

Online Supplementary Materials

Methods (supplemental)

Study Setting

A key difference between Sarnia, Windsor and London, Ontario, the three major urban centres within the study sub-regions of interest, is the major industry present in each. While Sarnia is a Canadian hub for petrochemical processing, the major industries in Windsor include automobile assembly plants, and scrap metal recycling. Windsor has high exposure to transboundary air and water pollution from Ohio, Illinois and, Michigan, and is also immediately downwind of major steel mills in Detroit, and 100 km down river from Sarnia. The city of London-Middlesex is the home of many branches of industry, corporate offices, medical and educational facilities. It is also a manufacturing, distribution and financial center, with less emphasis on manufacturing in the last few decades.

Secondary exposures

While NO₂ and O₃ are known to be markers of traffic related air pollution, SO₂, though also found in traffic related air pollution, is often used as a marker of industry related air pollution.^[1] There are various sources for PM_{2.5} including residential fireplace and wood stoves, pollen, industrial processes, as well as traffic.^[2] ** NO₂ and O₃ data were available between 1996 – 2009; PM_{2.5} data were available between 2003-2009; SO₂ data were available between 1993 – 2009. Exposure measures for NO₂, O₃ and PM_{2.5} were assigned to each child based on the forward sortation area (FSA) where the child was born. FSA's are small geographical units, which correspond to the first 3 digits of the postal code and represent approximately 400-700 persons. SO₂ exposure was assigned to each child based on the city region of birth which is a larger geographic area than the FSA.

Additional Covariates

Information on additional covariates that have been previously shown to be associated with risk of childhood asthma were also collected at the time of the child's birth including: sex, rural (community size <10,000 persons) versus urban location of residence, neighbourhood income

quintile (approximated by linking the child's postal code at birth to the nearest Canadian census information), ONMarg index (with each of its four dimensions included separately in the multivariable logistic regression model), maternal age, maternal history of asthma, maternal diabetes, caesarian versus vaginal delivery, and preterm, small for gestational age or low birthweight.

Secondary outcomes

Our secondary outcome, persistent asthma, was defined as those children with incident asthma who continued to have a subsequent health care encounter (outpatient visit or hospitalization) for asthma after the age of six years, or who newly developed asthma after the age of six years. This secondary outcome was explored due to the likelihood of asthma symptoms persisting in to adulthood in these children and specific definitions were chosen as per previous studies on phenotyping of asthma in children.^[3]

References

- [1] E. Garcia *et al.*, "Association of Changes in Air Quality With Incident Asthma in Children in California, 1993-2014," *JAMA*, vol. 321, no. 19, pp. 1906–1915, May 2019, doi: 10.1001/jama.2019.5357.
- [2] A. F. Pennington *et al.*, "Exposure to Mobile Source Air Pollution in Early-life and Childhood Asthma Incidence: The Kaiser Air Pollution and Pediatric Asthma Study," *Epidemiol. Camb. Mass*, vol. 29, no. 1, pp. 22–30, Jan. 2018, doi: 10.1097/EDE.0000000000000754.
- [3] G. Bowatte *et al.*, "The influence of childhood traffic-related air pollution exposure on asthma, allergy and sensitization: a systematic review and a meta-analysis of birth cohort studies," *Allergy*, vol. 70, no. 3, pp. 245–256, Mar. 2015, doi: 10.1111/all.12561.

