WEB APPENDIX

Case ascertainment

This study was approved by the IRB at the Beth Israel Deaconess Medical Center (BIDMC). We identified consecutive patients ≥21 years of age admitted to the BIDMC between April 1, 1999, and October 31, 2008, with neurologist-confirmed ischemic stroke and residing in the Boston metropolitan region. Patients with in-hospital strokes or transient ischemic attacks were excluded. Trained abstractors recorded data on patient demographics, presenting symptoms and medical history from medical records. As in previous studies (1), we restricted our analysis to patients who lived within 40 km of the air pollution monitoring site to reduce exposure error. This analysis was limited to dates when data on constituents are available (January 1, 2003 to October 31, 2008).

Exposure assessment

$PM_{2.5}$ and particle constituents. We obtained continuous measurements of $PM_{2.5}$ and daily (9AM-9AM) constituent concentrations from the Harvard–U.S. Environmental Protection Agency (EPA) Supersite in Boston, MA, located <1 km from the study site (2). $PM_{2.5}$ measured at this site is a strong proxy for personal exposure to ambient particles in communities surrounding Boston (3, 4). Where $PM_{2.5}$ data were missing (<10% of hourly measurements), levels were imputed using regression modeling, including a long-term time trend, day of week, hour of day, temperature, relative humidity, barometric pressure and nitrogen dioxide as predictors.

Covariates. Daily (9AM-9AM) meteorological data including temperature, relative humidity, and barometric pressure were calculated from the hourly surface observations of the National Weather Service First Order Station at Logan Airport.

Statistical analysis

We used the time-stratified case-crossover study design (5, 6) to assess the association between ischemic stroke onset and levels of constituents in the 24 hours preceding each event. In this design, each subject's exposure prior to a case-defining event (case period) is compared with his or her exposure during periods when the subject did not become a case (control period). $PM_{2.5}$ levels during the 24 hours preceding each event were compared to levels on other days of the same month and same day of the week as the case period. This design has been shown to effectively control for seasonality, time-trends, and chronic and slowly-varying potential confounders (7).

In all analyses, constituents were assessed relative to the time of stroke symptom onset. When the date of stroke onset is known but the time cannot be estimated (n=123), we assumed that symptom onset occurred at 9AM. We estimated the level of each constituent by taking a weighted average of the levels from the two days containing the 24 hours prior to stroke onset.

We performed conditional logistic regression stratifying on each hospitalization to obtain estimates of odds ratios (OR) and 95 percent confidence intervals (CI) associated with an interquartile-range increase in each constituent in separate models. Because of the sampling strategy, these OR's are unbiased estimates of the incidence rate ratio (IRR). We controlled for ambient temperature and dew point temperature using natural cubic splines (3 degrees of freedom each) and barometric pressure (linear continuous variable). We calculated estimates separately for the warm (April to November) and cold season (October to March). Analyses were performed using the R statistical package (R v 2.8.1) (8).

References

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Web Table 1. Incidence Rate Ratio and 95% Confidence Intervals for the Association between an IQR Increase in Constituent Proportion and Ischemic Stroke Onset in the following 24 Hours.

Constituent	Incidence Rate Ratio	95% Confidence Interval
Silicon	0	0, 9.16E+03
Chlorine	0.67	0, 1.04E+03
Potassium	6.03	0, 3.22E+05
Manganese	0	3.31E-322, 9.48E+85
Zinc	0	0, 2.27E+23
Sodium	0	0, 6.10
Copper	0	0, 7.45E+106
Aluminum	0	0, 2.88E+12
Calcium	0	0, 1.03E+13
Bromine	9.814E+22	0, 1.23E+293
Lead	1.371E+09	0, 3.51E+192
Selenium	0	0, 3.03E+287
Titanium	0	0, 1.67E+168
Vanadium	7.535E+55	0, 3.18E+176
Iron	0	0, 9.77E+06
Sulfur	0.53	0, 21.74
Nickel	3.37E+84	0, 2.33E+264
Black Carbon	0.761	0.07, 8.55

Web Table 2. Estimates for the Association between an IQR Increase in Constituent Concentration and Ischemic Stroke Onset in the following 24 Hours and the Interaction between Constituent and $PM_{2.5}$.

