Associations between environmental factors and hospital admissions for sickle cell disease

Frédéric B. Piel,[1,2] Sanjay Tewari,[3] Valentine Brousse,[4] Antonis Analitis,[5] Anna Font,[6] Stephan Menzel,[3] Subarna Chakravorty,[3] Swee Lay Thein,[3,7] Baba Inusa,[8] Paul Telfer,[9] Mariane de Montalembert,[4] Gary W. Fuller,[6] Klea Katsouyanni[5,6] and David C. Rees[3]

[1]Department of Epidemiology and Biostatistics, MRC-PHE Centre for Environment and Health, School of Public Health, Imperial College London, UK; [2]Department of Zoology, University of Oxford, UK; [3]Department of Molecular Haematology, King's College London School of Medicine, King's College Hospital, UK; [4]Reference Centre for Sickle-Cell Disease, Pediatric Department, Hôpital Universitaire Necker-Enfants Malades, APHP, Paris, Université Paris Descartes, France; [5]Department of Hygiene, Epidemiology and Medical Statistics, Medical School, National and Kapodistrian University of Athens, Greece; [6]Environmental Research Group, MRC-PHE Centre for Environment and Health, King's College London, UK; [7]National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, MD, USA; [8]Department of Paediatric Haematology, Evelina Children's Hospital, King's College London, UK and [9]Department of Paediatric Haematology and Oncology, Barts Health NHS Trust, Royal London Hospital, UK

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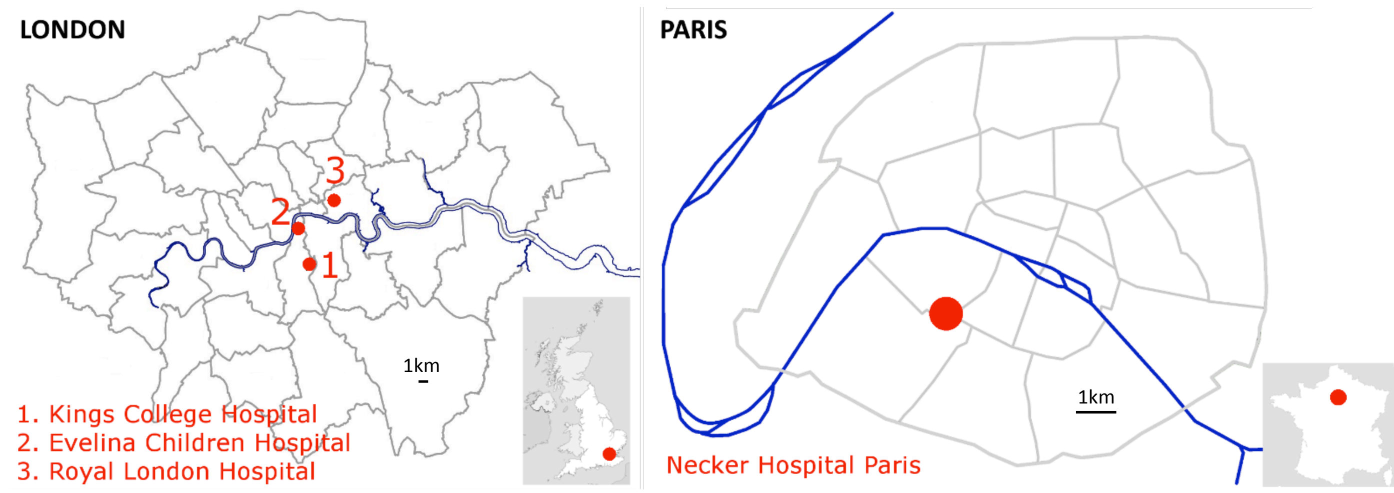
Correspondence: f.piel@imperial.ac.uk

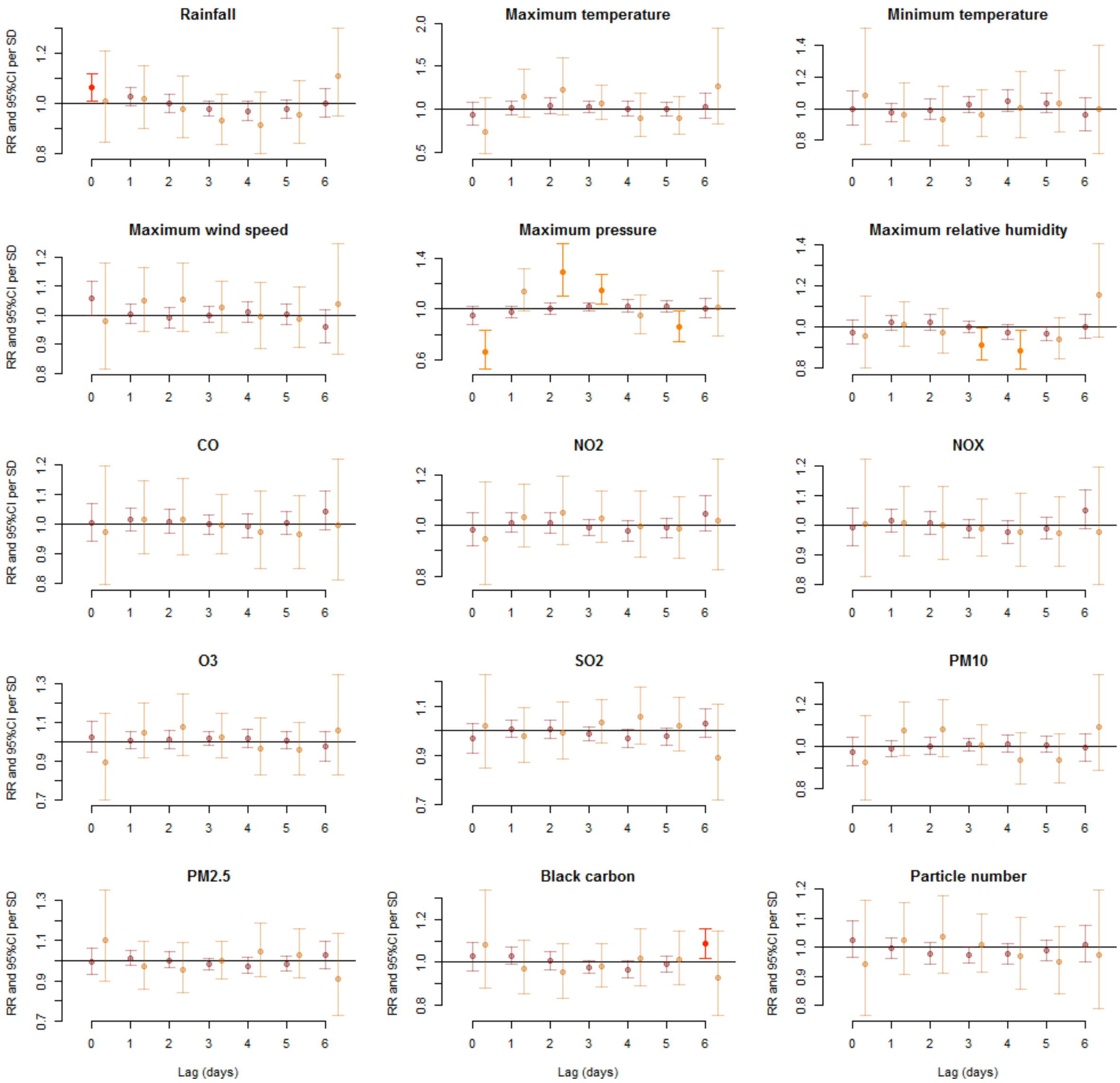
Associations between environmental factors and hospital admissions for sickle cell disease – Supplementary Information

Frédéric B. Piel, Sanjay Tewari, Valentine Brousse, Antonis Analitis, Anna Font, Stephan Menzel, Subarna Chakravorty, Swee Lay Thein, Baba Inusa, Paul Telfer, Mariane de Montalembert, Gary W. Fuller, Klea Katsouyanni & David C. Rees