Table S1. Database descriptions

Database	Description
Ontario Health Insurance Plan (OHIP) Claims History Database	<p>The OHIP claims database contains information on inpatient and outpatient services provided to Ontario residents eligible for the province's publicly funded health insurance system by fee-for-service health care practitioners (primarily physicians) and "shadow billings" for those paid through non-fee-for-service payment plans.</p> <p>Billing codes on the claims (OHIP fee codes) identify the care provider, their area of specialization and the type and location of service. OHIP billing claims also contain a 3-digit diagnosis code - the main reason for the service - captured using a modified version of the ICD, 8th revision coding system. OHIP claims are well completed, but the validity of the diagnosis coding is highly variable.¹</p>
OHIP Registered Persons Database (RPDB)	<p>The OHIP RPDB provides basic demographic information (age, sex, location of residence, date of birth, and date of death for deceased individuals) for those issued an Ontario health insurance number. The RPDB also indicates the time periods for which an individual was eligible to receive publicly funded health insurance benefits and the best known postal code for each registrant on July 1st of each year.</p>
Discharge Abstract Database (DAD)	<p>The DAD is compiled by the Canadian Institute for Health Information (CIHI) and contains administrative, clinical (diagnoses and procedures/interventions), demographic, and administrative information for all admissions to acute care hospitals in Ontario. At ICES, consecutive DAD records are linked together to form 'episodes of care' among the hospitals to which patients have been transferred after their initial admission. Prior to April 1, 2002, diagnoses (up to 16 on a given DAD record) are captured using the International Statistical Classification of Diseases, Injuries, and Causes of Death, 9th Revision (ICD-9) coding system and procedures (up to 10 on a given DAD record) are captured using the Canadian Classification of Diagnostic, Therapeutic, and Surgical Procedures (CCP) coding system. Following April 1, 2002, diagnoses (up to 25 on a given DAD record) are captured using the International Statistical Classification of Diseases and Related Health Problems, 10th Revision, Canada (ICD-10-CA) coding system and interventions (up to 20 on a given DAD record) are captured using the Canadian Classification of Health Interventions (CCI) coding system.</p> <p>In a hospital medical record reabstraction study of 14,500 hospital discharges from 18 hospital sites between April 2002 and March 2004, DAD records were demonstrated to have excellent agreement (over 99%) for nonmedical information such as demographic and administrative data. Regarding diagnoses, median agreement between the original DAD records and the reabstracted records for the 50 most common most</p>

	responsible diagnoses was 81% (Sensitivity 82%; Specificity 82%). ² The corresponding median agreement for the 50 most frequently performed surgical procedures was 92% (sensitivity 95%, positive predictive value 91%).
ICES Mother-Baby Linked Database (MOMBABY)	The ICES MOMBABY Database links the DAD inpatient admission records of delivering mothers and their newborns. From 2002 onward, this linkage is performed deterministically using a maternal-newborn chart matching number. Prior to 2002, mothers were linked to their children by matching on the institutions they were admitted, their postal codes, and their admission/discharge dates.
Ontario Ministry of Environment air quality data	The Ontario Ministry of Environment has a network of 38 outdoor air monitoring stations providing hourly concentrations of pollutants including, ozone, nitrogen dioxide and fine particulate matter.
Environment Canada national air pollution surveillance data (NAPS)	The NAPS database provides long-term air quality data for the purpose of monitoring and assessing the quality of outdoor air across Canada. Currently there are 286 sites in 203 communities in every province and territory providing continuous measurement of sulphur dioxide, nitrogen dioxide, ozone, fine particulate matter and carbon monoxide.
Ontario Marginalization Index (ONMarg)	This is a neighbourhood level measure of socioeconomic status that comprises multiple factors that may adversely impact health. The four dimensions of the Ontario Marginalization Index are i) residential instability: includes measures of crowding, marital status, etc., ii) material deprivation: incorporates education, low income and unemployment, iii) dependency: measures the proportion of seniors or young children versus employed individuals and iv) ethnic concentration: reflects the proportion of visible minorities or recent immigrants. ³ Each dimension of the Ontario Marginalization Index is divided into quintiles (Quintile 1 = least amount of marginalization). ³

1. Williams J, Young W. A summary of the quality of health care administrative databases in Canada. In: Goel V, Williams J, Anderson G, Blackstien-Hirsch P, Fooks C, Naylor C, editors. *Patterns of Health Care in Ontario: The ICES Practice Atlas*. 2nd Edition. Ottawa: Canadian Medical Association; 1996. 339-346.

