Web appendix - Further methodological details and additional results

Clinical data – identification of cases for inclusion in MINAP for and details of database

The identification of admissions for entry into the MINAP database is managed at the individual hospital level; guidelines recommend identifying eligible admissions through a combination of avenues including biochemistry records (specifically troponin measurements), admission notes, and discharge slips. The database includes 123 fields covering basic demographic data, timing of onset of symptoms, electrocardiograph changes, markers of myocardial necrosis, final diagnosis, thrombolytic or other treatment received, as well as the geographical co-ordinates of the super-output area containing the patient's place of residence (a super output area is an unit of geography used in the UK representing a small area with mean population 1500). Also recorded are pre-existing co-morbidities including hypertension, diabetes and previous cardiovascular events.

Imputation of missing daily temperature data using complete regional data series

After combining daily temperature data in conurbations with multiple stations, 8 conurbations had some missing data. However, 10 complete temperature series were available at a broader "regional" level, based on the following regions: North East, North West, Yorkshire and the Humber, East Midlands, West Midlands, East, London, South East, South West, and Wales. These regional series draw from all available monitoring data in the region to produce a representative series for the whole region; these regional data were very strongly correlated with non-missing conurbation-level data ($r \geq 0.98$ in each conurbation). We therefore used the regional series as a basis for imputing data for days with missing temperature at the narrower conurbation level. Specifically, for each conurbation, a simple linear regression model was fitted over all days in the period 2003-2006 relating daily conurbation temperature to daily regional temperature; this model was estimated using days with non-missing conurbation temperature, and then used to predict conurbation temperature on days with missing data.

Pollution monitoring stations and missing pollutant data

Data from multiple pollution monitoring stations were available within Greater London (n=8 stations), West Midlands (5), Greater Manchester (4), Sheffield (2) and West Yorkshire (2), and were combined into a single series. Within these conurbations, median correlations

between hourly data series from pairs of monitors were 0.67, 0.89, 0.63, 0.73 and 0.51 for PM_{10}, ozone, CO, NO_2 and SO_2 respectively. In all other conurbations a single monitor series was available for each pollutant. Thus, after initial data processing, there was a single hourly pollution series for each pollutant, in each conurbation. Exposure levels on the case and control days for each individual were then drawn directly from the relevant single pollution series for the conurbation.

5 average lag terms covering 1-6, 7-12, 13-18, 19-24, and 25-72 hours were generated for each pollutant for use in the models. For example, the 1-6 hour term was generated as the mean of the pollutant levels at lags 1, 2, 3, 4, 5 and 6 hours. In some cases pollutant data at individual hours was missing. Where at least 2/3 of individual hourly measurements were available (i.e. 4 measurements for lag terms 1-6, 7-12, 13-18, 19-24 hours; 32 measurements for lag term 25-72 hours), the average lag term was generated as the mean of the remaining hours; where less than 2/3 of individual hourly measurements were available, the average lag term was set to missing and the associated observation excluded from models involving that pollutant. This resulted in 2107 (2.7%), 1952 (2.5%), 2447 (3.1%), 2216 (2.8%), and 2208 (2.8%) events being excluded from the single pollutant models for PM_{10}, ozone, CO, NO_2 and SO_2 respectively, and 4931 (6.2%) events being excluded from the multi-pollutant model.

