

Maternal Second-Hand Smoke Exposure in Pregnancy Is Associated With Childhood Asthma Development

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What is already known about this topic? Active maternal smoking during pregnancy has been associated with childhood asthma development in previous longitudinal studies.

What does this article add to our knowledge? Maternal home second-hand smoke exposure during pregnancy is also longitudinally associated with physician-diagnosed childhood asthma development and current asthma symptoms up to age 7 years, even in the absence of active maternal smoking during pregnancy.

How does this study impact current management guidelines? In addition to recommending smoking cessation for all pregnant women, management guidelines should recommend smoking cessation for all household contacts of pregnant women, whether or not the mother smokes actively during pregnancy.

BACKGROUND: Childhood asthma development has been associated with active maternal smoking during pregnancy, but its association with maternal second-hand smoke exposure in pregnancy needs to be evaluated.

OBJECTIVE: We investigated longitudinal associations between maternal smoke exposure in pregnancy and childhood asthma development.

METHODS: In a population-based cohort of 5619 seven-year-old Toronto children, parents reported age of physician-diagnosed asthma development, maternal smoking during pregnancy, home second-hand smoke exposure from pregnancy until 7 years, demographics, and family history of atopy. By using Cox proportional and discrete-time hazard survival analyses, we evaluated associations between asthma and maternal smoking or home second-hand smoke exposure in pregnancy.

RESULTS: During pregnancy, 5.0% of mothers smoked and 6.2% were nonsmokers and exposed to home second-hand smoke; 15.5% of children developed asthma. Children whose mothers smoked or were exposed to home second-hand smoke during pregnancy were more likely to develop asthma (adjusted hazard ratio [HR] 1.30 [95% CI, 1.06-1.60]). The association persisted for children of nonsmoking mothers with home second-hand smoke exposure during pregnancy (adjusted HR 1.34 [95% CI, 1.01-1.76]), children with asthma symptoms in the past year (adjusted HR 1.36 [95% CI, 1.03-1.79]), and after adjusting for home second-hand smoke exposure from birth to age 7 years.

CONCLUSIONS: Maternal home second-hand smoke exposure during pregnancy is associated with incident physician-diagnosed childhood asthma, even if the mother does not smoke actively during pregnancy. Childhood asthma prevention programs should include smoking cessation strategies targeted toward smokers who live in the homes of smoking and nonsmoking pregnant women as well as pregnant women who smoke. © 2014 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2014;2:201-7)

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Childhood asthma affects up to 20%^{1,2} of children in Canada, and exposure to second-hand smoke remains widespread among Canadian children (9%-12%).^{3,4} Cross-sectional associations between the development of childhood asthma or wheezing and smoke exposure in pregnancy or childhood (odds ratios ranging from 1.2-3.5)⁵⁻¹⁷ have been consistently demonstrated. Results of studies that have evaluated childhood exposure to second-hand smoke at different ages have suggested that the timing of exposure may affect the magnitude of association with asthma development.^{6-8,11,15,17} The results of 1 longitudinal analysis also have suggested an association between maternal smoking in pregnancy

Abbreviations used*HR- Hazard ratio**RR- Relative risk*

and asthma development in the first 5 years of life.¹⁸ However, the longitudinal association between childhood asthma development and maternal home second-hand smoke exposure in pregnancy, independent of active maternal smoking, has not been previously reported. We evaluated the associations between childhood asthma development from birth to age 7 years and maternal active smoking and home second-hand smoke exposure during pregnancy in a population-based cohort of children living in Toronto, Canada.

METHODS

Study design and population

A population-based cohort of 5619 grades 1 and 2 school children were recruited from a random sample of 283 public schools in the Greater Toronto Area¹ during the 2006 Toronto Child Health Evaluation Questionnaire Study. In phase 1, cross-sectional exposure data and lifetime outcome data from birth until age 6 or 7 years were collected by validated parent- or guardian-completed questionnaires for all 5619 children. In phase 2, parents or guardians of a randomly selected nested case-control subset of 1497 children, half of whom had reported a history of asthma or wheezing in phase 1, participated in a detailed telephone survey that included information on lifetime home exposures from pregnancy until age 6 or 7 years. The study was approved by the Hospital for Sick Children Research Ethics Board.

Exposures

For all 5619 participants, the parents or guardians reported maternal smoking during pregnancy, in the child's first year of life, and at age 6 or 7 years; they also reported any smokers currently living in the child's home at age 6 or 7 years. For the nested case-control sample of 1497 children, retrospective longitudinal data were collected regarding the presence of any smokers living in every home inhabited by the child from pregnancy until age 6 or 7 years. The month and year of moving into each home were also recorded.

