WEB APPENDIX

Clinical data

Identification of cases for inclusion in MINAP 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.

Data on temperature and potential confounders

Multiple weather/pollution monitoring stations within a conurbation

Where 2 or more monitoring stations within a conurbation were available, temperature, relative humidity, and pollutant data from these multiple stations were combined into a single hourly series using the AIRGENE algorithm;[1] relative humidity data were arcsin-transformed before this step in order to recover an approximate normal distribution, and then back-transformed afterwards to a percentage scale.

Data on infectious disease levels for sensitivity analysis

As a measure of level of circulating viral infections (used in a sensitivity analysis), we obtained data on weekly consultation rates for influenza-like illness from the Royal College of General Practitioners Research and Surveillance Centre, Birmingham.[2] We generated a daily series for these data by linearly interpolating between the weekly rates. We also obtained daily counts of laboratory-confirmed influenza A and respiratory syncytial virus (RSV) from the UK Health Protection Agency.

Statistical analysis

Choosing between heat threshold models, and estimation of the threshold

To estimate the temperature threshold, we ran the model using every possible heat threshold in turn (in 1°C steps). At each possible threshold, the maximum likelihood estimates were found for all other parameters, and the log-likelihood was recorded, resulting in an evaluation of the profile likelihood for the threshold parameter. A 95% confidence region for the estimated threshold (T_h) included those threshold values T satisfying the criterion 2x(log-likelihood(T_h) – log-likelihood(T)) ≤ 3.84, based on comparison with a X_1^2 distribution.[3] We allowed for a threshold in each lag period individually, and then for all lag periods combined. The best overall threshold model was chosen based on minimizing the AIC (or, equivalently maximizing the model likelihood, since the total number of parameters estimated was constant throughout).

Post hoc analyses: Effect modification by time of day/night

We conducted an analysis to assess whether a heat effect with different characteristics or threshold might operate at times when temperatures rarely exceeded our estimated heat threshold temperature (i.e. at night). We fitted a model with non-linear terms for lag 1-6 hour temperature, and linear terms for other lags, but allowing separate short-lag effects for the periods 1am-midday and 1pm-midnight;

we chose this division of time because for events occurring in the hours 1pm-midnight, the 1-6 hour lagged temperature referred to temperature in the period 7am to 11pm, and exceeded our overall estimated threshold of 20℃ in 25% of observations, compared with less than 3% of observations at other times of day; we investigated other possible choices of day/night split but they produced less separation by this measure.

Table A: Estimated temperature-MI associations in sensitivity analyses

	OR for MI (per °C) and 95% CI						
	Lag period (hours)						
	1-6 (threshold at 20°C)	7-12	13-18	19-24	25-48	49-192	193-360
Main "final" model	1.019 (1.005 to 1.033)	1.002 (0.991 to 1.014)	1.011 (0.997 to 1.026)	0.989 (0.977 to 1.001)	0.991 (0.981 to 1.001)	0.996 (0.986 to 1.006)	0.991 (0.981 to 1.002)
Time symptom onset available	1.018 (0.999 to 1.037)	1.002 (0.986 to 1.017)	1.013 (0.994 to 1.033)	0.983 (0.966 to 0.999)	0.992 (0.978 to 1.005)	0.989 (0.976 to 1.003)	0.978 (0.965 to 0.992)
Corroborative evidence for MI	1.024 (1.009 to 1.039)	0.999 (0.988 to 1.011)	1.013 (0.998 to 1.028)	0.988 (0.976 to 1.001)	0.990 (0.980 to 1.001)	0.995 (0.984 to 1.005)	0.993 (0.982 to 1.004)
Robust standard errors	1.019 (1.005 to 1.033)	1.002 (0.991 to 1.014)	1.011 (0.997 to 1.026)	0.989 (0.977 to 1.001)	0.991 (0.981 to 1.001)	0.996 (0.986 to 1.006)	0.991 (0.981 to 1.002)
Restrict to largest 4 conurbations	1.020 (1.005 to 1.035)	1.003 (0.991 to 1.016)	1.009 (0.993 to 1.025)	0.993 (0.979 to 1.006)	0.990 (0.979 to 1.001)	0.992 (0.982 to 1.003)	0.990 (0.979 to 1.001)
Adjust for PM_{10}	1.017 (1.002 to 1.031)	1.003 (0.992 to 1.015)	1.011 (0.997 to 1.026)	0.991 (0.979 to 1.003)	0.992 (0.981 to 1.002)	0.999 (0.987 to 1.011)	0.985 (0.972 to 0.998)
Adjust for ozone	1.024 (1.009 to 1.040)	1.005 (0.993 to 1.017)	1.005 (0.990 to 1.021)	0.991 (0.978 to 1.004)	0.992 (0.981 to 1.002)	0.997 (0.987 to 1.007)	0.989 (0.979 to 1.000)
Adjust for influenza/RSV	1.019 (1.004 to 1.033)	1.002 (0.991 to 1.013)	1.011 (0.997 to 1.026)	0.989 (0.977 to 1.001)	0.991 (0.981 to 1.001)	0.995 (0.985 to 1.005)	0.991 (0.981 to 1.001)
Match on day of week	1.018 (1.002 to 1.034)	1.007 (0.994 to 1.020)	1.009 (0.993 to 1.025)	0.989 (0.975 to 1.002)	0.986 (0.975 to 0.998)	0.998 (0.988 to 1.008)	0.990 (0.980 to 1.001)