***Web Table A**: Estimated excess risk of MI associated with pollution increases from 2-pollutant models*

Pollutant and lag (hrs)		Excess Risk (%) and 95% CI per 10µg/m3 increase (except CO: per 0.1mg/m3 increase)" — 2 pollutant model adjusted for…									
		PM_{10}		Ozone		CO		NO_2		SO_2	
PM_{10}	*Lag 1-6*	-		1.2	[0.3 to 2.0]	1.3	[0.4 to 2.3]	0.8	[-0.1 to 1.8]	1.2	[0.3 to 2.1]
	7-12	-		-0.6	[-1.6 to 0.5]	-0.8	[-1.9 to 0.4]	-0.2	[-1.4 to 0.9]	-0.6	[-1.7 to 0.4]
	13-18	-		-0.5	[-1.6 to 0.5]	-0.4	[-1.5 to 0.8]	-0.4	[-1.5 to 0.7]	-0.3	[-1.4 to 0.7]
	19-24	-		-0.3	[-1.2 to 0.6]	-0.2	[-1.2 to 0.8]	-0.3	[-1.3 to 0.7]	-0.4	[-1.3 to 0.6]
	25-72	-		-0.9	[-1.9 to 0.2]	-0.1	[-1.3 to 1.1]	-0.6	[-1.9 to 0.6]	-1.1	[-2.2 to 0.1]
	Σ(1-72)	-		*-1.1*	*[-2.1 to -0.0]*	*-0.1*	*[-1.4 to 1.1]*	*-0.8*	*[-2.1 to 0.6]*	*-1.2*	*[-2.4 to -0.0]*
Ozone	*Lag 1-6*	0.0	[-0.6 to 0.6]	-		-0.1	[-0.7 to 0.5]	0.7	[-0.1 to 1.5]	-0.2	[-0.8 to 0.4]
	7-12	0.3	[-0.4 to 1.0]	-		0.6	[-0.2 to 1.3]	-0.2	[-1.2 to 0.8]	0.5	[-0.3 to 1.2]
	13-18	-0.6	[-1.4 to 0.1]	-		-0.7	[-1.5 to 0.0]	-1.0	[-2.0 to -0.0]	-0.6	[-1.3 to 0.1]
	19-24	-0.1	[-0.7 to 0.5]	-		-0.2	[-0.8 to 0.5]	-0.1	[-0.9 to 0.8]	-0.1	[-0.7 to 0.5]
	25-72	-0.3	[-1.0 to 0.4]	-		-0.6	[-1.3 to 0.2]	-0.7	[-1.5 to 0.2]	-0.3	[-1.0 to 0.4]
	Σ(1-72)	*-0.8*	*[-1.6 to -0.0]*	-		*-1.1*	*[-1.9 to -0.2]*	*-1.3*	*[-2.2 to -0.4]*	*-0.7*	*[-1.5 to 0.1]*
CO	*Lag 1-6*	-0.1	[-0.7 to 0.5]	0.2	[-0.4 to 0.8]	-		-0.5	[-1.2 to 0.2]	0.2	[-0.4 to 0.7]