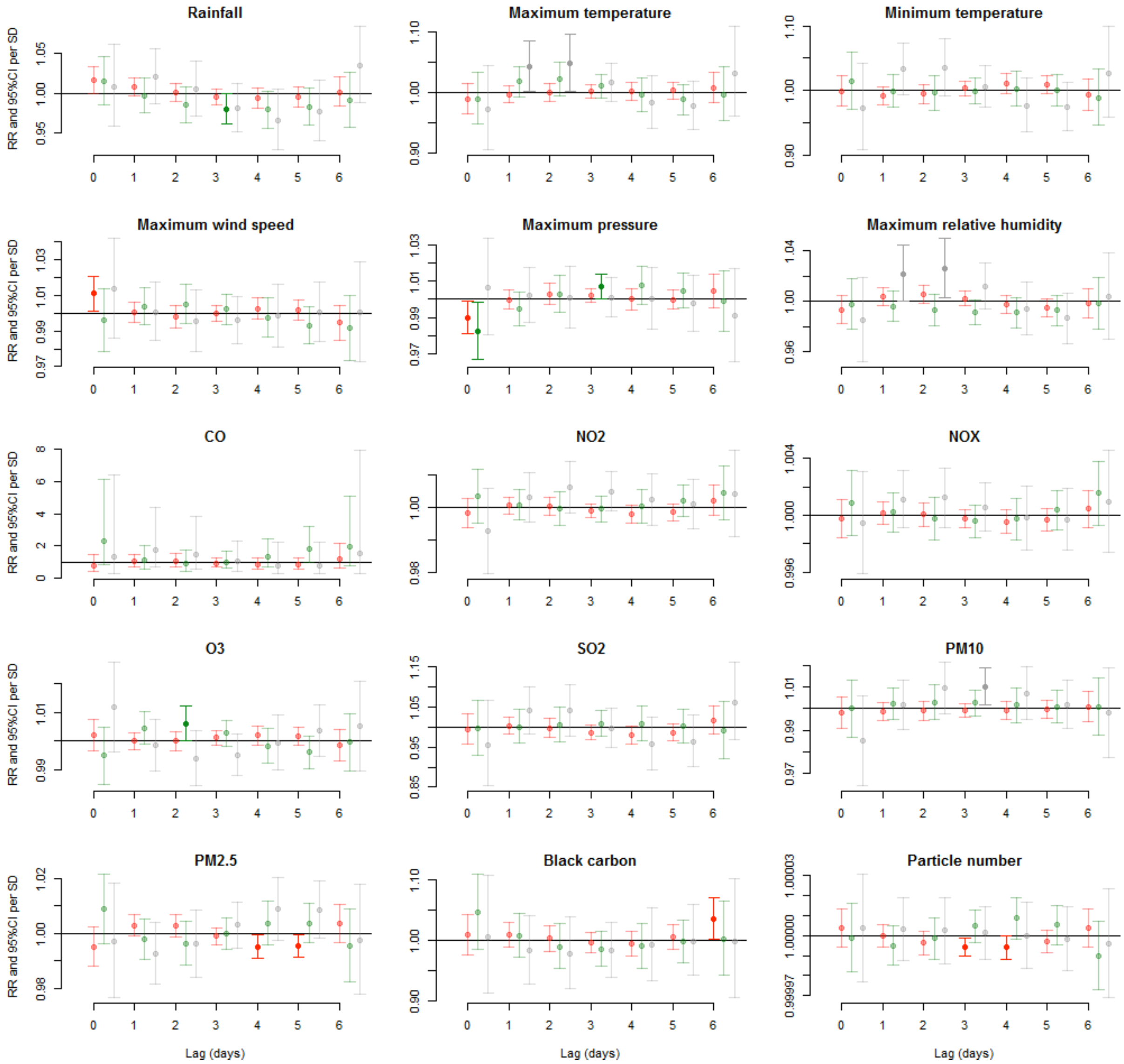
Supplementary Figure 1. Map of the hospitals included in this study, in London (left) and Paris (right).



Supplementary Figure 2. Lag plots of relative risks (RR) and 95% confidence intervals (CI) per standard deviation (SD) increase in 15 exposure variables (6 for meteorological conditions and 9 for air quality) based on distributed lag non-linear models (DLNM) with all lags (0-6 days) modelled together using a polynomial constraint for HbSS (red) and HbSC (orange) hospital admissions in London between 1st January 2008 and 31st December 2012. Statistically significant risks are shown in brighter colours.



Supplementary Figure 3. Lag plots of relative risks (RR) and 95% confidence intervals (CI) per standard deviation (SD) increase in 15 exposure variables (6 for meteorological conditions and 9 for air quality) based on distributed lag non-linear models (DLNM) with all lags (0-6 days) modelled together using a polynomial constraint for sickle cell disease hospital admissions in London for pain (red), fever (green) and acute chest syndrome (grey) between 1st January 2008 and 31st December 2012. Statistically significant risks are shown in brighter colours.



Supplementary Table 1. Number of monitoring stations with more than 80% of records available, root mean squared error (RMSE) and normalised root mean square error (NRMSE) associated with the expectation–maximization imputation algorithm for multiple-exposure normal time-series, based on cross-validation using a left-out sample of 100 daily records, in London and Paris over the 5-year study period (1st January 2008 – 31st December 2012).

			CO	**NO2**	**NOX**	**O3**	**SO2**	**PM10**	**PM2.5**
London	Background	# of stations included	3 (out of 10)	9 (out of 37)	9 (out of 37)	5 (out of 20)	3 (out of 16)	0 (out of 0)	0 (out of 0)
		RMSE (%)	0.09	6.13	14.43	4.95	1.8	NA	NA
		NRMSE (%)	7.32	7.02	5.85	5.96	15.09	NA	NA
	Roadside	# of stations included	4 (out of 11)	21 (out of 76)	21 (out of 76)	6 (out of 13)	2 (out of 15)	16 (out of 71)	1 (out of 12)
		RMSE (%)	0.13	8.78	32.04	5.54	2.84	4.75	NA
		NRMSE (%)	14.37	7.77	6.65	7.00	16.47	7.41	NA
Paris		# of stations included	4 (out of 10)	32 (out of 46)	31 (out of 45)	19 (out of 29)	0 (out of 11)	13 (out of 29)	4 (out of 8)
		RMSE (%)	160.9	6.00	16.03	4.28	NA	3.61	3.57
		NRMSE (%)	11.46	8.75	9.2	4.77	NA	4.04	5.53

Supplementary Table 2. Relative risks (RR) and 95% confidence intervals (CI) from the generalized additive models (GAM) for sickle cell disease admissions and various environmental factors in London and Paris between 1st January 2008 and 31st December 2012. Exposure factors associated to increased/reduced relative risks are shown in red/blue, respectively. The number of admissions falling into each subgroup is shown as N. ACS = Acute chest syndrome.

