PureGene Kits (Gentra Systems, Minneapolis MN). Depending on the white blood cell count, extraction on average yielded 20-40 μg of DNA per ml whole blood. Using optical density, DNA concentration was determined and a 260/280 ratio > 1.7 was considered satisfactory. For additional quality control, every sample before use was subjected to

polymerase chain reaction (PCR) amplification using a primer set amplifying the ACE D/I polymorphism. Samples were after DNA quantification adjusted to TE buffer, partitioned into aliquots, and stored at –80°C.

Participants were genotyped for 2 gene deletions [*GSTM1* (Glutathione S-transferase mu 1, UniGene Hs.301961) (UniGene 2009a) and *GSTT1* (Glutathione S-transferase theta 1, UniGene Hs.268573) (UniGene 2009b)], 8 single nucleotide polymorphism (SNP) [*GSTP1 Ile105Val and Ala114Val* (Glutathione S-transferase pi 1, UniGene Hs.523836) (UniGene 2009c), *HFE C282Y and H63D* (Hemochromatosis, UniGene Hs.233325) (UniGene 2009d), *NQO1 C609T* (NAD(P)H dehydrogenase, quinone 1, UniGene Hs.406515) (UniGene 2009e), and *CAT RS2300181*, *RS2284367* and *RS769217* (Catalase, UniGene Hs.502302) (UniGene 2009f)], and a microsatellite GTn-repeat polymorphism [*HMOX1* (Heme oxygenase 1, UniGene Hs.517581) (UniGene 2009g)].

Using Sequenom SpectroDESIGNER software, multiplex PCR assays were designed by inputting sequence containing the SNP site and 100 bp of flanking sequence on either side of the SNP. 8 SNPs were multiplexed including *GSTP1 Ile105Val, GSTP1 Ala114Val, HFE C282Y, HFE H63D, CAT RS2300181*, *CAT RS2284367* and *CAT RS769217.* The SNPs were grouped into multiplexes 1) that are most likely to produce a PCR product in multiplex, 2) that all use the same mix of terminating nucleotides, and 3) that will produce an extension product over the SNP site that does not overlap in mass with any other oligonucleotide present in the reaction mix. In 384-well reaction plates, the PCR was carried out in a volume of 5 µl using 2.5 ng genomic DNA. Multiplex PCR was carried out to generate short PCR products (> 100 bp) containing one SNP or

insertion deletion. In a 5 µl reaction containing 1 x HotStar Taq PCR buffer (Qiagen), 0.1 U HotStar Taq (Qiagen), 2.5 mM $MgCl_2$, 200 µM each dNTP, and 50 nM each PCR primer, 2.5 ng genomic DNA was amplified. At 95 ^oC, the reaction was incubated for 15 minutes followed by 45 cycles of 95^oC for 20 seconds, 56^oC for 30 seconds, 72^oC for 1 minute, and finally 3 minutes more at 72^oC. The removal of excess dNTPs from the reaction was done by incubation with 0.3 U shrimp alkaline phosphatase (USB) at 37^oC for 20 minutes followed by 5 minutes at 85^oC to deactivate the enzyme. Single primer extension was carried out over the SNP or insertion/deletion in a final concentration of 600 nM each extension primer, 0.126 U Thermosequenase (Solis Biodyne) and 50 µM d/ddNTP and was incubated at 94^oC for 2 minutes followed by 45 cycles of 94 ^oC for 5 seconds, 52 ^oC for 5 seconds, and 72 ^oC for 5 seconds. Addition of a cation exchange resin was done to desalt the reaction, followed by mixing and centrifugation to settle the contents of the tube. The extension product was then spotted onto a 384 well spectro CHIP before being flown in the MALDI-TOF mass spectrometer.

Genotyping for the *GSTM1* and *GSTT1* deletion polymorphisms was also done and the assay consists of polymerase chain reaction (PCR) amplifications. As these polymorphisms are gene deletions, the PCR product indicates the presence of one or more copies of the gene. As a positive control, concomitant amplification of the *CYP1A1* gene was done in every case. The PCR amplification of *CYP1A1* results in a 312-bp product that is easily visualized in absence or presence of the *GSTM1* or *GSTT1* 273-bp PCR product. For DNA template preparation, the whole blood (0.5–1.0µl) was mixed with reaction buffer and primers, followed by incubation. 2.5 U of Amplitaq was added to it and PCR was performed, yielding the 273-bp product.