2. Juurlink D, Preyra C, Croxford R, Chong A, Austin P, Tu J et al. *Canadian Institute for Health Information Discharge Abstract Database: A Validation Study*. 2006. Toronto, Institute for Clinical Evaluative Sciences. Ref Type: Report

3. Matheson FI, Dunn JR, Smith KL, Moineddin R, Glazier RH. Development of the Canadian Marginalization Index: a new tool for the study of inequality. *Canadian journal of public health Revue canadienne de sante publique*. 2012;103(8 Suppl 2):S12-16.

Table S2. Health administrative codes used to define exposure variables and outcomes

Variable	Database	Codes	Details
Live births	MOMBABY	B_date	
Local Health Integration Network (LHIN) sub-region	Registered Persons Database (RPDB)	PSTLCODE	Used postal code recorded on a child's OHIP registration at birth within Lambton, Windsor and London-Middlesex sub-regions
Asthma	Ontario Asthma Surveillance Information System (OASIS)	ICD9: 493 ICD10: J45, J46 OHIPdx: 493	One hospital admission with a most responsible diagnosis of asthma, or two outpatient physician visits for asthma within a two-year period
Air pollutant concentrations	Ontario Ministry of Environment Air Quality Data and Environment Canada National Air Pollution Surveillance Data	Nitrogen dioxide Ozone Sulfur dioxide Particulate matter $\leq 2.5 \mu\text{m}$	

ICD = International Classification of Diseases, OHIP = Ontario Health Insurance Plan, MOMBABY = an ICES derived dataset that includes all mothers linked to their hospital-born children,

Table S3. Time stratified adjusted hazard of asthma

		HR (95% CI)	p-value
Lambton		REF	
	0 - < 2 years	0.50 (0.45, 0.54)	< 0.0001
London-Middlesex (N=31,115)	2 - < 6 years	0.83 (0.74, 0.92)	< 0.0001
	≥ 6 years	0.82 (0.69, 0.97)	0.023
Lambton		REF	
	0 - < 2 years	0.54 (0.49, 0.60)	< 0.0001
Windsor (N=20,209)	2 - < 6 years	0.89 (0.79, 1.00)	0.064
	≥ 6 years	1.07 (0.89, 1.29)	0.0447

* Adjusted for maternal age, maternal asthma, sex, rural geography, neighbourhood maternal deprivation, neighbourhood ethnic concentration, caesarian section delivery, fiscal year, restricted to only those children with data available for all pollutants exposures.

HR: Hazard ratio, CI: Confidence Intervals

Table S4. Cox proportional hazards estimates for the development of persistent asthma

	HR (95% CI)	
	Unadjusted	Adjusted*
Lambton		REF
Windsor	0.88 (0.84-0.93)	0.76 (0.72-0.80)
London-Middlesex	0.68 (0.65-0.71)	0.62 (0.59-0.65)

Persistent asthma = asthma diagnosis after age 6 and/or asthma diagnosis prior to age 6 and subsequent asthma health care encounter after age 6. Cohort N = 114,427; Number of events excluded = 7,593 children who did not have an asthma related health care encounter after the age of 6 years. Number of asthma events = 14,780.

*Adjusted for maternal age, maternal asthma, sex, rural geography, neighbourhood material deprivation, neighbourhood ethnic concentration, caesarian section delivery, fiscal year.