Outcomes

Among the full cohort of 5619 children, age of asthma diagnosis by a physician was reported retrospectively for children who developed asthma between birth and 6 or 7 years. The presence of current wheezing within the past 12 months also was reported.

Definitions of covariates and derived variables

Questionnaire data were collected regarding the child's current age, height, weight, and sex; the duration of breastfeeding (at least 6 months vs less than 6 months, dichotomized based on the current breastfeeding recommendations);¹⁹ preterm birth (born more than 3 weeks early); birth weight (<2500 g vs $\geq$ 2500 g); the presence of older or younger siblings; daycare attendance; maternal and paternal histories of asthma, hayfever, and eczema; the highest education level of the parent or guardian; and income bracket and number of people per household for determination of income adequacy.¹

For children who participated in phase 2, home second-hand smoke exposure in each year of life was derived by subtracting

the child's month and year of birth from the month and year of moving into each home inhabited by the child from pregnancy until age 6 or 7 years and separating the ages of exposure into each year of life. If a child was exposed at any time during a year, he or she was considered exposed in that year. For children who did not participate in phase 2, nonmaternal home smoking in pregnancy was imputed as being present for children whose mothers did not smoke but were exposed to home second-hand smoke at age 6 or 7 years.

Missing data

Data coded as 'unknown' were recoded as missing. Data regarding age of asthma development were missing for 200 children (3.6%), and data regarding maternal smoking or maternal home second-hand smoke exposure during pregnancy were missing for 411 children (7.3%). The majority of covariates had missing data for fewer than 5% of participants. Data about preterm birth were missing for 459 children (8.2%), and income adequacy derived from household income and number of people living in the household could not be calculated for 378 children (6.7%). Breastfeeding duration was not reported for 961 children (17.1%); status of breastfeeding duration for at least 6 months was imputed first as 0 and then as 1 for all children with unknown breastfeeding duration. Reported current age was missing for 838 children (14.9%). Subtracting the child's date of birth from the date of interview allowed determination of age for another 36 children and the remainder of current ages were imputed as the median current age (7 years; interquartile range, 1.0 years). Body mass index was imputed as the median (16.0 kg/m², interquartile range, 3.5 kg/m²) for the 45.0% of children with missing data. After imputation, complete data were present for 4703 children in the final model.

Bias

We attempted to minimize selection bias by using a population-based sampling strategy for the original cohort. For the nested case-control study, multiple attempts were made to contact families, and telephone interviews were offered in the family's first language by using a commercial translation service. We attempted to minimize information bias by collecting questionnaire data with a validated instrument. To minimize recall bias, the parents were advised that the study was about breathing, nose, and skin problems in children, but they were not aware of the primary exposure and outcome. For the retrospective, nested case-control data, we also tried to minimize recall bias of second-hand smoke exposure by grouping the exposures by home to aid recall.

Statistical analysis

The effect of maternal smoking and home second-hand smoke exposure on age of physician-diagnosed childhood asthma development was determined by using time-to-event analysis to generate asthma-free survival curves for children with and without second-hand smoke exposure in each year of life from pregnancy to age 6 or 7 years. Cox proportional hazard models were used to estimate adjusted hazard ratios (HR) of childhood asthma development for home second-hand smoke exposure in pregnancy and the first year of life. Discrete-time hazard models²⁰ were performed to confirm the results of the Cox proportional hazard models and to allow simultaneous evaluation of home second-hand smoke exposure from pregnancy until age 6 or 7 years, and asthma development from birth until age 6 or 7

years. As described in supplementary Table E1 (in this article's Online Repository at www.jaci-inpractice.org), data on home smoke exposure from ages 1 to 5 years were imputed for children who did not participate in phase 2.

All analyses were conducted by using SAS 9.3 (SAS Institute, Cary, NC). Adjusted models were generated by including the child's current age, body mass index, sex, history of preterm birth, breastfeeding for at least 6 months, older or younger siblings, ever being in childcare; the highest parental education, income adequacy, and maternal asthma as covariates in the full models; and removing single variables by backward elimination ($P > .05$). For covariates with *a priori* likelihood of interaction with second-hand smoke exposure, the analysis was repeated, including interaction terms. For covariates with possible interaction based on this model, the analysis was repeated by using indicator variables for each of the 4 categories of home second-hand smoke exposure (0, 1) and the covariate (0, 1). Validity of the proportional hazards assumption was confirmed for the primary exposure and all covariates that remained in the final models (sex, preterm birth, breastfeeding for at least 6 months, and maternal asthma). Goodness of fit for the final models was verified by using deviance residuals to evaluate for influential outliers.

RESULTS

Participants

Details regarding school (80%) and child (25%) participation in the study have been previously reported.¹ In phase 2, the response rate was 90.9%.