Constituent	Model Term	Parameter Estimate	Standard Error	P	IRR	95% CI
Silicon	$PM_{2.5}$	0.171	0.083	0.04	1.187	1.008, 1.398
	Constituent	-0.046	0.105	0.66	0.955	0.778 1.173
	$PM_{2.5}$xConstituent	-0.013	0.040	0.74	0.987	0.912, 1.068
Chlorine	$PM_{2.5}$	0.108	0.063	0.088	1.114	0.984, 1.260
	Constituent	-0.003	0.006	0.64	0.997	0.985, 1.009
	$PM_{2.5}$xConstituent	0.003	0.004	0.38	1.003	0.996, 1.011
Potassium	$PM_{2.5}$	0.134	0.062	0.032	1.143	1.011, 1.291
	Constituent	0.017	0.031	0.59	1.017	0.957, 1.080
	$PM_{2.5}$xConstituent	-0.005	0.009	0.59	0.995	0.977, 1.013
Manganese	$PM_{2.5}$	0.078	0.096	0.42	1.081	0.896, 1.305
	Constituent	-0.096	0.107	0.37	0.908	0.737, 1.120
	$PM_{2.5}$xConstituent	0.039	0.049	0.43	1.039	0.944, 1.144
Zinc	$PM_{2.5}$	0.123	0.089	0.17	1.131	0.950, 1.347
	Constituent	-0.072	0.082	0.38	0.931	0.793, 1.093
	$PM_{2.5}$xConstituent	0.016	0.032	0.61	1.016	0.955, 1.081
Sodium	$PM_{2.5}$	0.198	0.100	0.048	1.219	1.002, 1.483
	Constituent	-0.099	0.123	0.42	0.905	0.712, 1.151
	$PM_{2.5}$xConstituent	-0.009	0.043	0.84	0.992	0.911, 1.079
Copper	$PM_{2.5}$	0.117	0.065	0.073	1.124	0.989, 1.278
	Constituent	-0.020	0.073	0.78	0.980	0.849, 1.131
	$PM_{2.5}$xConstituent	0.008	0.023	0.73	1.008	0.964, 1.054
Aluminum	$PM_{2.5}$	0.164	0.090	0.07	1.178	0.986, 1.406
	Constituent	-0.029	0.103	0.78	0.971	0.794, 1.188
	$PM_{2.5}$xConstituent	-0.007	0.034	0.84	0.993	0.928, 1.062
Calcium	$PM_{2.5}$	0.231	0.126	0.066	1.260	0.985, 1.613
	Constituent	0.051	0.120	0.67	1.053	0.832, 1.331
	$PM_{2.5}$xConstituent	-0.047	0.055	0.39	0.954	0.856, 1.063
Bromine	$PM_{2.5}$	0.216	0.103	0.036	1.241	1.014, 1.517
	Constituent	0.068	0.111	0.54	1.070	0.861, 1.330
	$PM_{2.5}$xConstituent	-0.049	0.049	0.32	0.952	0.865, 1.048
Lead	$PM_{2.5}$	0.136	0.086	0.11	1.146	0.969, 1.355
	Constituent	0.014	0.108	0.89	1.014	0.821, 1.253

	$PM_{2.5}$xConstituent	-0.007	0.045	0.87	0.993	0.909, 1.084
Selenium	$PM_{2.5}$	0.082	0.074	0.27	1.085	0.939, 1.254
	Constituent	-0.026	0.082	0.75	0.974	0.830, 1.143
	$PM_{2.5}$xConstituent	0.026	0.031	0.4	1.027	0.966, 1.091
Titanium	$PM_{2.5}$	0.156	0.092	0.089	1.169	0.977, 1.400
	Constituent	0.064	0.127	0.62	1.066	0.830, 1.368
	$PM_{2.5}$xConstituent	-0.024	0.046	0.61	0.977	0.892, 1.069
Vanadium	$PM_{2.5}$	0.101	0.082	0.21	1.107	0.943, 1.299
	Constituent	0.042	0.079	0.6	1.043	0.893, 1.218
	$PM_{2.5}$xConstituent	-0.00001	0.031	1.000	1.000	0.941, 1.063
Iron	$PM_{2.5}$	0.122	0.129	0.34	1.130	0.878, 1.455
	Constituent	0.011	0.114	0.92	1.011	0.808, 1.265
	$PM_{2.5}$xConstituent	-0.0002	0.053	1.000	1.000	0.902, 1.109
Sulfur	$PM_{2.5}$	0.171	0.128	0.18	1.186	0.923, 1.524
	Constituent	0.033	0.139	0.81	1.034	0.787, 1.359
	$PM_{2.5}$xConstituent	-0.016	0.026	0.53	0.984	0.935, 1.035
Nickel	$PM_{2.5}$	0.107	0.083	0.2	1.113	0.945, 1.310
	Constituent	0.082	0.103	0.43	1.085	0.887, 1.328
	$PM_{2.5}$xConstituent	-0.008	0.039	0.84	0.992	0.920, 1.070
Black Carbon	$PM_{2.5}$	0.020	0.122	0.87	1.020	0.804, 1.295
	Constituent	0.186	0.126	0.14	1.205	0.942, 1.542
	$PM_{2.5}$xConstituent	-0.003	0.045	0.94	0.997	0.913, 1.088

Abbreviations: CI, confidence interval; IRR, incidence rate ratio