	7-12	0.2	[-0.5 to 0.9]	0.2	[-0.4 to 0.9]	-		0.7	[-0.1 to 1.5]	0.0	[-0.6 to 0.7]
	13-18	-0.2	[-0.9 to 0.5]	-0.5	[-1.2 to 0.1]	-		-0.3	[-1.0 to 0.5]	-0.2	[-0.8 to 0.4]
	19-24	-0.1	[-0.7 to 0.5]	-0.3	[-0.9 to 0.3]	-		-0.3	[-1.0 to 0.4]	-0.2	[-0.8 to 0.3]
	25-72	-0.6	[-1.4 to 0.2]	-0.8	[-1.5 to -0.1]	-		-0.6	[-1.5 to 0.4]	-0.7	[-1.4 to 0.0]
	Σ(1-72)	*-0.8*	*[-1.6 to 0.1]*	*-1.2*	*[-1.9 to -0.4]*	-		*-1.0*	*[-2.0 to 0.1]*	*-0.9*	*[-1.7 to -0.2]*
NO_2	*Lag 1-6*	0.8	[0.0 to 1.6]	1.7	[0.7 to 2.7]	1.5	[0.6 to 2.5]	-		1.1	[0.4 to 1.9]
	7-12	-0.9	[-1.8 to 0.0]	-0.9	[-2.2 to 0.3]	-1.5	[-2.6 to -0.5]	-		-1.0	[-1.9 to -0.1]
	13-18	0.1	[-0.9 to 1.1]	-1.1	[-2.3 to 0.1]	0.1	[-1.0 to 1.2]	-		0.0	[-0.9 to 1.0]
	19-24	0.2	[-0.6 to 1.0]	0.0	[-1.0 to 1.0]	0.3	[-0.7 to 1.2]	-		-0.1	[-0.9 to 0.7]
	25-72	-0.2	[-1.2 to 0.8]	-0.8	[-1.8 to 0.1]	0.1	[-1.1 to 1.3]	-		-0.6	[-1.6 to 0.3]
	Σ(1-72)	*0.0*	*[-1.1 to 1.1]*	*-1.2*	*[-2.2 to -0.2]*	*0.4*	*[-0.8 to 1.6]*	-		*-0.6*	*[-1.6 to 0.4]*
SO_2	*Lag 1-6*	-0.6	[-2.9 to 1.8]	-0.1	[-2.3 to 2.2]	0.4	[-1.9 to 2.8]	-0.7	[-3.1 to 1.7]	-	
	7-12	0.6	[-2.0 to 3.4]	0.3	[-2.2 to 3.0]	-0.2	[-2.8 to 2.5]	0.9	[-1.8 to 3.6]	-	
	13-18	-1.2	[-3.7 to 1.4]	-2.2	[-4.7 to 0.3]	-1.2	[-3.8 to 1.4]	-1.7	[-4.2 to 1.0]	-	
	19-24	1.8	[-0.5 to 4.2]	1.6	[-0.7 to 3.9]	1.5	[-0.8 to 3.9]	2.0	[-0.4 to 4.4]	-	
	25-72	1.2	[-2.3 to 4.7]	-1.0	[-4.0 to 2.2]	0.6	[-2.6 to 4.0]	0.6	[-2.9 to 4.2]	-	
	Σ(1-72)	*1.8*	*[-2.1 to 5.9]*	*-1.4*	*[-4.7 to 2.1]*	*1.2*	*[-2.4 to 5.0]*	*1.0*	*[-2.9 to 5.1]*	-	