Descriptive data

The prevalence of maternal smoking in pregnancy was 5.0%, and 6.2% of the mothers were nonsmokers but were exposed to home second-hand smoke during pregnancy; 15.5% of children developed physician-diagnosed asthma by age 6 or 7 years, 49.7% were boys, 8.4% had a history of preterm birth, 65.2% had been breastfed for at least 6 months, and 9.8% had a history of maternal asthma (Table I).

Cross-sectional analysis

In bivariate analyses, maternal smoking or home second-hand smoke exposure in pregnancy and the first year of life carried increased risk of physician-diagnosed asthma development (relative risk [RR] 1.45 [95% CI, 1.21-1.74] and RR 1.23 [95% CI, 1.04-1.47], respectively). Other factors related to physician-diagnosed asthma development included male sex (RR 1.59 [95% CI, 1.40-1.80]), preterm birth (RR 1.55 [95% CI, 1.29-1.86]), and a history of maternal asthma (RR 2.64 [95% CI, 2.31-3.01]). Being breastfed for at least the first 6 months of life showed a protective association against asthma development (RR 0.79 [95% CI, 0.69-0.91]) (Table I).

Survival analysis

After adjustment for sex, preterm birth, maternal asthma, and breastfeeding duration, maternal active smoking or home second-hand smoke exposure during pregnancy was associated with a 30% increased adjusted hazard of childhood asthma development (adjusted HR 1.30 [95% CI, 1.06-1.60]) (Table II). The association between physician-diagnosed childhood asthma and maternal home second-hand smoke exposure in pregnancy persisted in children without active maternal smoking in pregnancy ($n = 4384$; adjusted HR 1.34 [95% CI, 1.01-1.76]) (Table II). The association also was present for the 539 children (10.0%) with

physician-diagnosed asthma and current wheezing in the past 12 months (adjusted HR 1.36 [95% CI, 1.03-1.79]).

Maternal home second-hand smoke exposure in pregnancy showed evidence of possible interaction with income adequacy ($P = .015$), history of maternal asthma ($P = .012$), breastfeeding ($P = .09$), and sex ($P = .08$). Among children with maternal home second-hand smoke exposure in pregnancy, only children from families with higher income adequacy had an increased risk of incident childhood asthma (adjusted HR 1.52 [95% CI, 1.17-1.99]) (Table III). Children with maternal asthma were at risk for incident asthma, regardless of whether they were unexposed (adjusted HR 3.03 [95% CI, 2.50-3.66]) or exposed (adjusted HR 2.76 [95% CI, 1.88-4.06]) to maternal second-hand smoke in pregnancy (Table IV); the risk of incident asthma associated with maternal home second-hand smoke exposure in pregnancy was lower for children without maternal asthma (adjusted HR 1.49 [95% CI, 1.17-1.89]).

When considering the interaction with income adequacy and maternal asthma in a single model, maternal home second-hand smoke exposure was associated with incident asthma only among children of high income adequacy (adjusted HR 1.81 [95% CI, 1.34-2.44]) for children without maternal asthma; children with maternal asthma had an increased risk of asthma regardless of their income adequacy status (see Table E2 in this article's Online Repository at www.jaci-inpractice.org). The risk of incident asthma associated with maternal home second-hand smoke exposure in pregnancy also was greater among children breastfed for fewer than 6 months (adjusted HR 1.45 [95% CI, 1.13-1.87]) (see Table E3 in this article's Online Repository at www.jaci-inpractice.org) and boys (adjusted HR 1.96 [95% CI, 1.45-2.64]) (see Table E4 in this article's Online Repository at www.jaci-inpractice.org).

The association between maternal smoking or home second-hand smoke exposure in pregnancy and childhood asthma development persisted after adjustment for child second-hand smoke exposure in the first year of life (see Table E5 in this article's Online Repository at www.jaci-inpractice.org). All discrete-time hazard models showed increased odds of childhood asthma development associated with maternal smoking or home second-hand smoke exposure in pregnancy after adjusting for child second-hand smoke exposure from birth until age 7 years (see Table E1 in this article's Online Repository at www.jaci-inpractice.org). Child second-hand smoke exposures in the first year and from birth to age 7 years were not associated with asthma development in multivariable Cox proportional and discrete-time hazard models, with or without adjustment for maternal smoking and home second-hand smoke exposure in pregnancy (Tables E1, E5, and E6 in this article's Online Repository at www.jaci-inpractice.org). There was collinearity between the variables for second-hand smoke exposure in pregnancy, the first year of life, and childhood until age 7 years, so direct conclusions cannot be drawn regarding the relative associations of these exposures from a single model. The increased risks of childhood asthma development associated with male sex, history of preterm birth, and maternal asthma, and the decreased risk associated with being breastfed for at least 6 months remained consistent among all multivariable Cox proportional and discrete-time hazard models. Accounting for cluster sampling by school did not change the associations.