City	Genotype	Exposure variable	Reason for admission														
			All			Pain			Fever			ACS			Other		
			RR	CI Low	CI Up	RR	CI Low	CI Up	RR	CI Low	CI Up	RR	CI Low	CI Up	RR	CI Low	CI Up
London	SCD	N	1472			934			300			108			130		
		Rainfall	**1.06**	**1.01**	**1.12**	**1.07**	**1.01**	**1.14**	1.05	0.95	1.18	1.02	0.84	1.23	1.08	0.92	1.26
		Maximum temperature	0.99	0.88	1.11	0.95	0.83	1.09	1.08	0.85	1.38	1.17	0.79	1.73	0.93	0.65	1.35
		Minimum temperature	1.01	0.91	1.11	0.98	0.87	1.10	1.06	0.85	1.31	1.02	0.73	1.43	1.07	0.78	1.48
		Maximum wind speed	1.06	1.00	1.12	**1.08**	**1.01**	**1.16**	0.98	0.87	1.11	1.05	0.87	1.27	1.03	0.86	1.24
		Maximum pressure	**0.93**	**0.88**	**0.99**	**0.93**	**0.87**	**1.00**	**0.84**	**0.75**	**0.95**	1.07	0.88	1.31	1.08	0.88	1.31
		Maximum relative humidity	0.97	0.91	1.02	0.96	0.90	1.03	0.95	0.84	1.08	0.96	0.78	1.18	1.04	0.86	1.26
		CO	1.00	0.94	1.07	0.96	0.89	1.04	1.12	0.99	1.26	1.09	0.89	1.32	0.93	0.73	1.18
		NO_2	0.99	0.93	1.06	0.97	0.90	1.05	1.08	0.94	1.24	0.97	0.77	1.21	0.97	0.78	1.20
		NO_X	0.99	0.93	1.06	0.98	0.90	1.05	1.05	0.92	1.20	1.03	0.84	1.27	0.94	0.75	1.17
		O_3	1.03	0.96	1.11	1.05	0.97	1.14	0.98	0.84	1.15	1.13	0.89	1.43	0.96	0.76	1.22
		SO_2	0.97	0.91	1.03	0.98	0.92	1.06	0.99	0.86	1.13	0.94	0.75	1.17	0.83	0.64	1.06
		PM_{10}	0.97	0.91	1.03	0.96	0.89	1.03	1.04	0.91	1.19	0.91	0.73	1.14	0.93	0.75	1.17
		$PM_{2.5}$	1.00	0.94	1.06	0.96	0.90	1.03	1.08	0.95	1.22	0.92	0.74	1.14	**1.22**	**1.02**	**1.46**
		Black carbon	1.04	0.97	1.10	1.03	0.95	1.11	1.09	0.95	1.25	1.01	0.81	1.26	1.03	0.84	1.26
		Particle number	1.02	0.96	1.08	1.03	0.96	1.11	0.98	0.86	1.12	1.03	0.83	1.27	1.03	0.85	1.25
	HbSS	N	1350			859			268			104			119		
		Rainfall	**1.07**	**1.02**	**1.13**	**1.07**	**1.00**	**1.14**	1.06	0.95	1.19	1.04	0.86	1.25	1.10	0.95	1.29
		Maximum temperature	1.00	0.89	1.12	0.93	0.81	1.07	1.12	0.87	1.45	1.26	0.84	1.88	0.97	0.66	1.42
		Minimum temperature	1.01	0.91	1.12	0.97	0.86	1.09	1.07	0.85	1.35	1.08	0.76	1.51	1.12	0.80	1.57
		Maximum wind speed	**1.06**	**1.00**	**1.12**	**1.09**	**1.02**	**1.16**	0.98	0.86	1.11	1.07	0.89	1.30	1.06	0.88	1.27
		Maximum pressure	**0.94**	**0.89**	**1.00**	0.93	0.87	1.00	**0.86**	**0.76**	**0.98**	1.09	0.89	1.33	1.06	0.86	1.30
		Maximum relative humidity	0.97	0.91	1.03	0.96	0.90	1.04	0.95	0.83	1.08	0.97	0.79	1.20	1.04	0.85	1.27
		CO	1.00	0.94	1.07	0.96	0.89	1.05	**1.14**	**1.01**	**1.30**	1.07	0.88	1.32	0.90	0.70	1.16
		NO_2	0.99	0.92	1.06	0.97	0.90	1.06	1.07	0.92	1.24	0.95	0.75	1.20	0.96	0.77	1.21
		NO_X	0.99	0.93	1.06	0.98	0.90	1.06	1.06	0.91	1.22	1.01	0.82	1.26	0.92	0.73	1.17
		O_3	1.04	0.97	1.12	1.05	0.97	1.15	0.99	0.84	1.17	1.17	0.91	1.49	0.98	0.77	1.26
		SO_2	0.97	0.91	1.03	0.98	0.91	1.06	0.98	0.85	1.14	0.94	0.75	1.18	0.85	0.66	1.09
		PM_{10}	0.96	0.90	1.03	0.95	0.88	1.03	1.05	0.91	1.21	0.90	0.72	1.13	0.92	0.72	1.17
		$PM_{2.5}$	0.99	0.94	1.06	0.95	0.88	1.02	1.09	0.95	1.24	0.93	0.75	1.16	**1.24**	**1.03**	**1.49**
		Black carbon	1.03	0.97	1.10	1.03	0.95	1.12	1.07	0.93	1.24	0.98	0.78	1.23	1.03	0.84	1.27
		Particle number	1.02	0.96	1.09	1.03	0.96	1.12	1.00	0.87	1.15	1.01	0.81	1.25	1.02	0.84	1.25
	HbSC	N	122			75			32			4			11		
		Rainfall	1.01	0.85	1.22	1.09	0.89	1.33	0.95	0.66	1.39	/	/	/	/	/	/
		Maximum temperature	0.95	0.66	1.36	1.17	0.74	1.84	0.83	0.38	1.84	/	/	/	/	/	/
		Minimum temperature	0.99	0.73	1.36	1.13	0.76	1.70	0.95	0.52	1.72	/	/	/	/	/	/
		Maximum wind speed	0.99	0.82	1.19	1.03	0.81	1.30	0.97	0.67	1.39	/	/	/	/	/	/
		Maximum pressure	0.85	0.70	1.02	0.88	0.69	1.11	0.75	0.52	1.08	/	/	/	/	/	/
		Maximum relative humidity	0.95	0.78	1.15	0.94	0.74	1.19	0.93	0.62	1.40	/	/	/	/	/	/
		CO	0.99	0.80	1.21	0.95	0.71	1.26	1.01	0.69	1.46	/	/	/	/	/	/
		NO_2	1.00	0.81	1.24	0.91	0.69	1.20	1.25	0.84	1.86	/	/	/	/	/	/
		NO_X	1.02	0.84	1.24	0.98	0.75	1.28	1.07	0.77	1.49	/	/	/	/	/	/
		O_3	0.93	0.73	1.18	1.01	0.76	1.36	0.82	0.49	1.36	/	/	/	/	/	/
		SO_2	1.00	0.83	1.22	1.04	0.82	1.30	1.13	0.80	1.59	/	/	/	/	/	/
		PM_{10}	1.01	0.82	1.24	1.03	0.80	1.32	1.05	0.68	1.64	/	/	/	/	/	/
		$PM_{2.5}$	1.08	0.89	1.30	1.14	0.91	1.43	1.09	0.72	1.65	/	/	/	/	/	/
		Black carbon	1.06	0.86	1.32	0.97	0.74	1.28	1.24	0.85	1.83	/	/	/	/	/	/
		Particle number	0.96	0.78	1.20	0.97	0.74	1.28	0.83	0.55	1.26	/	/	/	/	/	/
Paris	HbSS	N	347			201			51			12			83		
		Rainfall	0.98	0.87	1.11	1.02	0.88	1.19	0.64	0.37	1.11	/	/	/	1.02	0.82	1.27
		Maximum temperature	0.80	0.62	1.01	0.75	0.55	1.02	0.94	0.50	1.77	/	/	/	0.84	0.52	1.36
		Minimum temperature	0.85	0.69	1.06	**0.75**	**0.57**	**0.99**	0.93	0.53	1.63	/	/	/	0.96	0.63	1.45
		Maximum wind speed	1.02	0.91	1.14	1.01	0.88	1.17	0.99	0.75	1.32	/	/	/	1.01	0.81	1.27
		Maximum pressure	0.98	0.88	1.10	0.94	0.81	1.08	1.12	0.84	1.50	/	/	/	1.12	0.89	1.40
		Maximum relative humidity	1.07	0.93	1.22	1.11	0.93	1.32	0.87	0.63	1.21	/	/	/	0.98	0.75	1.28
		CO	0.92	0.80	1.05	0.93	0.78	1.11	1.05	0.77	1.43	/	/	/	0.81	0.61	1.09
		NO_2	0.92	0.79	1.06	0.96	0.79	1.15	1.09	0.77	1.55	/	/	/	0.77	0.57	1.05
		NO_x	0.92	0.80	1.06	0.95	0.80	1.13	1.01	0.74	1.39				0.85	0.63	1.13
		O_3	1.04	0.89	1.23	1.02	0.82	1.25	1.34	0.90	1.99	/	/	/	1.07	0.78	1.48
		PM_{10}	0.97	0.85	1.09	1.03	0.89	1.20	1.09	0.82	1.43	/	/	/	0.78	0.59	1.03
		$PM_{2.5}$	0.97	0.86	1.10	1.05	0.90	1.22	1.04	0.78	1.38	/	/	/	0.77	0.58	1.02

Supplementary Table 3. Relative risks (RR) from the distributed lag non-linear models (DLNM) for sickle cell disease admissions and various environmental factors, at lags up to 6 days, in London and Paris between 1st January 2008 and 31st December 2012. Statistically significant RRs are highlighted in bold. Exposure factors associated to increased/reduced relative risks are shown in red/blue, respectively.