Note: Models included the presented pollutant effects, and were adjusted for temperature (5 lag terms covering days 0-28 inclusive), relative humidity (average of lags 0-3 days), day of week, influenza, RSV, and residual seasonality within calendar month strata (single sin/cos pair per conurbation)
Σ(1-72) effect for each pollutant estimated by summing regression coefficients for the 5 lag terms

***Web Table B**: Estimated excess risk of MI in key sensitivity analyses*

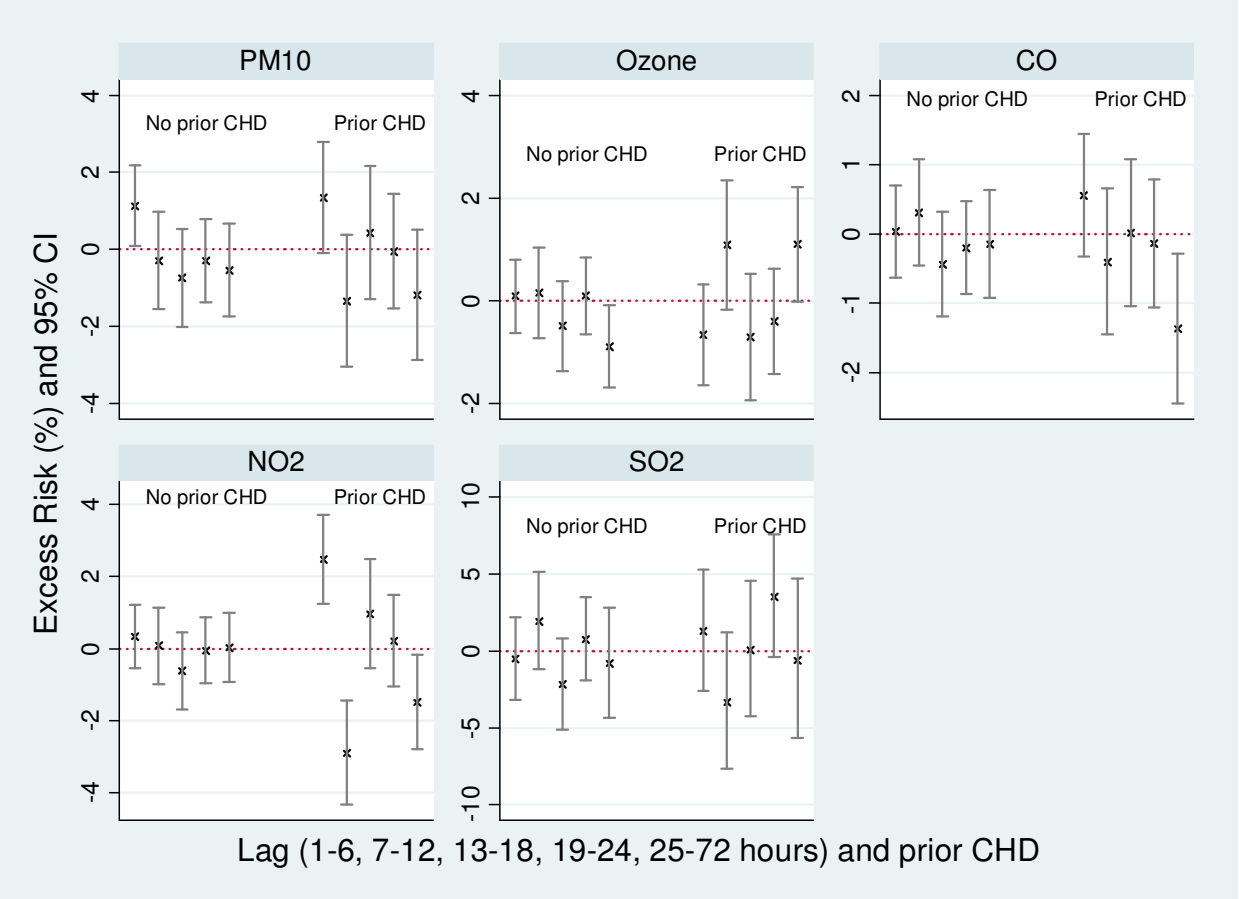
Pollutant and lag (hrs)		Excess Risk (%) and 95% CI per 10μg/m^3 increase (except CO: per 0.1mg/m^3 increase)					
		Symptom onset only		Evidence of MI		Adjust clustering	
PM_{10}	*Lag 1-6*	0.9	[-0.1 to 1.9]	1.3	[0.4 to 2.2]	1.3	[0.2 to 2.4]
	7-12	-0.5	[-1.7 to 0.7]	-0.8	[-1.8 to 0.3]	-0.8	[-1.9 to 0.4]
	13-18	0.1	[-1.0 to 1.3]	-0.2	[-1.3 to 0.9]	-0.2	[-1.1 to 0.7]
	19-24	-0.2	[-1.2 to 0.8]	-0.4	[-1.3 to 0.6]	-0.4	[-1.1 to 0.4]
	25-72	-1.1	[-2.3 to 0.1]	-1.0	[-2.0 to 0.1]	-1.0	[-1.5 to -0.5]
	Σ(*1-72)*	-0.8	[-1.9 to 0.4]	-1.0	[-2.1 to 0.0]	-1.0	[-2.0 to -0.1]
Ozone	*Lag 1-6*	0.1	[-0.5 to 0.8]	-0.3	[-0.9 to 0.4]	-0.3	[-0.9 to 0.4]
	7-12	0.3	[-0.6 to 1.1]	0.5	[-0.3 to 1.3]	0.5	[-0.3 to 1.3]
	13-18	-0.8	[-1.6 to 0.0]	-0.6	[-1.4 to 0.1]	-0.6	[-1.2 to -0.1]
	19-24	0.0	[-0.7 to 0.7]	0.0	[-0.6 to 0.7]	0.0	[-0.4 to 0.5]