An assay design by Yamada et al. (Yamada et al. 2000) was used for the *HMOX-1* microsatellite (GT)n length polymorphism. Briefly, the amplification of *HMOX-1* locus was done by PCR at the 5′ promoter flanking region containing (GT)n repeats with primers as described by Yamada. Using a laser-based automated DNA sequencer (AB 3100; Applied Biosystems, Foster City, CA), the sizes of the PCR products were analyzed. Even though the exact cutoff for *HMOX-1* modulation is still unknown, constructs with lengths of > 25 repeats showed reduced *HMOX-1* basal promoter activity and decreased transcriptional upregulation in response to various stimuli like H_2O_2 compared with lengths < 25 repeats (Yamada et al. 2000; Chen et al. 2002). In the analysis of the data, we used the 25-repeat cutoff to categorize the study subjects in two categories [≤ 24 (GT)n repeats in at least one allele or > 24 (GT)n repeats in both alleles] based on the *HMOX-1* microsatellite length.

Effect Size Estimates

All effect size estimate findings were reported as change in mean QTc per IQR of pollutant, using the formula: (ES = β x IQR), with 95% confidence intervals (CI) ES = [(β ± 1.96 x SE) x IQR]. In addition, effect size estimates were scaled to percent of a SD change in QTc per IQR change of a pollutant, using the formula: [ES = (β x IQR)/SD] x 100%, with 95% CI {ES = [(β ± 1.96 x SE) x IQR]/SD}. β and SE are the estimated regression coefficient and its standard error, IQR is the interquartile range of the pollutant, and SD is the standard deviation of QTc.

Statistical Models

Quadratic Polynomial Distributed Lag Model

$$Y_{ij} = u_i + \beta_0 + \alpha_0\left(\sum_{k=0}^{10} k^0 w_{ij-k}\right) + \alpha_1\left(\sum_{k=0}^{10} k^1 w_{ij-k}\right) + \alpha_2\left(\sum_{k=0}^{10} k^2 w_{ij-k}\right) + f(s_{ij}) + \beta_1 X_1 + \ldots + \beta_p X_p + \varepsilon_{ij}$$
$$Y_{ij} = u_i + \beta_0 + \alpha_0 v_{0ij} + \alpha_1 v_{1ij} + \alpha_2 v_{2ij} + f(s_{ij}) + \beta_1 X_1 + \ldots + \beta_p X_p + \varepsilon_{ij} \quad [1]$$

Quadratic Polynomial Distributed Lag Model with Effect Modifier M

$$Y_{ij} = u_i + \beta_0 + \alpha_0 v_{0ij} + \alpha_1 v_{1ij} + \alpha_2 v_{2ij} +$$
$$(\alpha_3 v_{0ij} + \alpha_4 v_{1ij} + \alpha_5 v_{2ij}) M_{ij} + \alpha_6 M_{ij} + f(s_{ij}) + \beta_1 X_1 + \ldots + \beta_p X_p + \varepsilon_{ij} \quad [2]$$

Hourly Lag Model

$$Y_{ij} = u_i + \beta_0 + \alpha_0 w_{ij-k} + f(s_{ij}) + \beta_1 X_1 + \ldots + \beta_p X_p + \varepsilon_{ij} \qquad k = 0, 1, \ldots, or\ 10 \quad [3]$$

Hourly Lag Model with Effect Modifier M

$$Y_{ij} = u_i + \beta_0 + \alpha_0 w_{ij-k} + \alpha_1 w_{ij-k} M_{ij} + \alpha_2 M_{ij} + f(s_{ij}) + \beta_1 X_1 + \ldots + \beta_p X_p + \varepsilon_{ij} \quad k = 0, 1, \ldots, or\ 10 \quad [4]$$

where Y_{ij} is the QTc interval of subject *i* at time *j*, β_0 is the overall intercept, u_i is the random intercept for subject *i*, M_{ij} is the effect modifier of subject *I* at time *j*. w_{ij-k} is either the current or the previous 10 lagged concentration value of the pollution. v_{0ij}, v_{1ij}, and v_{2ij} are linear combinations of the current and the previous 10 lagged concentration values of pollution w_{ij-k}. $f(s_{ij})$ is the smooth function of calendar date (natural spline with 4 degrees of freedom per year), and $X_1, \ldots, X_p$ are the fixed covariates terms measured at each of the visits in which the ECG measurements were taken.