City	Exposure	Lag (days)						
		0	1	2	3	4	5	6
London	Rainfall	**1.06**	1.03	1.00	0.98	0.97	0.98	1.00
	Maximum temperature	0.94	1.02	1.04	1.03	1.00	1.00	1.03
	Minimum temperature	1.00	0.98	0.99	1.03	1.05	1.04	0.96
	Maximum wind speed	1.06	1.00	0.99	1.00	1.01	1.00	0.96
	Maximum pressure	0.95	0.98	1.00	1.02	1.03	1.02	1.01
	Maximum relative humidity	0.97	1.02	1.02	1.00	0.97	0.97	1.00
	CO	1.00	1.01	1.01	1.00	0.99	1.00	1.04
	NO_2	0.98	1.01	1.01	0.99	0.98	0.99	1.05
	NO_X	0.99	1.01	1.01	0.99	0.98	0.99	1.05
	O_3	1.03	1.01	1.01	1.02	1.02	1.01	0.97
	SO_2	0.97	1.01	1.01	0.99	0.97	0.98	1.03
	PM_{10}	0.97	0.99	1.00	1.01	1.01	1.01	0.99
	$PM_{2.5}$	1.00	1.01	1.00	0.99	0.97	0.98	1.03
	Black carbon	1.03	1.03	1.01	0.98	0.97	0.99	**1.08**
	Particle number	1.03	1.00	0.98	0.97	0.98	0.99	1.01
Paris	Rainfall	0.99	1.01	1.02	1.01	1.00	0.97	0.94
	Maximum temperature	0.86	0.98	0.98	0.92	0.88	0.89	1.05
	Minimum temperature	0.97	0.99	0.96	0.92	0.89	0.90	0.97
	Maximum wind speed	1.00	1.04	1.06	**1.08**	1.06	1.02	0.94
	Maximum pressure	0.98	1.02	1.01	0.98	0.95	0.95	1.02
	Maximum relative humidity	1.09	1.00	0.99	1.00	1.00	0.97	0.88
	CO	0.93	0.97	0.97	0.95	0.95	1.00	**1.14**
	NO_2	0.94	0.95	0.96	0.97	0.98	1.02	1.08
	NO_x	0.91	0.99	1.00	0.98	0.96	0.98	1.10
	O_3	1.06	1.02	1.00	0.99	0.99	0.98	0.97
	PM_{10}	0.99	0.99	0.97	0.95	0.96	0.99	1.09
	$PM_{2.5}$	1.00	0.97	0.96	0.96	0.98	1.01	1.05

Supplementary Table 4. Relative risks and 95% confidence intervals from the time-series case-crossover generalized additive models (GAM) for sickle cell disease admissions and various environmental factors in London and Paris between 1st January 2008 and 31st December 2012. Exposure factors associated to increased/reduced relative risks are shown in red/blue, respectively. The number of admissions falling into each subgroup is shown as N. ACS = Acute chest syndrome.

City	Genotype	Exposure variable	Reason for admission														
			ALL			PAIN			FEVER			ACS			OTHER		
			RR	Min	Max	RR	Min	Max	RR	Min	Max	RR	Min	Max	RR	Min	Max
London	SS	N		1350			859			268			104			119	
		Rainfall	**1.10**	**1.03**	**1.17**	**1.12**	**1.04**	**1.21**	1.04	0.91	1.19	1.10	0.86	1.41	1.12	0.91	1.38
		Maximum temperature	0.93	0.81	1.06	0.84	0.71	0.99	1.19	0.88	1.61	1.19	0.75	1.90	0.88	0.56	1.38
		Minimum temperature	0.99	0.88	1.11	0.94	0.81	1.08	1.14	0.88	1.48	1.03	0.68	1.58	1.03	0.70	1.52
		Maximum wind speed	**1.07**	**1.00**	**1.15**	**1.10**	**1.01**	**1.19**	0.94	0.81	1.09	1.12	0.88	1.43	1.18	0.94	1.49
		Maximum pressure	**0.91**	**0.84**	**0.97**	**0.90**	**0.82**	**0.98**	0.87	0.74	1.02	0.96	0.76	1.22	0.99	0.76	1.29
		Maximum relative humidity	0.96	0.89	1.03	0.96	0.88	1.05	0.97	0.82	1.14	0.96	0.75	1.23	0.94	0.72	1.21
		CO	0.99	0.91	1.07	0.95	0.85	1.05	1.08	0.93	1.25	1.20	0.93	1.54	0.79	0.56	1.11
		NO_2	0.96	0.88	1.05	0.95	0.86	1.06	1.02	0.84	1.23	1.02	0.75	1.38	0.87	0.66	1.15
		NO_X	0.97	0.90	1.06	0.96	0.87	1.06	1.01	0.85	1.21	1.20	0.91	1.58	0.82	0.62	1.09
		O_3	1.07	0.98	1.18	1.09	0.98	1.21	0.99	0.80	1.22	1.15	0.83	1.58	1.11	0.82	1.49
		SO_2	0.95	0.88	1.03	0.97	0.89	1.06	0.95	0.78	1.16	1.00	0.79	1.26	0.78	0.58	1.05
		PM_{10}	0.95	0.87	1.03	0.91	0.82	1.01	1.12	0.93	1.35	0.97	0.71	1.32	0.86	0.65	1.14
		$PM_{2.5}$	0.99	0.92	1.06	0.93	0.85	1.02	1.15	0.97	1.37	0.94	0.73	1.21	1.15	0.92	1.45
		Black carbon	1.03	0.95	1.11	1.01	0.92	1.12	1.06	0.89	1.27	0.92	0.68	1.24	1.10	0.85	1.43
		Particle matter	0.96	0.89	1.04	0.96	0.87	1.06	0.94	0.79	1.12	1.02	0.77	1.34	0.93	0.71	1.22
	SC	N		122			75			32			4			11	
		Rainfall	1.04	0.83	1.32	1.13	0.87	1.46	1.02	0.57	1.82	/	/	/	/	/	/
		Maximum temperature	0.86	0.55	1.35	1.00	0.57	1.75	1.04	0.40	2.71	/	/	/	/	/	/
		Minimum temperature	1.05	0.71	1.56	1.20	0.73	1.99	1.14	0.53	2.46	/	/	/	/	/	/
		Maximum wind speed	0.98	0.78	1.24	0.99	0.74	1.33	1.08	0.70	1.67	/	/	/	/	/	/
		Maximum pressure	0.87	0.68	1.10	0.88	0.65	1.19	0.80	0.51	1.27	/	/	/	/	/	/
		Maximum relative humidity	0.95	0.75	1.21	0.94	0.70	1.25	1.00	0.61	1.64	/	/	/	/	/	/
		CO	0.88	0.67	1.17	0.88	0.60	1.30	0.77	0.44	1.35	/	/	/	/	/	/
		NO_2	0.82	0.62	1.10	0.76	0.53	1.10	0.94	0.53	1.68	/	/	/	/	/	/
		NO_X	0.89	0.68	1.16	0.90	0.63	1.27	0.80	0.48	1.35	/	/	/	/	/	/
		O_3	0.94	0.69	1.27	0.97	0.67	1.40	1.05	0.52	2.13	/	/	/	/	/	/
		SO_2	0.86	0.64	1.15	0.93	0.66	1.32	0.85	0.48	1.51	/	/	/	/	/	/
		PM_{10}	0.81	0.60	1.08	0.83	0.58	1.18	0.64	0.32	1.27	/	/	/	/	/	/
		$PM_{2.5}$	1.08	0.84	1.39	1.12	0.83	1.52	1.26	0.68	2.34	/	/	/	/	/	/
		Black carbon	1.00	0.77	1.31	0.89	0.63	1.26	1.04	0.64	1.67	/	/	/	/	/	/
		Particle matter	0.85	0.65	1.13	0.82	0.58	1.15	0.69	0.38	1.26	/	/	/	/	/	/
Paris	SS	N		347			201			51			12			83	
		Rainfall	0.99	0.87	1.14	1.01	0.85	1.20	0.77	0.42	1.39	/	/	/	1.01	0.79	1.28
		Maximum temperature	0.94	0.71	1.24	0.94	0.66	1.35	0.96	0.46	2.01	/	/	/	0.88	0.50	1.55
		Minimum temperature	0.83	0.65	1.06	0.80	0.58	1.10	0.71	0.38	1.35	/	/	/	0.90	0.56	1.45
		Maximum wind speed	0.99	0.86	1.13	1.00	0.83	1.21	1.09	0.76	1.57	/	/	/	0.92	0.70	1.22
		Mean pressure	1.02	0.89	1.17	1.01	0.84	1.21	1.05	0.77	1.43	/	/	/	1.08	0.83	1.42
		Maximum relative humidity	1.05	0.89	1.23	1.08	0.87	1.34	1.00	0.66	1.51	/	/	/	0.93	0.66	1.29
		CO	0.89	0.75	1.05	0.92	0.73	1.17	1.07	0.68	1.68	/	/	/	0.80	0.57	1.13
		NO_2	0.90	0.75	1.07	0.94	0.74	1.18	1.06	0.68	1.65	/	/	/	0.79	0.55	1.14
		NO_X	0.90	0.76	1.07	0.95	0.76	1.20	0.96	0.63	1.47	/	/	/	0.85	0.61	1.19
		O_3	1.04	0.86	1.26	1.06	0.82	1.38	1.19	0.79	1.80	/	/	/	0.99	0.66	1.49
		PM_{10}	1.00	0.87	1.16	1.13	0.93	1.37	1.07	0.71	1.63	/	/	/	0.79	0.57	1.10
		$PM_{2.5}$	1.02	0.88	1.18	1.16	0.95	1.41	1.04	0.69	1.57	/	/	/	0.79	0.57	1.10