	25-72	-0.2	[-1.0 to 0.6]	-0.3	[-1.0 to 0.4]	-0.3	[-0.8 to 0.2]
	Σ(*1-72)*	-0.6	[-1.5 to 0.2]	-0.6	[-1.4 to 0.1]	-0.6	[-1.2 to -0.0]
CO	*Lag 1-6*	0.3	[-0.3 to 0.9]	0.2	[-0.3 to 0.8]	0.2	[-0.4 to 0.9]
	7-12	0.0	[-0.7 to 0.7]	-0.1	[-0.7 to 0.6]	-0.1	[-0.7 to 0.6]
	13-18	0.0	[-0.7 to 0.8]	-0.2	[-0.9 to 0.4]	-0.2	[-0.9 to 0.4]
	19-24	-0.3	[-0.9 to 0.3]	-0.2	[-0.7 to 0.4]	-0.2	[-0.6 to 0.3]
	25-72	-0.6	[-1.4 to 0.1]	-0.6	[-1.3 to 0.1]	-0.6	[-1.1 to -0.1]
	Σ(*1-72)*	-0.6	[-1.4 to 0.2]	-0.8	[-1.5 to -0.1]	-0.8	[-1.4 to -0.2]
NO_2	*Lag 1-6*	0.5	[-0.3 to 1.3]	1.1	[0.4 to 1.9]	1.1	[0.3 to 2.0]
	7-12	-0.7	[-1.7 to 0.3]	-1.1	[-2.0 to -0.1]	-1.1	[-1.8 to -0.3]
	13-18	0.2	[-0.8 to 1.3]	0.1	[-0.8 to 1.1]	0.1	[-0.4 to 0.6]
	19-24	0.0	[-0.9 to 0.9]	-0.2	[-1.0 to 0.6]	-0.2	[-0.7 to 0.2]
	25-72	-0.5	[-1.4 to 0.4]	-0.5	[-1.3 to 0.4]	-0.5	[-1.0 to 0.0]
	Σ(*1-72)*	-0.5	[-1.4 to 0.5]	-0.5	[-1.4 to 0.4]	-0.5	[-1.0 to -0.0]
SO_2	*Lag 1-6*	-1.1	[-3.6 to 1.5]	-0.3	[-2.6 to 2.1]	-0.3	[-3.0 to 2.5]
	7-12	1.2	[-1.8 to 4.1]	0.8	[-1.9 to 3.6]	0.8	[-3.2 to 5.0]
	13-18	-1.6	[-4.4 to 1.2]	-1.6	[-4.2 to 1.1]	-1.6	[-5.0 to 2.0]
	19-24	2.7	[0.2 to 5.4]	1.5	[-0.9 to 3.9]	1.5	[-1.3 to 4.3]
	25-72	-2.6	[-5.9 to 0.8]	-1.7	[-4.8 to 1.5]	-1.7	[-4.7 to 1.5]
	Σ(*1-72)*	-1.5	[-5.1 to 2.3]	-1.3	[-4.6 to 2.2]	-1.3	[-4.2 to 1.7]