RESULTS

Eligible study participants included 580 NAS participants, who had a total of 926 valid ECG recordings available for analysis. Subjects were male with a mean age of 74.8 years (SD=6.8 years) and were mostly overweight with a mean BMI of 27.9 kg/m^2 (SD=4.1 kg/m^2). Approximately, 20 percent of the participants were diabetic and two-thirds of them were former smokers. QTc values were approximately normally distributed with a mean of 393.3 msec (SD=29.7). QTc was not significantly correlated with BMI, MAP or total cholesterol, but was positively and significantly correlated with age (Pearson correlation coefficient r=0.16, P-value <0.01).

All pollutant concentrations during the actual hour of ECG monitoring (0 hr lag) were significantly correlated with each other, with BC and $PM_{2.5}$ having the highest correlation (Spearman correlation coefficient $\rho = 0.69$, P-value < 0.01). Among the gaseous pollutants, NO_2 and CO were most strongly correlated ($\rho = 0.64$), while the correlation between particulate and gaseous pollutant was highest for BC and NO_2 ($\rho = 0.60$). In contrast, ozone was negatively correlated with every other pollutant ($\rho < -0.12$).

Supplemental Material, Table 1. Genetic Polymorphisms and a prior-hypothesized interactions with traffic-related pollution for prolonged ventricular repolarization QTc interval.

Gene name/Gene product function	Gene	Amino acid change or Polymorphic region	Chromosome	rsID	A priori hypothesized gene-air pollution interaction
Catalase enzyme					Air pollutants may play a role in the production of reactive oxygen species. (No prior studies were found.)
Heme enzyme present in the peroxisome of nearly all aerobic cells and converts the reactive oxygen species H_2O_2 to H_20 and O_2.	*CAT*	C/T	11p	769217	
	CAT	A/G	11p	2284367	
	CAT	A/G	11p	2300181	
Glutathione-S-transferase enzyme					Air pollutants are inducers & substrates for *GSTs.* (Chahine et al. 2007) (Probst-Hensch et al. 2008)
Detoxification enzymes(Phase 2) that can deactivate drugs, carcinogens, environmental toxins and products of oxidative stress by conjugation with glutathione	*GSTM1*	- / +	1p		
	GSTP1	V105I	11q	1695	
	GSTP1	A114V	11q	1799811	
	GSTT1	- / +	22q		
Heme oxygenase 1 enzyme					Air pollutants are inducers & substrates for *HMOX1.* (Chahine et al. 2007)
An essential enzyme in the heme catabolism, it cleaves heme to form biliverdin, which is converted to bilirubin by biliverdin reductase, and carbon monoxide, a putative neurotransmitter,	*HMOX1*	any ≤ 24 (GT)n/ > 24 (GT)n repeat	22q		
Hemochromatosis enzyme					Air pollutants are inducers & substrates for *HFE.* (Park et al. 2006)
Membrane enzyme that regulates iron absorption by regulating the interaction of transferrin receptor with transferrin	*HFE*	H63D	6p	1799945	
	HFE	C282Y	6p	1800562	
NAD(P)H dehydrogenase quinone 1					Air pollutants are inducers & substrates for *NQ01.* (Billet et al. 2007)
Detoxificaiton enzyme (Phase 2) that catalyzes the 4- or 2-electron reduction of quinones to prevent redox cycling, which leads to the generation of free radicals.	*NQ01*	C609T	16q	1800566	

Supplemental Material, Table 2. Effect estimates for change in mean QTc and % SD change in QTc with an IQR increase in pollutant exposures [cumulative over the 10 hours prior to ECG measurement (QCDL Model) and 4 hours prior to ECG measurement (4-Hr Lag Model)].