Supplementary Table 5. Relative risks and 95% confidence intervals from multiple-exposure generalized additive models (GAM) for sickle cell anemia (HbSS) admissions and selected environmental factors (based on results from single-exposure models) in London and Paris between 1st January 2008 and 31st December 2012. Exposure factors associated to increased/reduced relative risks are shown in red/blue, respectively. The number of admissions falling into each subgroup is shown as N. ACS = Acute chest syndrome.

City	Genotype	Exposure variable (lags 0 & 1)	Reason for admission														
			ALL			PAIN			FEVER			ACS			OTHER		
			RR	Min	Max	RR	Min	Max	RR	Min	Max	RR	Min	Max	RR	Min	Max
London	SS	N	1350			859			268			104			119		
		Rainfall + Ozone	1.07	1.01	1.13	1.07	1.00	1.14	1.07	0.95	1.20	1.02	0.84	1.25	1.09	0.93	1.28
		Rainfall + CO	1.07	1.01	1.13	1.07	1.00	1.14	1.08	0.96	1.20	1.03	0.85	1.25	1.09	0.93	1.27
		Rainfall + $PM_{2.5}$	1.07	1.02	1.13	1.07	1.01	1.14	1.07	0.96	1.20	1.02	0.84	1.24	1.11	0.95	1.29
		Maximum wind speed + Ozone	1.08	1.00	1.17	1.13	1.02	1.24	0.98	0.82	1.17	0.95	0.72	1.26	1.09	0.84	1.40
		Maximum wind speed + CO	1.08	1.01	1.16	1.11	1.02	1.21	1.03	0.88	1.20	1.07	0.84	1.35	1.00	0.79	1.26
		Maximum wind speed + PM2.5	1.09	1.02	1.17	1.14	1.05	1.24	0.96	0.82	1.12	1.01	0.80	1.27	1.15	0.92	1.43
		Mean pressure + Ozone	0.91	0.82	1.00	0.93	0.82	1.05	0.73	0.59	0.91	1.14	0.80	1.62	1.08	0.77	1.52
		Mean pressure + CO	0.91	0.82	1.00	0.92	0.82	1.04	0.73	0.59	0.90	1.10	0.77	1.56	1.11	0.79	1.56
		Mean pressure + PM2.5	0.90	0.81	0.99	0.92	0.81	1.03	0.73	0.59	0.91	1.12	0.79	1.59	1.03	0.73	1.45
Paris	SS	N	347			201			51			12			83		
		Rainfall + Ozone	0.97	0.86	1.10	1.01	0.87	1.18	0.59	0.33	1.05	/	/	/	1.01	0.81	1.26
		Rainfall + CO	0.96	0.85	1.09	1.01	0.86	1.18	0.62	0.35	1.09	/	/	/	1.00	0.80	1.25
		Rainfall + $PM_{2.5}$	0.96	0.85	1.09	1.02	0.88	1.19	0.58	0.32	1.06	/	/	/	0.98	0.77	1.24
		Maximum wind speed + Ozone	1.01	0.87	1.16	1.07	0.89	1.28	0.80	0.56	1.15	/	/	/	0.91	0.69	1.20
		Maximum wind speed + CO	0.96	0.83	1.11	1.01	0.84	1.22	0.92	0.63	1.33	/	/	/	0.83	0.62	1.12
		Maximum wind speed + PM2.5	0.98	0.86	1.12	1.06	0.90	1.26	0.90	0.63	1.28	/	/	/	0.81	0.61	1.08
		Mean pressure + Ozone	0.91	0.75	1.11	0.85	0.67	1.08	1.22	0.73	2.02	/	/	/	1.15	0.78	1.69
		Mean pressure + CO	0.94	0.78	1.14	0.88	0.69	1.12	1.17	0.71	1.93	/	/	/	1.21	0.82	1.78
		Mean pressure + PM2.5	0.94	0.78	1.14	0.84	0.66	1.08	1.18	0.71	1.97	/	/	/	1.31	0.89	1.93

Supplementary Code 1. Expectation–maximization imputation for multiple-exposure normal time-series of concentrations of air pollutants in London and Paris.

```
# Change variable name accordingly
# Options: "background" or "road"
mytype <- "background"
# Options: "CO, "NO2", "NOX", "O3", "SO2" (and "PM10", "PM25" if "road")
myvar <- "NOX"

# Set Dir as the directory containing the input files
mydata <- read.table(paste(Dir,mytype,"DailyConcentrations_2008to2014_",myvar,".CSV",sep=""), header=T,
sep=",")
# Use only data for the study period (2008-2012)
mydata <- mydata[1:1827,]

mydata2 <- data.frame(mydata[,1])
colname <- "date"
j=1
f="~"
# Identify columns for which missing data for less than 20% of days
for (i in c(2:ncol(mydata))){
  if (sum(is.na(mydata[,i]))<(0.2*nrow(mydata))){
    mydata2 <- cbind(mydata2,mydata[,i])
    colname <- c(colname, paste(myvar,colnames(mydata[i]),sep="_"))
    if (j==1) f <- paste(f,myvar,"_",colnames(mydata[i]),sep="") else f <-
paste(f,"+",myvar,"_",colnames(mydata[i]),sep="")
    j=j+1
    }
}
colnames(mydata2)<-colname

# Fill in the gaps
library (mtsdi)
i <- mnimput(as.formula(f), mydata2, eps=1e-3 ,ts = TRUE ,method="spline", log = FALSE,
sp.control=list(df=rep(7,ncol(mydata2)-1)))
Var.nogap <- predict(i)
# Save the output
write.table(Var.nogap, paste(Dir,mytype,"_",myvar,"_nogap.csv",sep=""))

### Sensitivity analysis

# Replace some measurements with NAs, independently for each column
mydata3 <- na.omit(mydata2)
mydata4 <- mydata3
N <- 100
inds <- matrix(NA,ncol=N,nrow=ncol(mydata3)-1)
for (i in c(2:ncol(mydata3))){
  inds[i-1,] <- round(runif(N,1,nrow(mydata3)))
  mydata4[,i][inds[i-1,]] <- NA
}
i4 <- mnimput(as.formula(f), mydata4, eps=1e-3,ts = TRUE, method = "spline", log = TRUE, sp.control =
list(df=rep(7,ncol(mydata2)-1)))
Var.nogap4 <- predict(i4)

### Assess prediction performance
```

```
library(Hmisc)
# Function that returns Root Mean Squared Error
rmse <- function(error) 21

myrmse <- rep(0,ncol(Var.nogap4))
mynrmse <- rep(0,ncol(Var.nogap4))

for (j in c(1:(ncol(mydata3)-1))){
  mypred <- Var.nogap4[,j][inds[j,]]
  myobs <- mydata3[,j+1][inds[j,]]
  mycor <- rcorr(mypred,myobs)
  error <- myobs - mypred
  myrmse[j] <- rmse(error)
  mynrmse[j] <- rmse(error)/(max(myobs)-min(myobs))*100
}
```