Note: "Symptom onset only" results are restricted to patients for whom the time of symptom onset was specifically recorded; "Evidence of MI" results are restricted to patients with ECG or marker levels corroborating the MI diagnosis; "Adjust clustering" results use robust standard errors to account for any possible clustering by conurbation

Note: Results are from single-pollutant models adjusted for temperature (5 lag terms covering days 0-28 inclusive), relative humidity (average of lags 0-3 days), day of week, influenza, RSV, and residual seasonality within calendar month strata (single sin/cos pair per conurbation)

Σ(1-72) represents the cumulative effect over lag 1-72 hours for each pollutant, estimated by summing regression coefficients for the 5 lag terms

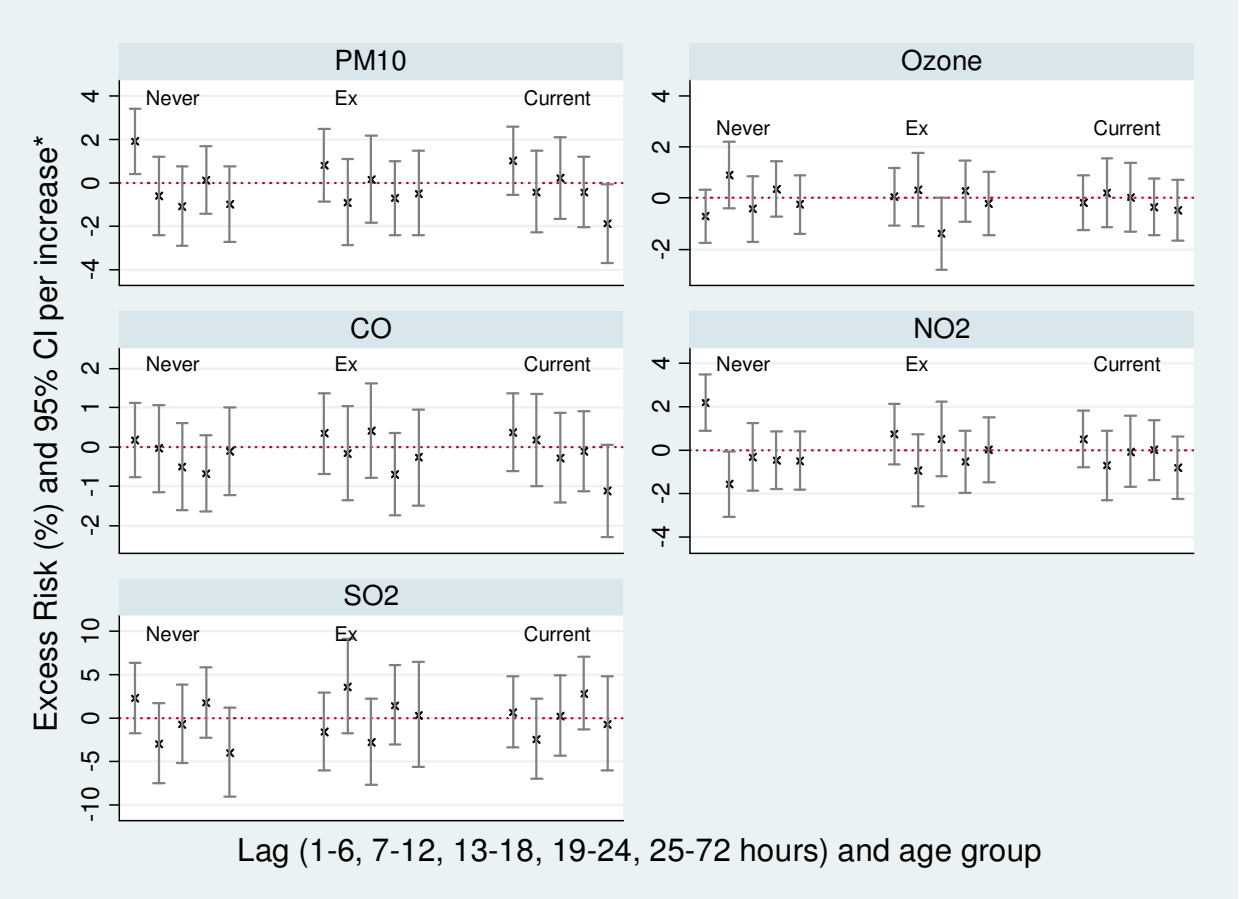
***Web Fig A**: Estimated excess risk of MI associated with pollution increases, stratified by pre-existing coronary heart disease*



p-interaction = 0.82, 0.05, 0.44, 0.007, 0.31 for PM_{10}, ozone, CO, NO_2, and SO_2 respectively

Note: Separate models for each pollutant, with 5 lag terms and interactions between each lag term and an indicator for prior heart disease, adjusted for temperature (5 lag terms covering days 0-28 inclusive), relative humidity (average of lags 0-3 days), day of week, influenza, RSV, and residual seasonality within calendar month strata (single sin/cos pair per conurbation)
CHD = coronary heart disease