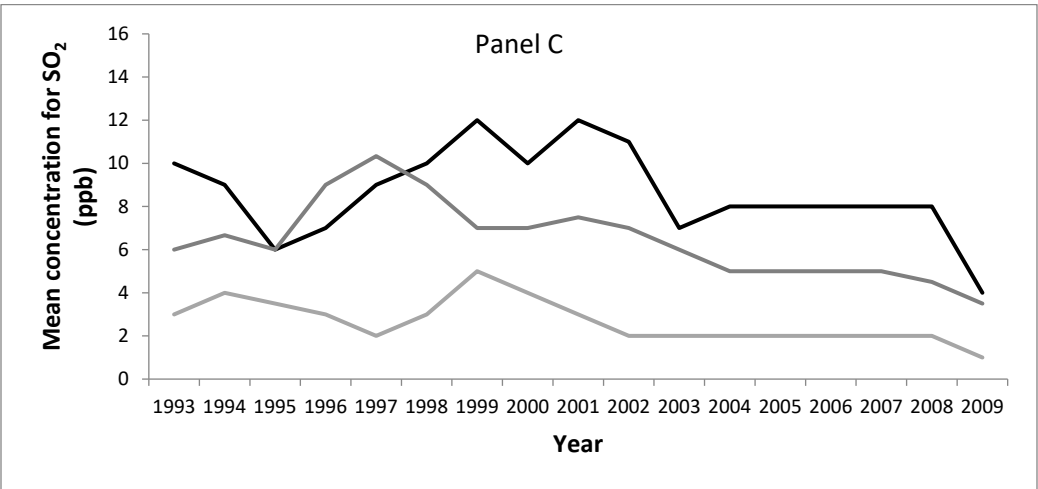
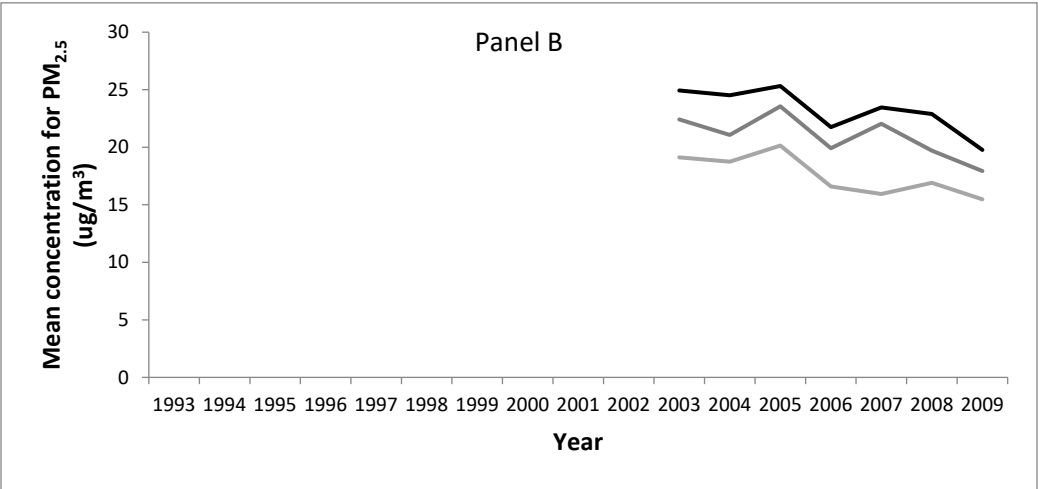
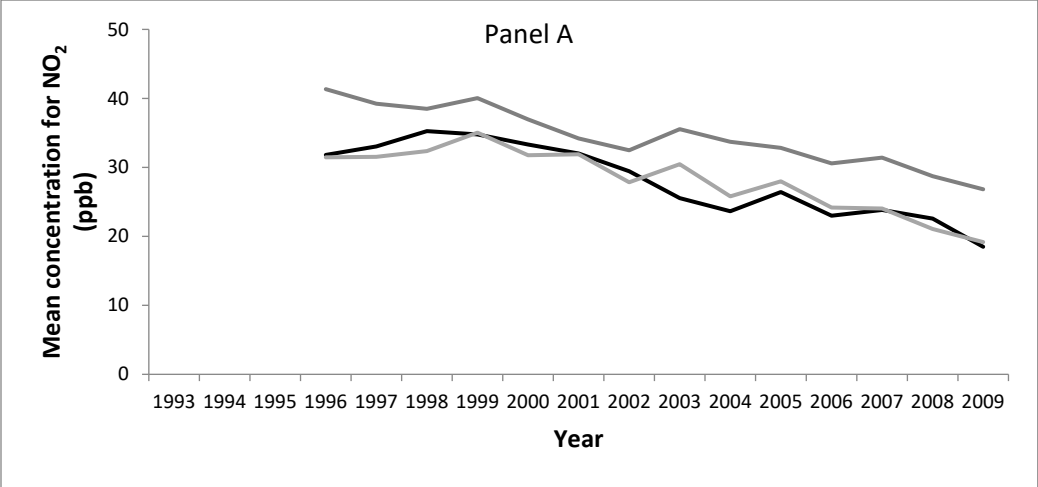
HR: Hazard Ratio; CI: Confidence Intervals