Supplementary Code 2. GAM models and plots

```
####################################################################################
# Code used by Piel et al (2016) Associations between environmental factors and hospital admissions for sickle cell disease
# Last updated: 25 October 2016
# Author: Fred B. Piel
####################################################################################

library(mgcv)
library(Epi)
library(forestplot)
library(splines)

setwd("path")
mydata <- read.table("data file", sep=",", header=T)

## Tested for "Road air pollution data

#mydata <- mydata[1:1827,]
mydata$time <- seq(nrow(mydata))

### Calculate RR, CIs and P-values for London (SCD, SS, SC) and Paris (SS)
mymodel <- matrix(NA, nrow = 17, ncol=16)
colnames(mymodel) <-
c("SCD","SCD.CI.low","SCD.CI.high","SCD.p","SS","SS.CI.low","SS.CI.high","SS.p","SC","SC.CI.low","SC.CI.high","SC.p","Paris","Paris.CI.low","Paris.CI.high","Paris.p")
rownames(mymodel) <- c("Rainfall", "Maximum temperature","Minimum temperature","Maximum wind speed","Maximum pressure","Maximum relative humidity","Apparent temperature","Wind chill",
          "CO","NO2","NOX","O3","SO2","PM10","PM2.5","Black carbon","Particle matter")
mymodel <- as.data.frame(mymodel)
y <- 1

# Fill in the data frame for London - SCD, SS, SC
for (j in c(68:70)){
 k <- 1
 for (i in c(37:53)){
  myexpo1 <- mydata[,i]
  #myexpolag <- cbind(myexpo1, lag(myexpo1,1))
  myoutcome <- mydata[,j]
  mygam1 <- gam(myoutcome ~ myexpo1 + ns(time,df=20) + as.factor(WeekDay), data=mydata,family=quasipoisson)
  eff1 <- ci.lin(mygam1,subset="y",Exp=T)
  mymodel[k,c(y,y+1,y+2,y+3)] <- eff1[1,c(5:7,4)]
  k <- k+1
 }
y <- y+4
}

# Fill in the data frame for Paris - SS
j <- 83
k <- 1
for (i in c(54:67)){
 myexpo2 <- mydata[,i]
 myoutcome <- mydata[,j]
```

```
  mygam2 <- gam(myoutcome ~ myexpo2 + ns(time,df=20) + as.factor(WeekDay),
data=mydata,family=quasipoisson)
  eff2 <- ci.lin(mygam2,subset="y",Exp=T)
  mymodel[k,c(y,y+1,y+2,y+3)] <- eff2[1,c(5:7,4)]
  if (i == 65) k <- k+2
  else k <- k+1
}
mymodel

# Save the table of GAM results
library(xlsx)
write.xlsx(mymodel, "GAM results 20161025.xlsx")

##################################################################################

### Create a forest plot from the above
mymodel2 <- cbind(rownames(mymodel),mymodel[,1:15])
# Using log if large range of values
#mymodel2 <- cbind(rownames(mymodel),log(mymodel[,1:15]))

### Panel A
mymodelA <- mymodel2[c(1,4:5),]
#png(filename = paste("GAM",colnames(mydata[j]),".png"))
forestplot(mean=cbind(mymodelA$SCD, mymodelA$SS, mymodelA$SC, mymodelA$Paris),
        lower=cbind(mymodelA$SCD.CI.low, mymodelA$SS.CI.low, mymodelA$SC.CI.low,
mymodelA$Paris.CI.low),
        upper=cbind(mymodelA$SCD.CI.high, mymodelA$SS.CI.high, mymodelA$SC.CI.high,
mymodelA$Paris.CI.high),
        labeltext=paste(mymodelA[,1]),
        is.summary=c(F, rep(FALSE, times=nrow(mymodelA))),
        txt_gp = fpTxtGp(label = gpar(fontfamily="", cex=1), ticks = gpar(fontfamily="", cex=1)),
        legend=c("London - SCD","London - SS","London - SC","Paris - SS"),
        zero=1,
        boxsize=0.1,
        new_page=T,
        # Change the "1" in the middle to "0" if using log above.
        xticks=c(round(min(mymodelA[,c(3,7,11,15)], na.rm=T),3),1,round(max(mymodelA[,c(4,8,12,16)],
na.rm=T),3)),
        # Tricky to highlight significant variables - TO WORK ON
        col=fpColors(box=c("red","darkred","light coral","blue"),line=c("red","darkred","light coral","blue")),
        title="Relative risks (per 1 SD increment) for sickle cell hospital admissions")
#dev.off()

### Panel B
mymodelB <- cbind(rownames(mymodel[c(2:3,6:17),]), mymodel[c(2:3,6:17),])
forestplot(mean=cbind(mymodelB$SCD, mymodelB$SS, mymodelB$SC, mymodelB$Paris),
        lower=cbind(mymodelB$SCD.CI.low, mymodelB$SS.CI.low, mymodelB$SC.CI.low,
mymodelB$Paris.CI.low),
        upper=cbind(mymodelB$SCD.CI.high, mymodelB$SS.CI.high, mymodelB$SC.CI.high,
mymodelB$Paris.CI.high),
        labeltext=paste(mymodelB[,1]),
        is.summary=c(F, rep(FALSE, times=nrow(mymodelB))),
        txt_gp = fpTxtGp(label = gpar(fontfamily="", cex=1), ticks = gpar(fontfamily="", cex=1)),
        zero=1,
        boxsize=0.1,
        new_page=T,
        # Change the "1" in the middle to "0" if using log above.
```

```
	xticks=c(round(min(mymodelB[,c(3,7,11,15)], na.rm=T),3),1,round(max(mymodelB[,c(4,8,12,16)], 
na.rm=T),3)),
	col=fpColors(box=c("red","darkred","light coral","blue"),line=c("red","darkred","light coral","blue")))
```