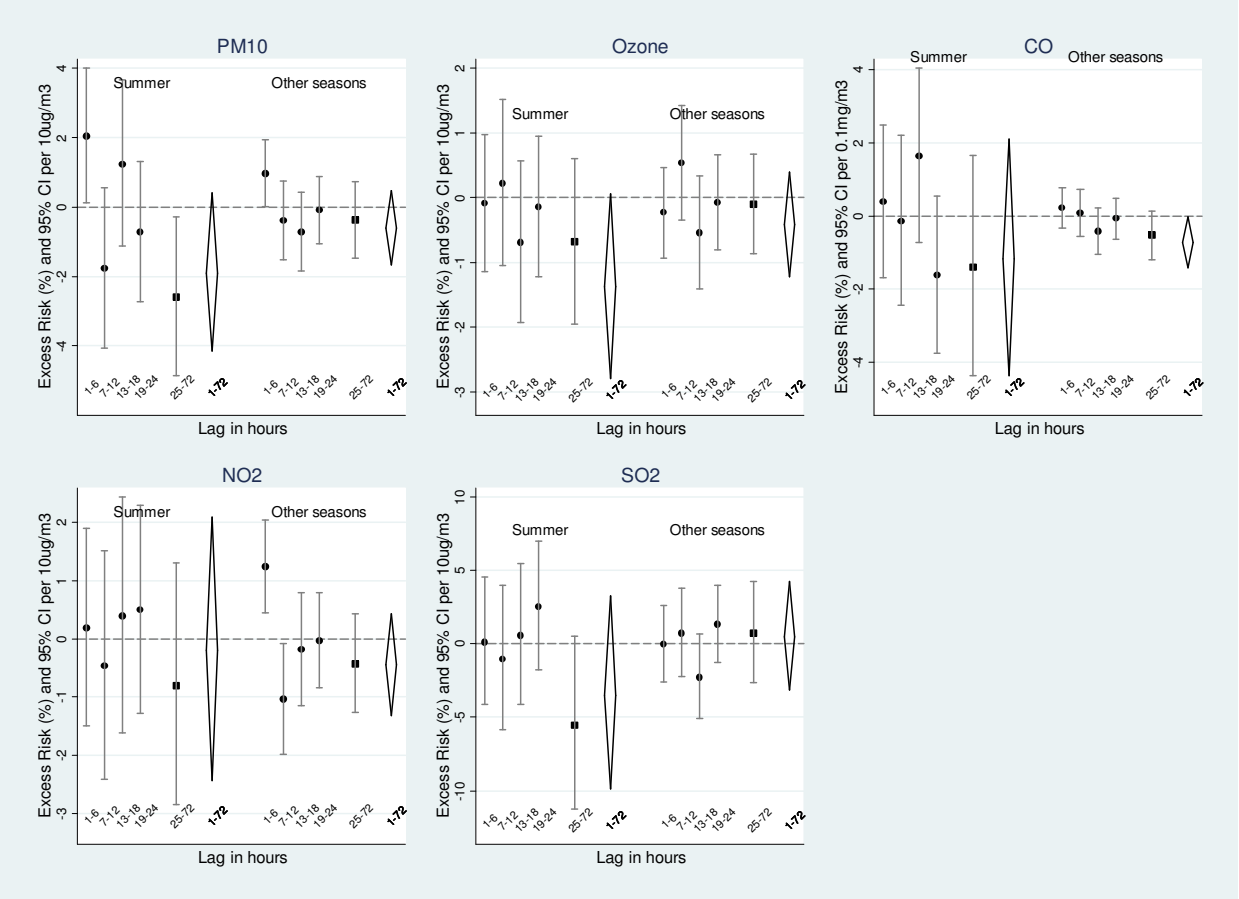
***Web Fig B**: Estimated excess risk of MI associated with pollution increases, stratified by smoking status*



p-interaction = 0.95, 0.73, 0.86, 0.82, 0.74 for PM_{10}, ozone, CO, NO_2, and SO_2 respectively

Note: Separate model for each pollutant, with 5 lag terms and interactions between each lag term and indicators for smoking status, adjusted for temperature (5 lag terms covering days 0-28 inclusive), relative humidity (average of lags 0-3 days), day of week, influenza, RSV, and residual seasonality within calendar month strata (single sin/cos pair per conurbation)
Σ(1-72) effect for each pollutant estimated by summing (on the log scale) regression coefficients for the 5 lag terms