Table S5. Examining the Hazard Ratios of developing asthma, for a model with and without air pollutants fitted with and without cubic splines.

		without splines				with splines			
		Hazard Ratio	LCL	UCL	p-value	Hazard Ratio	LCL	UCL	p-value
Model without air pollution	London-Middlesex vs. Lambton	0.649	0.608	0.694	<0.0001	-	-	-	-
	Windsor vs. Lambton	0.719	0.668	0.773	<0.0001	-	-	-	-
Model with all 4 pollutants	London-Middlesex vs. Lambton	0.891	0.641	1.238	0.490	1.177	0.635	2.184	0.604
	Windsor vs. Lambton	0.790	0.619	1.009	0.059	0.763	0.532	1.093	0.140

*Adjusted for maternal age, maternal asthma, sex, rural geography, neighbourhood material deprivation, neighbourhood ethnic concentration, caesarian section delivery, fiscal year; restricted to only those children with data available for all pollutant exposures.

HR: Hazard Ratio; CI: Confidence Intervals



Appendix 1, as supplied by the authors. Appendix to: Radhakrishnan D, Bota SE, Price A, et al. Comparison of childhood asthma incidence in 3 neighbouring cities in southwestern Ontario: a 25-year longitudinal cohort study. *CMAJ Open* 2021. doi:10.9778/cmajo.20200130. Copyright © 2021 The Author(s) or their employer(s). To receive this resource in an accessible format, please contact us at cmajgroup@cmaj.ca. Appendices are posted as supplied by authors.