Pollutant	QCDL Model		4-Hr Lag Model	
	Change in Mean QTc (msec) (95% CI)	% SD Change in QTc % (95% CI)	Change in Mean QTc (msec) (95% CI)	% SD Change in QTc % (95% CI)
BC	1.89 (-0.16–3.93)	6.46 (-0.54–13.45)	2.54 (0.28–4.80)	8.70 (0.95–16.45)
NO_2	2.56 (-0.88–6.00)	8.63 (-2.98–20.23)	2.72 (-0.01–5.44)	9.15 (-0.04–18.34)
CO	3.83 (-0.17–7.82)	13.13 (-0.58–26.84)	2.36 (-0.07–4.80)	8.10 (-0.24–16.45)
$PM_{2.5}$	0.22 (-3.01–3.44)	0.72 (-9.99–11.43)	0.64 (-1.60–2.89)	2.14 (-5.33–9.60)
SO_2	1.03 (-1.22–3.28)	3.46 (-4.10–11.02)	0.61 (-1.16–2.39)	2.06 (-3.91–8.02)
O_3	-0.74 (-3.73–2.25)	-2.58 (-13.01–7.85)	-1.29 (-4.44–1.85)	-4.50 (-15.46–6.46)

Supplemental Material, Table 3. Adjusted effect estimates for percent SD change in QTc with an IQR increase in traffic pollutant exposures [cumulative over the 10 hours prior to ECG measurement (QCDL Model) and 4 hours prior to ECG measurement (4-Hr Lag Model)] by patient characteristics (diabetic status, obesity, and smoking status).

Pollutant	Modifier	QCDL Model		4-Hr Lag Model	
		% SD Change in QTc % (95% CI)	*P-value* Interaction	% SD Change in QTc % (95% CI)	*P-value* Interaction
Diabetic Status					
BC	DM	18.09 (2.28–33.90)	0.26	28.38 (12.16–44.60)	<0.01
	Non-DM	4.90 (-2.71–12.51)		4.31 (-4.03–12.65)	
NO_2	DM	23.93 (-0.40–48.26)	<0.01	24.02 (6.67–41.37)	<0.05
	Non-DM	4.12 (-9.00–17.24)		4.92 (-5.16–15.01)	
CO	DM	12.95 (-12.30–38.20)	0.15	5.49 (-10.97–21.95)	0.72
	Non-DM	13.41 (-2.12– 28.94)		8.74 (-0.28–17.76)	
Obesity Status					
BC	Obese	13.60 (-0.23–27.44)	0.54	17.85 (3.50–32.20)	0.14
	Non-Obese	4.21 (-3.90–12.32)		5.68 (-3.04–14.40)	
NO_2	Obese	13.53 (-10.13–37.20)	<0.01	20.92 (2.90–38.95)	0.13
	Non-Obese	7.68 (-5.56–20.92)		6.01 (-4.01–16.02)	
CO	Obese	11.58 (-14.63–37.79)	0.29	12.84 (-0.64–26.32)	0.38
	Non-Obese	13.38 (-1.97–28.72)		6.25 (-3.11–15.61)	
Smoking Status					
BC	Never	14.79 (1.85–27.73)	0.74	13.51 (0.75–26.27)	0.36
	Ever	1.96 (-6.26–10.19)		6.42 (-2.78–15.62)	
NO_2	Never	14.07 (-8.13–36.27)	<0.01	16.14 (0.27–32.02)	0.30
	Ever	6.62 (-6.81–20.05)		6.70 (-3.65–17.06)	
CO	Never	16.03 (-8.00–40.06)	0.14	14.60 (-0.17–29.36)	0.30
	Ever	11.23 (-4.82–27.29)		6.08 (-3.10–15.25)	

Supplemental Material, Table 4. Adjusted effect estimates for percent SD change in QTc with an IQR increase in traffic pollutant exposures [cumulative over the 10 hours prior to ECG measurement (QCDL Model) and 4 hours prior to ECG measurement (4-Hr Lag Model)] by genetic susceptibility to oxidative stress (High GSS vs. Low GSS).

Pollutant	Modifier	QCDL Model		4-Hr Lag Model	
		% SD Change in QTc (msec) (95% CI)	*P-value* Interaction	% SD Change in QTc (msec) (95% CI)	*P-value* Interaction
Genetic Susceptibility Score Status					
BC	High	13.63 (2.76–24.49)	0.57	9.97 (-3.08–23.03)	0.53
	Low	-1.99 (-13.81–9.83)		4.74 (-6.50–15.98)	
NO_2	High	12.57 (-6.65–31.78)	<0.01	10.07 (-3.31–23.45)	0.85
	Low	1.05 (-16.34–18.45)		11.76 (-1.16–24.68)	
CO	High	23.81 (1.78–45.84)	0.08	12.66 (0.74–24.57)	0.87
	Low	14.83 (-4.68–33.44)		13.88 (2.49–25.26)	

Supplemental Material, Table 5. Adjusted effect estimates for change in mean QTc and % SD change in QTc with an IQR change in cumulative traffic pollutant exposure (during the 10 hours prior to ECG measurement) by genotype.