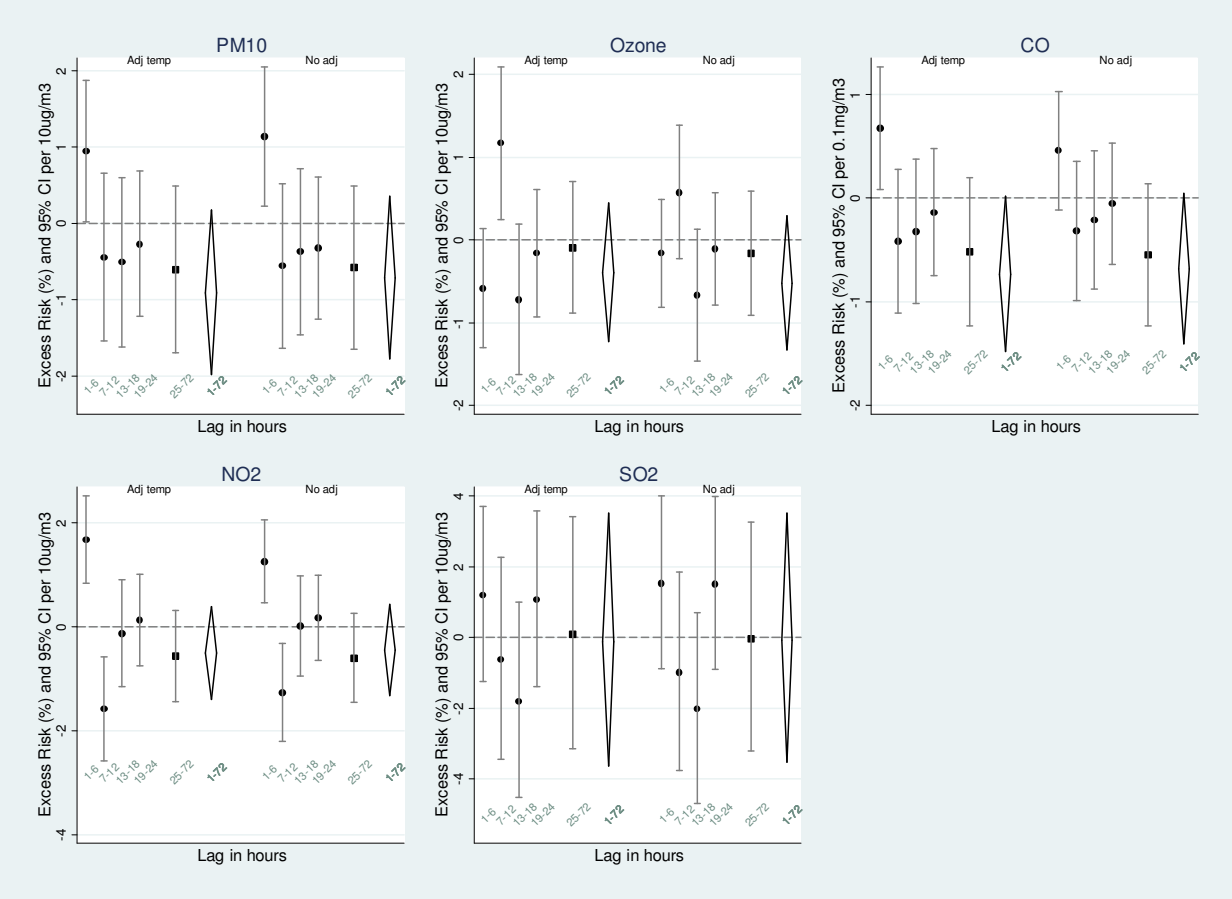
***Web Fig C**: Estimated excess risk of MI associated with pollution increases, stratified by season*



p-interaction = 0.33, 0.88, 0.56, 0.73, 0.47 for PM_{10}, ozone, CO, NO_2, and SO_2 respectively

Note: Separate model for each pollutant, with 5 lag terms and interactions between each lag term and an indicator for season, adjusted for temperature (5 lag terms covering days 0-28 inclusive), relative humidity (average of lags 0-3 days), day of week, influenza, RSV, and residual seasonality within calendar month strata (single sin/cos pair per conurbation)
Σ(1-72) effect for each pollutant estimated by summing (on the log scale) regression coefficients for the 5 lag terms

***Web Fig D**: The impact of adjusting for hourly temperature on the estimated excess risk of MI associated with pollution increases*



Note: Separate model for each pollutant, adjusted for daily mean temperature (5 lag terms covering days 0-28 inclusive), relative humidity (average of lags 0-3 days), day of week, influenza, RSV, and residual seasonality within calendar month strata (single sin/cos pair per conurbation)
Further adjustment for hourly temperature comprised 5 lag terms matching hourly pollution lags (1-6, 7-12, 13-18, 19-24, 25-72 hours)
Analysis was restricted to the 9 conurbations in which hourly temperature data were available
Adj temp = adjusted for hourly temperature; No adj = no adjustment for hourly temperature