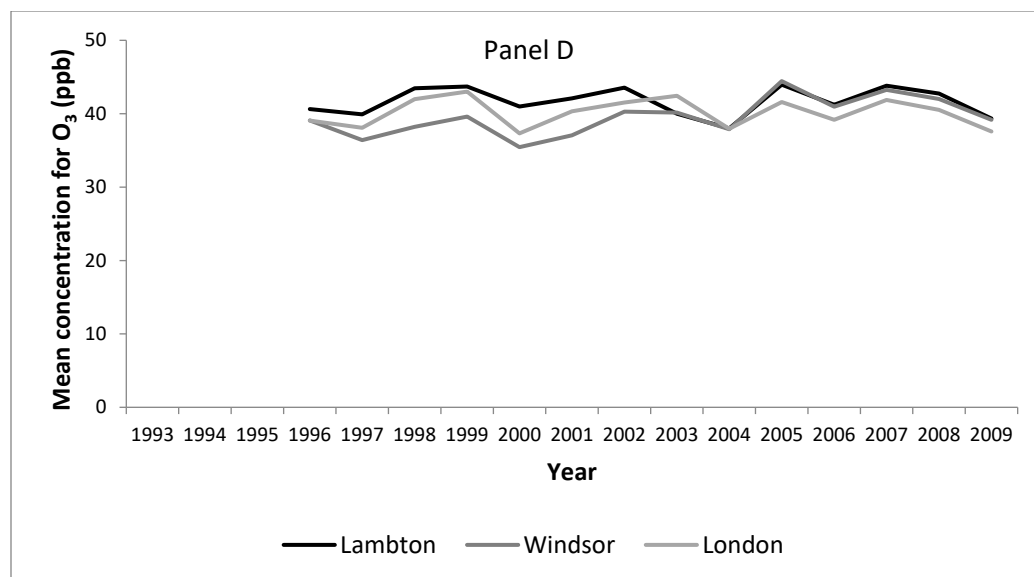
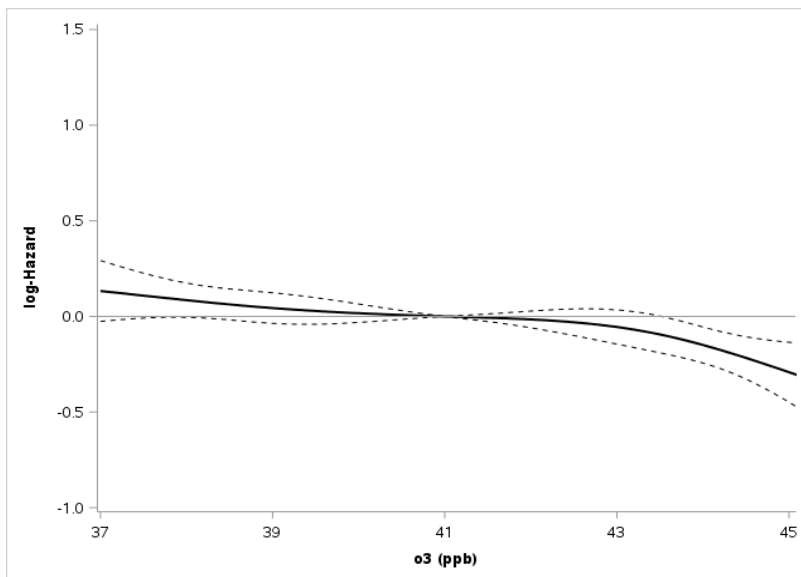
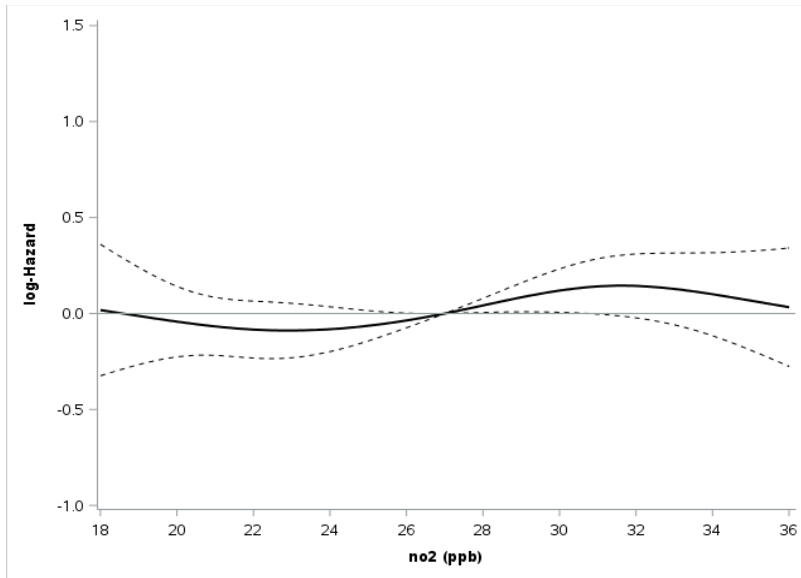


Figure S1. Mean air pollution concentrations for A) Nitrogen dioxide, NO₂, B) fine particulate matter, PM_{2.5}, C) Sulphur dioxide, SO₂, and D) Ozone, O₃ assigned to children at the time of birth and summarized by city.