Note: All models adjusted for relative humidity, holiday, day of week, residual seasonality within calendar months (using a single harmonic Fourier series[4]), and for NO_2 except where an alternative pollutant (PM_{10} or ozone) is specified

Figure A: Distribution of MI times in individual conurbations and overall

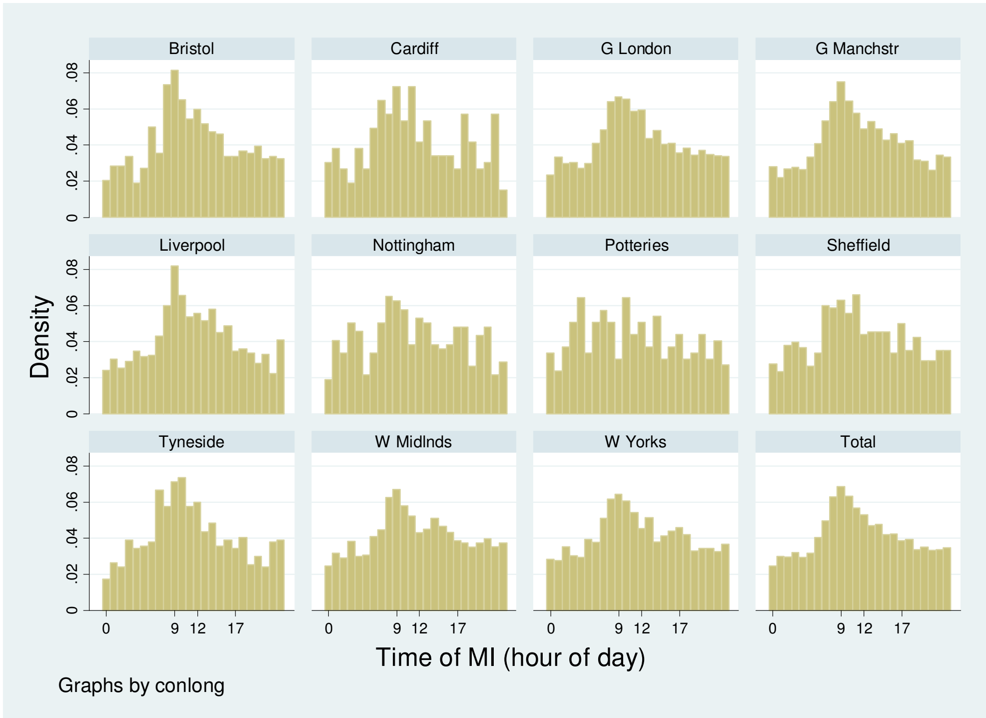
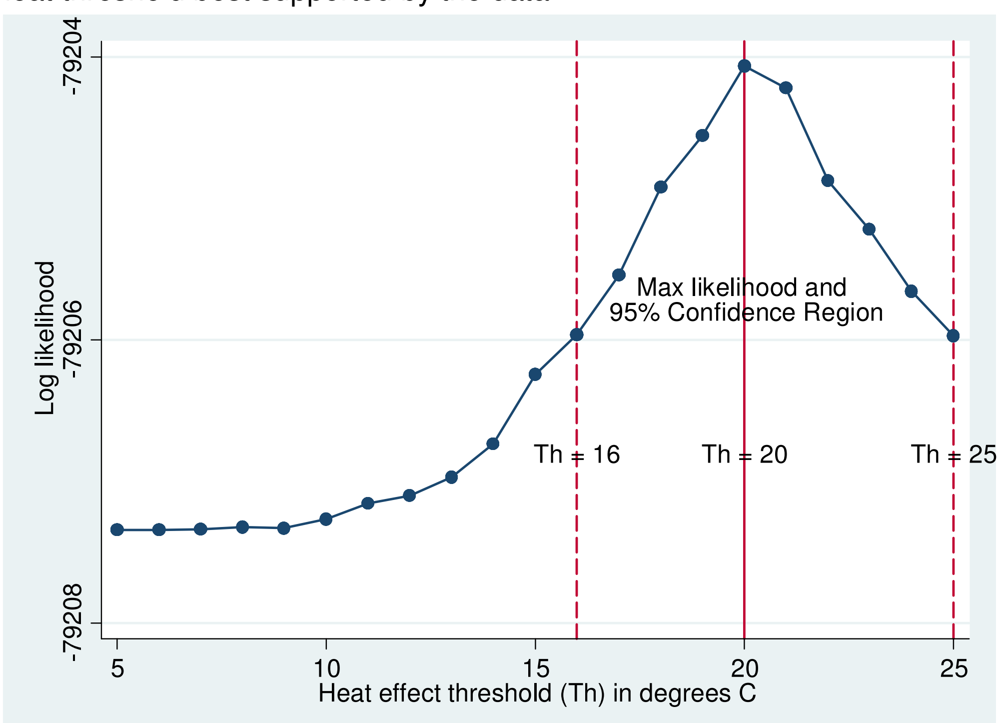
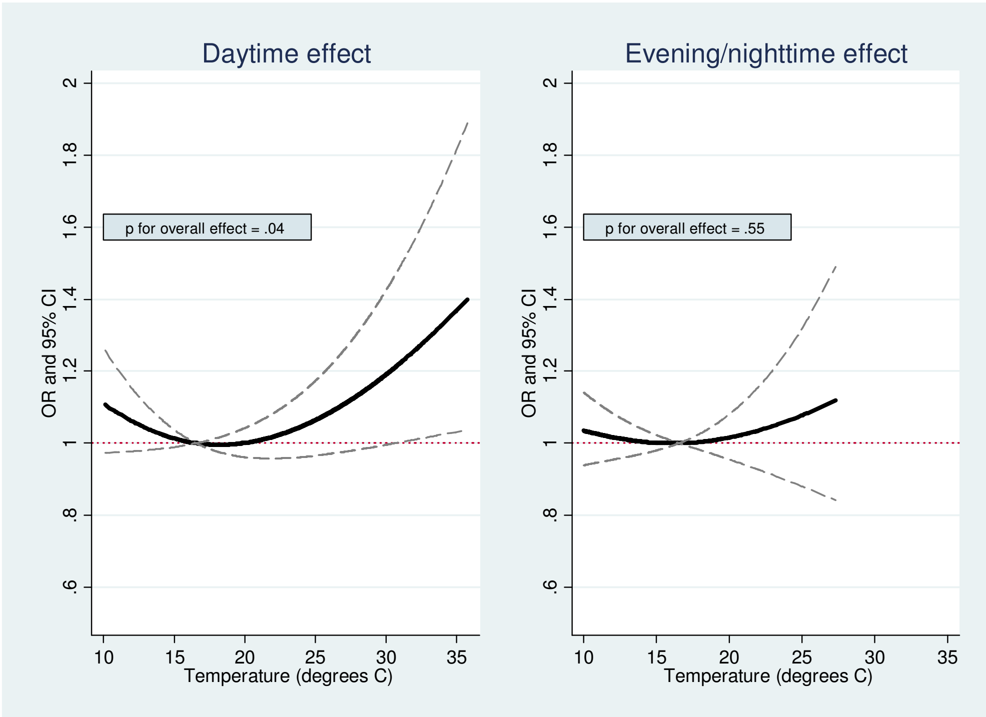