Supplementary Code 3. DLNM models and plots

```
##################################################################################
# Code used by Piel et al (2016) Associations between environmental factors and hospital admissions for sickle cell disease
# Last updated: 25 October 2016
# Author: Fred B. Piel
###################################################################################

library(dlnm)
library(splines)
library(foreign)
library(tsModel)
library(mgcv)

# LOAD THE DATA INTO THE SESSION
setwd("path")
mydata <- read.table("data file", sep=",", header=T)

mydata$time <- seq(nrow(mydata))

####################################################################################
# London and Paris plots all on the same figure
####################################################################################
par(mfrow=c(4,4), mar=(c(4,5,1.5,1)))
myvar <- c("Rainfall", "Maximum temperature","Minimum temperature","Maximum wind speed","Maximum pressure","Maximum relative humidity","Apparent temperature","CO","NO2","NOX","O3","SO2","PM10","PM2.5","Black carbon","Particle number")
nlag <- 6
mydlnm.table <- as.data.frame(matrix(NA, nrow = 17*(nlag+1), ncol=8))
colnames(mydlnm.table) <- c("Exposure", "Lag","RR_LON","ci.low_LON","ci.hi_LON", "RR_PAR","ci.low_PAR","ci.hi_PAR")
mydlnm.table[,1] <- c(rep("Rainfall",(nlag+1)), rep("Maximum temperature",(nlag+1)), rep("Minimum temperature",(nlag+1)), rep("Maximum wind speed",(nlag+1)), rep("Maximum pressure",(nlag+1)), rep("Maximum relative humidity",(nlag+1)), rep("Apparent temperature",(nlag+1)), rep("Wind chill",(nlag+1)), rep("CO",(nlag+1)),rep("NO2",(nlag+1)),rep("NOX",(nlag+1)),rep("O3",(nlag+1)),rep("SO2",(nlag+1)),rep("PM10",(nlag+1)),rep("PM2.5",(nlag+1)),rep("Black carbon",(nlag+1)),rep("Particle number",(nlag+1)))
x <- "lag0"
for (i in c(1:nlag)){
 x <- c(x,paste("lag",i,sep=""))
 }
mydlnm.table[,2] <- rep(x,17)

k <- 1
xx <- 1
for (i in c(37:52)){
 # For London - 16 exposure variables
 myexpo1 <- mydata[,i]
 cb1<-crossbasis(myexpo1, lag=nlag, argvar=list(fun="lin"), arglag=list(fun="poly",degree=3))
 #cb11<-crossbasis(mydata$London_Max_Temp, lag=nlag, argvar=list(fun="lin",cen=FALSE), arglag=list(fun="poly",degree=3))
 mydlnm1 <- gam(mydata$LON_SS ~ cb1 + ns(time,df=20) + WeekDay,family=quasipoisson(), data=mydata)
 pred1 <- crosspred(cb1,mydlnm1,at=1)
 j=0
 if (i %in% c(37:47)) j = i+16
```

```
  if (i %in% c(49:50)) j = i+15

  if (i %in% c(37:47,49:50)){
    # For Paris - 12 exposure variables
    myexpo2 <- mydata[,j]
    cb2<-crossbasis(myexpo2, lag=nlag, argvar=list(fun="lin"), arglag=list(fun="poly",degree=3))
    mydlnm2 <- gam(mydata$Paris_SS ~ cb2 + ns(time,df=20) + WeekDay,family=quasipoisson(), data=mydata)
    pred2 <- crosspred(cb2,mydlnm2,at=1)
    tablag <- cbind(with(pred1,t(rbind(matRRfit,matRRlow,matRRhigh))),
with(pred2,t(rbind(matRRfit,matRRlow,matRRhigh))))
    colnames(tablag) <- c("RR_LON","ci.low_LON","ci.hi_LON", "RR_PAR","ci.low_PAR","ci.hi_PAR")
    # Different types for x- and y-axis labels depending on position
    if (k %in% c(1,5,9)) {
      plot(-0.5:(nlag+.5),-0.5:(nlag+.5),type="n", bty="n", ylim=c(min(tablag),max(tablag)), main= myvar[k],
xlab="",ylab="RR and 95%CI per SD")
      }
    else if (k %in% c(2:4,6:8,10:12)) {
      plot(-0.5:(nlag+.5),-0.5:(nlag+.5),type="n", bty="n", ylim=c(min(tablag),max(tablag)), main= myvar[k],
xlab="",ylab="")
    }
    else if (k == 13) {
      plot(-0.5:(nlag+.5),-0.5:(nlag+.5),type="n", bty="n", ylim=c(min(tablag),max(tablag)), main= myvar[k],
xlab="Lag (days)",ylab="RR and 95%CI per SD")
    }
    else if (k == 14) {
      plot(-0.5:(nlag+.5),-0.5:(nlag+.5),type="n", bty="n", ylim=c(min(tablag),max(tablag)), main= myvar[k],
xlab="Lag (days)",ylab="")
    }
    abline(h=1)
    # London - Red
    arrows(0:nlag,tablag[,2],0:nlag,tablag[,3],length=0.05,angle=90,code=3,
col=ifelse(xor(pred1$matRRhigh<1,pred1$matRRlow>1),"#FF0000","#80000050"))
    points(0:nlag,tablag[,1],pch=19,
col=ifelse(xor(pred1$matRRhigh<1,pred1$matRRlow>1),"#FF0000","#80000050"))
    # Paris - Blue
    arrows(0.25:(nlag+.25),tablag[,5],0.25:(nlag+.25),tablag[,6],length=0.05,angle=90,code=3,
col=ifelse(xor(pred2$matRRhigh<1,pred2$matRRlow>1),"#0000FF","#00008050"))
    points(0.25:(nlag+.25),tablag[,4],pch=19,
col=ifelse(xor(pred2$matRRhigh<1,pred2$matRRlow>1),"#0000FF","#00008050"))
    mydlnm.table[xx:(xx+(nlag)),3:8] <- tablag
  } else {
    # London only - 4 exposure variables: Feel temp, SO2, Black carbon and particle number
    tablag <- with(pred1,t(rbind(matRRfit,matRRlow,matRRhigh)))
    colnames(tablag) <- c("RR_LON","ci.low_LON","ci.hi_LON")
    # Different types for x- and y-axis labels depending on position
    if (k %in% c(15,16)) {
      plot(-0.5:(nlag+.5),-0.5:(nlag+.5),type="n", bty="n", ylim=c(min(tablag),max(tablag)), main= myvar[k],
xlab="Lag (days)",ylab="")
    }
    else if (k == 12){
      plot(-0.5:(nlag+.5),-0.5:(nlag+.5),type="n", bty="n", ylim=c(min(tablag),max(tablag)), main= myvar[k],
xlab="",ylab="")
    }
    abline(h=1)
    # London - Red
    arrows(0:nlag,tablag[,2],0:nlag,tablag[,3],length=0.05,angle=90,code=3,
col=ifelse(xor(pred1$matRRhigh<1,pred1$matRRlow>1),"#FF0000","#80000050"))
```

```
   points(0:nlag,tablag[,1],pch=19,
col=ifelse(xor(pred1$matRRhigh<1,pred1$matRRlow>1),"#FF0000","#80000050"))
   mydlnm.table[xx:(xx+(nlag)),3:5] <- tablag
  }
 k <- k+1
 xx <- xx+(nlag+1)
}

# Save the table of DLNM results
library(xlsx)
write.xlsx(mydlnm.table, "DLNM results - 7 lags - 20161017.xlsx")

################################################################################
### 2-panel plots
################################################################################
# Panel 1 - Significant results
par(mfrow=c(2,2), mar=(c(4,5,1.5,1)))
myvar <- c("Rainfall", "Maximum wind speed","CO","Black carbon")
nlag <- 6
mydlnm.table <- as.data.frame(matrix(NA, nrow = length(myvar)*(nlag+1), ncol=8))
colnames(mydlnm.table) <- c("Exposure", "Lag","RR_LON","ci.low_LON","ci.hi_LON",
"RR_PAR","ci.low_PAR","ci.hi_PAR")
mydlnm.table[,1] <- c(rep("Rainfall",(nlag+1)), rep("Maximum wind speed",(nlag+1)), rep("CO",(nlag+1)),
rep("Black carbon",(nlag+1)))
x <- "lag0"
for (i in c(1:nlag)){
 x <- c(x,paste("lag",i,sep=""))
}
mydlnm.table[,2] <- rep(x,length(myvar))

k <- 1
xx <- 1
for (i in c(37,40,45,52)){
 # For London - 4 significant exposure variables
 myexpo1 <- mydata[,i]
 cb1<-crossbasis(myexpo1, lag=nlag, argvar=list(fun="lin"), arglag=list(fun="poly",degree=3))
 #cb11<-crossbasis(mydata$London_Max_Temp, lag=nlag, argvar=list(fun="lin",cen=FALSE),
arglag=list(fun="poly",degree=3))
 mydlnm1 <- gam(mydata$LON_SS ~ cb1 + ns(time,df=20) + WeekDay,family=quasipoisson(), data=mydata)
 pred1 <- crosspred(cb1,mydlnm1,at=1)
 j=0
 if (i %in% c(37:48)) j = i+17
 if (i %in% c(50:51)) j = i+16

 if (i %in% c(37:48,50:51)){
   # For Paris - 3 exposure variables
   myexpo2 <- mydata[,j]
   cb2<-crossbasis(myexpo2, lag=nlag, argvar=list(fun="lin"), arglag=list(fun="poly",degree=3))