Pollution values are based on annual summaries of pollution levels by forward sortation area (NO₂, PM_{2.5}, O₃) or city (SO₂). NO₂ and O₃ data were available between 1996 – 2009; PM_{2.5} data were available between 2003-2009; SO₂ data were available between 1993 – 2009. ppb: part per billion; ug/m³: microgram per cubic meter



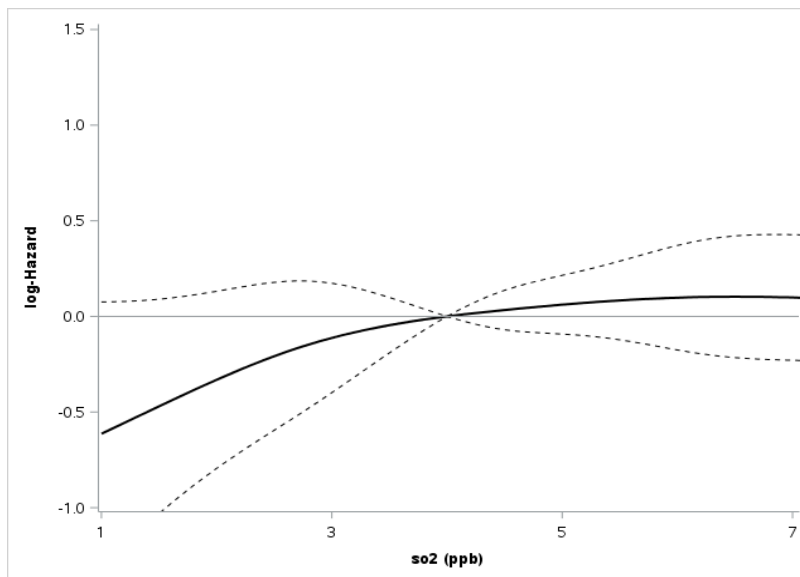
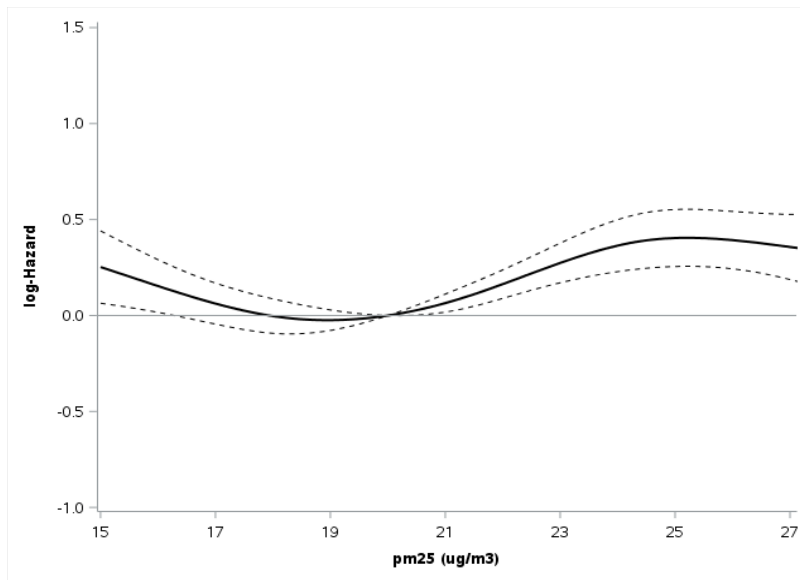


Figure S2. Effect of each pollutant on hazard of asthma using restricted cubic splines

Pollution values are based on annual summaries of pollution levels by forward sortation area (NO₂, PM_{2.5}, O₃) or city (SO₂). NO₂ and O₃ data were available between Jan 1, 1996 – Mar 31, 2009; PM_{2.5} data were available between Jan 1, 2003- Mar 31, 2009; SO₂ data were available between Apr 1, 1993 – Mar 31, 2009. ppb: part per billion; ug/m³: microgram per cubic meter