Figure B: Profile likelihood for lag 1-6 hours heat threshold showing the choice of heat threshold best supported by the data



Note: curve generated by fitting every possible threshold in turn (in 1℃ steps) and evaluating the model likelihood; models adjusted for linear temperature effects at longer lags, relative humidity, NO_2, holiday, day of week, and residual seasonality within calendar months (using a single harmonic Fourier series[4])

Figure C: Estimated 1-6 hour lagged temperature-MI association, by time of day/night



Note: "daytime" and "nighttime" effects include MIs occurring between 1pm-midnight, and 1am-midday respectively. In the "daytime" stratum, 1-6 hour lagged temperature referred to the interval 7am-11pm. Model adjusted for linear temperature effects at longer lags, relative humidity, NO_2, holiday, day of week, and residual seasonality within calendar months (using a single harmonic Fourier series[4])

Additional references for this appendix

1. Ruckerl R, Greven S, Ljungman P, Aalto P, Antoniades C, Bellander T, et al. Air pollution and inflammation (interleukin-6, C-reactive protein, fibrinogen) in myocardial infarction survivors. Environ Health Perspect. 2007; **115**(7): 1072-80.

2. Royal College of General Practitioners. The RCGP Research & Surveillance Centre (formerly the Birmingham Research Unit). [cited 2011 December]; Available from: http://www.rcgp.org.uk/clinical_and_research/rsc.aspx

3. Stryhn H, Christensen J. Confidence intervals by the profile likelihood method, with applications in veterinary epidemiology. International Symposia on Veterinary Epidemiology and Economics (ISVEE); 2003; Vina del Mar, Chile; 2003.

4. Woolhiser DA, Pegram GGS. Maximum likelihood estimation of Fourier coefficients to describe seasonal variation of parameters in stochastic daily precipitation models. Journal of Applied Meteorology. 1979; **18**: 34-42.