Genotype	Pollutant	Modifier	QCDL Model		
			Change in Mean QTc (msec) (95% CI)	% SD Change in QTc (%) (95% CI)	*P-value* Interaction
HFE C282Y	BC	Wild Type	2.52 (0.33–4.71)	8.77 (1.15–16.40)	0.10
		Any Variant	1.26 (-5.21–7.74)	4.40 (-18.14–26.95)	
	NO_2	Wild Type	3.51 (-0.28–7.31)	12.02 (-0.97–25.01)	<0.01
		Any Variant	-4.18 (-13.60–5.24)	-14.30 (-46.55–17.96)	
	CO	Wild Type	4.92 (0.79–9.04)	14.63 (2.36–26.91)	<0.01
		Any Variant	-4.55 (-16.00–6.89)	-13.55 (-47.61–20.51)	
HFE H63D	BC	Wild Type	3.19 (0.87–5.50)	11.09 (3.04–19.13)	0.48
		Any Variant	-2.31 (-6.87–2.26)	-8.03 (-23.92–7.87)	
	NO_2	Wild Type	3.21 (-0.82–7.23)	10.97 (-2.80–24.74)	<0.01
		Any Variant	0.23 (-6.97–7.44)	0.80 (-23.85–25.46)	
	CO	Wild Type	3.59 (-0.87–8.04)	12.63 (-3.06–28.31)	0.04
		Any Variant	3.36 (-4.22–10.95)	11.84 (-14.87–38.55)	
CAT rs769217	BC	Wild Type	2.74 (-0.26–5.75)	9.35 (-0.89–19.60)	0.62
		Any Variant	1.65 (-1.22–4.51)	5.61 (-4.16–15.39)	
	NO_2	Wild Type	6.10 (1.33–10.86)	20.51 (4.48–36.54)	<0.01
		Any Variant	-0.77 (-5.96–4.43)	-2.57 (-20.04–14.89)	
	CO	Wild Type	7.73 (1.68–13.78)	26.68 (5.79–47.57)	0.02
		Any Variant	1.89 (-3.68–7.46)	6.53 (-12.69–25.76)	
CAT rs2284367	BC	Wild Type	2.69 (-0.35–5.72)	9.10 (-1.17–19.37)	0.43
		Any Variant	1.95 (-0.98–4.89)	6.61 (-3.33–16.55)	
	NO_2	Wild Type	6.19 (1.37–11.01)	20.66 (4.57–36.75)	<0.01
		Any Variant	-0.68 (-6.07–4.70)	-2.27 (-20.25–15.70)	
	CO	Wild Type	7.86 (1.73–14.00)	26.94 (5.92–47.97)	0.01
		Any Variant	1.88 (-3.73–7.50)	6.45 (-12.79–25.69)	

Supplemental Material, Table 6. Adjusted effect estimates for change in mean QTc and % SD change in QTc with an IQR change in cumulative traffic pollutant exposure (during the 10 hours prior to ECG measurement) by genotype.