   mydlnm2 <- gam(mydata$Paris_SS ~ cb2 + ns(time,df=20) + WeekDay,family=quasipoisson(), data=mydata)
   pred2 <- crosspred(cb2,mydlnm2,at=1)
   tablag <- cbind(with(pred1,t(rbind(matRRfit,matRRlow,matRRhigh))),
with(pred2,t(rbind(matRRfit,matRRlow,matRRhigh))))
   colnames(tablag) <- c("RR_LON","ci.low_LON","ci.hi_LON", "RR_PAR","ci.low_PAR","ci.hi_PAR")
   # Different types for x- and y-axis labels depending on position
   if (k == 1) {
     plot(-0.5:(nlag+.5),-0.5:(nlag+.5),type="n", bty="n", ylim=c(min(tablag),max(tablag)), main= myvar[k],
xlab="",ylab="RR and 95%CI per SD")
```

```
    }
    else if (k == 2) {
      plot(-0.5:(nlag+.5),-0.5:(nlag+.5),type="n", bty="n", ylim=c(min(tablag),max(tablag)), main= myvar[k],
xlab="",ylab="")
    }
    else if (k == 3) {
      plot(-0.5:(nlag+.5),-0.5:(nlag+.5),type="n", bty="n", ylim=c(min(tablag),max(tablag)), main= myvar[k],
xlab="Lag (days)",ylab="RR and 95%CI per SD")
    }
    abline(h=1)
    # London - Red

arrows(0:nlag,tablag[,2],0:nlag,tablag[,3],length=0.05,angle=90,code=3,lwd=4,col=ifelse(xor(pred1$matRRhigh
<1,pred1$matRRlow>1),"#FF0000","#80000050"))
    points(0:nlag,tablag[,1],pch=19,
col=ifelse(xor(pred1$matRRhigh<1,pred1$matRRlow>1),"#FF0000","#80000050"))
    # Paris - Blue

arrows(0.25:(nlag+.25),tablag[,5],0.25:(nlag+.25),tablag[,6],length=0.05,angle=90,code=3,lwd=4,col=ifelse(xor(
pred2$matRRhigh<1,pred2$matRRlow>1),"#0000FF","#00008050"))
    points(0.25:(nlag+.25),tablag[,4],pch=19,
col=ifelse(xor(pred2$matRRhigh<1,pred2$matRRlow>1),"#0000FF","#00008050"))
    mydlnm.table[xx:(xx+(nlag)),3:8] <- tablag
  } else {
    # London only - 1 exposure variables: Black carbon
    tablag <- with(pred1,t(rbind(matRRfit,matRRlow,matRRhigh)))
    colnames(tablag) <- c("RR_LON","ci.low_LON","ci.hi_LON")
    # Different types for x- and y-axis labels depending on position
    if (k == 4) {
      plot(-0.5:(nlag+.5),-0.5:(nlag+.5),type="n", bty="n", ylim=c(min(tablag),max(tablag)), main= myvar[k],
xlab="Lag (days)",ylab="")
    }
    #else if (k == 12){
    #  plot(-0.5:(nlag+.5),-0.5:(nlag+.5),type="n", bty="n", ylim=c(min(tablag),max(tablag)), main= myvar[k],
xlab="",ylab="")
    #}
    abline(h=1)
    # London - Red

arrows(0:nlag,tablag[,2],0:nlag,tablag[,3],length=0.05,angle=90,code=3,lwd=4,col=ifelse(xor(pred1$matRRhigh
<1,pred1$matRRlow>1),"#FF0000","#80000050"))
    points(0:nlag,tablag[,1],pch=19,
col=ifelse(xor(pred1$matRRhigh<1,pred1$matRRlow>1),"#FF0000","#80000050"))
    mydlnm.table[xx:(xx+(nlag)),3:5] <- tablag
  }
  k <- k+1
  xx <- xx+(nlag+1)
}

# Panel 2 - Non significant associations
########################################
par(mfrow=c(5,3), mar=(c(4,5,1.5,0.3)))
myvar <- c("Maximum temperature","Minimum temperature","Maximum pressure","Maximum relative
humidity","Apparent temperature","Wind chill","NO2","NOX","O3","SO2","PM10","PM2.5","Particle number")
nlag <- 6
mydlnm.table <- as.data.frame(matrix(NA, nrow = length(myvar)*(nlag+1), ncol=8))
```

```
colnames(mydlnm.table) <- c("Exposure", "Lag","RR_LON","ci.low_LON","ci.hi_LON",
"RR_PAR","ci.low_PAR","ci.hi_PAR")
mydlnm.table[,1] <- c(rep("Maximum temperature",(nlag+1)), rep("Minimum temperature",(nlag+1)),
rep("Maximum pressure",(nlag+1)), rep("Maximum relative humidity",(nlag+1)), rep("Apparent
temperature",(nlag+1)), rep("Wind chill",(nlag+1)),
rep("NO2",(nlag+1)),rep("NOX",(nlag+1)),rep("O3",(nlag+1)),rep("SO2",(nlag+1)),rep("PM10",(nlag+1)),rep("P
M2.5",(nlag+1)),rep("Particle number",(nlag+1)))
x <- "lag0"
for (i in c(1:nlag)){
  x <- c(x,paste("lag",i,sep=""))
}
mydlnm.table[,2] <- rep(x,length(myvar))

k <- 1
xx <- 1
for (i in c(38:39,41:44,46:51,53)){
  # For London - 13 exposure variables
  myexpo1 <- mydata[,i]
  cb1<-crossbasis(myexpo1, lag=nlag, argvar=list(fun="lin"), arglag=list(fun="poly",degree=3))
  #cb11<-crossbasis(mydata$London_Max_Temp, lag=nlag, argvar=list(fun="lin",cen=FALSE),
arglag=list(fun="poly",degree=3))
  mydlnm1 <- gam(mydata$LON_SS ~ cb1 + ns(time,df=20) + WeekDay,family=quasipoisson(), data=mydata)
  pred1 <- crosspred(cb1,mydlnm1,at=1)
  j=0
  if (i %in% c(37:48)) j = i+17
  if (i %in% c(50:51)) j = i+16

  if (i %in% c(38:39,41:44,46:48,50:51)){
    # For Paris - 11 exposure variables
    myexpo2 <- mydata[,j]
    cb2<-crossbasis(myexpo2, lag=nlag, argvar=list(fun="lin"), arglag=list(fun="poly",degree=3))
    mydlnm2 <- gam(mydata$Paris_SS ~ cb2 + ns(time,df=20) + WeekDay,family=quasipoisson(), data=mydata)
    pred2 <- crosspred(cb2,mydlnm2,at=1)
    tablag <- cbind(with(pred1,t(rbind(matRRfit,matRRlow,matRRhigh))),
with(pred2,t(rbind(matRRfit,matRRlow,matRRhigh))))
    colnames(tablag) <- c("RR_LON","ci.low_LON","ci.hi_LON", "RR_PAR","ci.low_PAR","ci.hi_PAR")
    # Different types for x- and y-axis labels depending on position
    if (k %in% c(1,4,7)) {
      plot(-0.5:(nlag+.5),-0.5:(nlag+.5),type="n", bty="n", ylim=c(min(tablag),max(tablag)), main= myvar[k],
xlab="",ylab="RR & 95%CI per SD",cex=1.5)
    }
    else if (k %in% c(2:3,5:6,8:9)) {
      plot(-0.5:(nlag+.5),-0.5:(nlag+.5),type="n", bty="n", ylim=c(min(tablag),max(tablag)), main= myvar[k],
xlab="",ylab="", cex=1.5)
    }
    else if (k %in% c(11:12)) {
      plot(-0.5:(nlag+.5),-0.5:(nlag+.5),type="n", bty="n", ylim=c(min(tablag),max(tablag)), main= myvar[k],
xlab="Lag (days)",ylab="")
    }
    abline(h=1)
    # London - Red
    arrows(0:nlag,tablag[,2],0:nlag,tablag[,3],length=0.05,angle=90,code=3, lwd=2,
col=ifelse(xor(pred1$matRRhigh<1,pred1$matRRlow>1),"#FF0000","#80000050"))
    points(0:nlag,tablag[,1],pch=19,
col=ifelse(xor(pred1$matRRhigh<1,pred1$matRRlow>1),"#FF0000","#80000050"))
    # Paris - Blue
```

```
arrows(0.25:(nlag+.25),tablag[,5],0.25:(nlag+.25),tablag[,6],length=0.05,angle=90,code=3,lwd=2,col=ifelse(xor(
pred2$matRRhigh<1,pred2$matRRlow>1),"#0000FF","#00008050"))
    points(0.25:(nlag+.25),tablag[,4],pch=19,
col=ifelse(xor(pred2$matRRhigh<1,pred2$matRRlow>1),"#0000FF","#00008050"))
    mydlnm.table[xx:(xx+(nlag)),3:8] <- tablag
  } else {
    # London only - 4 exposure variables: SO2 and particle number
    tablag <- with(pred1,t(rbind(matRRfit,matRRlow,matRRhigh)))
    colnames(tablag) <- c("RR_LON","ci.low_LON","ci.hi_LON")
    # Different types for x- and y-axis labels depending on position
    if (k == 10) {
      plot(-0.5:(nlag+.5),-0.5:(nlag+.5),type="n", bty="n", ylim=c(min(tablag),max(tablag)), main= myvar[k],
xlab="",ylab="RR & 95%CI per SD")
    }
    else if (k == 13){
      plot(-0.5:(nlag+.5),-0.5:(nlag+.5),type="n", bty="n", ylim=c(min(tablag),max(tablag)), main= myvar[k],
xlab="Lag (days)",ylab="RR & 95%CI per SD")
    }
    abline(h=1)
    # London - Red
    arrows(0:nlag,tablag[,2],0:nlag,tablag[,3],length=0.05,angle=90,code=3, lwd=2,
col=ifelse(xor(pred1$matRRhigh<1,pred1$matRRlow>1),"#FF0000","#80000050"))
    points(0:nlag,tablag[,1],pch=19,
col=ifelse(xor(pred1$matRRhigh<1,pred1$matRRlow>1),"#FF0000","#80000050"))
    mydlnm.table[xx:(xx+(nlag)),3:5] <- tablag
  }
  k <- k+1
  xx <- xx+(nlag+1)
}
```