Genotype		Pollutant	Modifier	QCDL Model	
			Change in Mean QTc (msec)(95% CI)	% SD Change in QTc (%)(95% CI)	*P-value* Interaction
CAT rs2300181	BC	Wild Type	2.11 (-0.60–4.82)	7.18 (-2.06–16.42)	0.63
		Any Variant	2.33 (-0.89–5.55)	7.94 (-3.05–18.93)	
	NO_2	Wild Type	-1.18 (-6.10–3.74)	-3.98 (-20.53–12.57)	<0.01
		Any Variant	6.61 (1.58–11.64)	22.23 (5.31–39.15)	
	CO	Wild Type	2.21 (-3.24–7.67)	7.64 (-11.19–26.46)	<0.01
		Any Variant	8.47 (2.58–14.36)	29.23 (8.91–49.56)	
NQ01 C609T	BC	Wild Type	1.41 (-1.21–4.03)	4.81 (-4.11–13.74)	0.81
		Any Variant	3.55 (0.03–7.07)	12.09 (0.10–24.08)	
	NO_2	Wild Type	2.54 (-1.89–6.98)	8.54 (-6.36–23.45)	<0.01
		Any Variant	3.29 (-2.57–9.14)	11.04 (-8.62–30.70)	
	CO	Wild Type	5.20 (0.06–10.33)	17.96 (0.21–35.71)	0.04
		Any Variant	3.51 (-3.12–10.14)	12.14 (-10.78–35.06)	
GSTP1 Ile105Val	BC	Wild Type	1.66 (-1.22–4.53)	5.78 (-4.24–15.80)	0.23
		Any Variant	3.52 (0.57–6.47)	12.27 (1.98–22.56)	
	NO_2	Wild Type	1.57 (-3.26–6.40)	5.52 (-11.46–22.50)	<0.01
		Any Variant	2.08 (-2.61–6.77)	7.31 (-9.18–23.81)	
	CO	Wild Type	3.92 (-1.79–9.64)	13.72 (-6.26–33.70)	0.02
		Any Variant	5.34 (-0.08–10.76)	18.68 (-0.26–37.62)	
GSTP1 Ala114Val	BC	Wild Type	2.80 (0.53–5.06)	9.77 (1.86–17.68)	0.17
		Any Variant	-3.29 (-8.35–1.78)	-11.48 (-29.17–6.21)	
	NO_2	Wild Type	2.07 (-1.57–5.72)	7.30 (-5.55–20.14)	<0.01
		Any Variant	-1.80 (-11.24–7.64)	-6.33 (-39.59–26.93)	
	CO	Wild Type	4.73 (0.35–9.11)	16.59 (1.22–31.95)	0.01
		Any Variant	-3.76 (-13.26–5.74)	-13.18 (-46.51–20.15)	

Supplemental Material, Table 7. Adjusted effect estimates for change in mean QTc and % SD change in QTc with an IQR change in cumulative traffic pollutant exposure (during the 10 hours prior to ECG measurement) by genotype.

Genotype	Pollutant	Modifier	QCDL Model		
			Change in Mean QTc (msec) (95% CI)	% SD Change in QTc (%) (95% CI)	*P-value* Interaction
GSTT1	BC	Deletion	1.94 (-2.34–6.23)	6.59 (-7.94–21.13)	0.53
		No Deletion	2.42 (-0.23–5.06)	8.19 (-0.77–17.16)	
	NO_2	Deletion	2.55 (-5.47–10.56)	8.51 (-18.28–35.31)	<0.01
		No Deletion	3.01 (-1.18–7.20)	10.06 (-3.94–24.06)	
	CO	Deletion	6.44 (-2.53–15.40)	22.38 (-8.80–53.56)	0.04
		No Deletion	4.13 (-0.52–8.78)	14.35 (-1.82–30.53)	
GSTM1	BC	Deletion	0.16 (-2.75–3.08)	0.57 (-9.62–10.76)	0.99
		No Deletion	2.54 (-0.35–5.42)	8.86 (-1.22–18.95)	
	NO_2	Deletion	1.66 (-3.15–6.47)	5.70 (-10.81–22.20)	<0.01
		No Deletion	3.67 (-1.32–8.66)	12.60 (-4.52–29.72)	
	CO	Deletion	1.82 (-3.67–7.31)	6.35 (-12.85–25.54)	<0.05
		No Deletion	5.75 (1.15–10.34)	20.09 (4.02–36.15)	
HMOX-1	BC	Any Short Allele	-0.18 (-3.10–2.73)	-0.63 (-10.59–9.34)	0.51
		Long/Long Alleles	3.67 (0.77–6.58)	12.55 (2.62–22.47)	
	NO_2	Any Short Allele	0.27 (-4.32–4.87)	0.92 (-14.56–16.40)	<0.01
		Long/Long Alleles	5.22 (-0.21–10.65)	17.58 (-0.70–35.85)	
	CO	Any Short Allele	3.38 (-1.91–8.67)	11.68 (-6.59–29.95)	0.09
		Long/Long Alleles	4.60 (-1.41–10.61)	15.89 (-4.87–36.65)	

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