DISCUSSION

Key results

To our knowledge, this is the first population-based study that quantified a longitudinal association between maternal home

TABLE I. Physician-diagnosed incident asthma and home second-hand smoke exposure during pregnancy and the first year of life

Variable	N (%) [*]	Unadjusted RR (95% CI)		
		Home smoking in pregnancy	Home smoking in the first year	Physician-diagnosed asthma
Male sex	2772 (49.7)	0.88 (0.75-1.02)	0.82 (0.72-0.94) [†]	1.59 (1.40-1.80) [‡]
Low birth weight	546 (10.2)	1.03 (0.79-1.33)	0.97 (0.76-1.22)	1.06 (0.86-1.29)
Preterm birth	435 (8.4)	1.19 (0.91-1.56)	1.19 (0.94-1.51)	1.55 (1.29-1.86) [‡]
Breastfed				
Ever	4709 (86.0)	0.46 (0.38-0.54) [‡]	0.48 (0.41-0.55) [‡]	0.90 (0.76-1.07)
For at least 6 mo	3035 (65.2)	0.61 (0.51-0.73) [‡]	0.61 (0.52-0.71) [‡]	0.79 (0.69-0.91) [§]
Siblings				
Older	2748 (49.8)	1.12 (0.96-1.30)	1.05 (0.92-1.21)	0.97 (0.86-1.10)
Younger	2480 (44.9)	0.86 (0.73-1.00)	0.84 (0.73-0.96)	0.98 (0.87-1.12)
Ever in childcare	3183 (57.4)	0.84 (0.72-0.98)	0.91 (0.79-1.05)	1.04 (0.92-1.18)
Low income adequacy	2095 (40.0)	1.41 (1.21-1.66) [‡]	1.29 (1.12-1.49) [§]	1.00 (0.87-1.13)
Highest education high school/college vs university	2915 (54.4)	3.31 (2.73-4.01) [‡]	3.31 (2.73-4.01) [‡]	1.20 (1.06-1.36) [†]
Parental conditions				
Maternal asthma	552 (9.8)	1.54 (1.25-1.90) [‡]	1.44 (1.19-1.75) [§]	2.64 (2.31-3.01) [‡]
Maternal hayfever	719 (12.8)	0.93 (0.74-1.17)	0.88 (0.71-1.08)	1.57 (1.35-1.82) [‡]
Maternal eczema	645 (11.5)	1.07 (0.85-1.35)	1.13 (0.92-1.38)	1.50 (1.28-1.76) [‡]
Paternal asthma	414 (7.4)	1.11 (0.85-1.46)	0.95 (0.73-1.24)	2.60 (2.25-3.00) [‡]
Paternal hayfever	694 (12.4)	0.82 (0.64-1.05)	0.95 (0.77-1.16)	1.36 (1.15-1.60) [§]
Paternal eczema	428 (7.6)	1.01 (0.76-1.33)	0.98 (0.76-1.27)	1.56 (1.30-1.87) [‡]
Physician-diagnosed condition in child				
Asthma	846 (15.5)	1.45 (1.21-1.74) [‡]	1.23 (1.04-1.47)	-
Hayfever	531 (9.7)	1.04 (0.80-1.34)	1.16 (0.93-1.44)	1.67 (1.42-1.97) [‡]
Eczema	1177 (21.4)	0.99 (0.82-1.20)	1.01 (0.85-1.19)	2.41 (2.14-2.73) [‡]
Food allergy	322 (5.9)	0.86 (0.60-1.22)	0.99 (0.73-1.33)	3.38 (2.94-3.88) [‡]
Home smoking (pregnancy)	585 (11.2)	-	-	1.45 (1.21-1.74) [‡]
Maternal	256 (5.0)	-	-	1.53 (1.15-2.03) [†]
Nonmaternal only	329 (6.2)	-	-	1.42 (1.09-1.85)
Home smoking (first year)	708 (13.5)	-	-	1.23 (1.04-1.47)
Maternal	401 (7.8)	-	-	1.17 (0.92-1.50)
Nonmaternal only	307 (5.7)	-	-	1.31 (0.99-1.73)

*Total sample size = 5619; frequencies are adjusted for missing values.

[†]Significant associations, $P < .01$ level.

[‡]Significant associations, $P < .0001$ level.

[§]Significant associations, $P < .001$ level.

^{||}Significant associations, $P < .05$ level.

second-hand smoke exposure in pregnancy and childhood asthma development. Children whose mothers smoked actively or were exposed to home second-hand smoke during pregnancy were more likely to develop physician-diagnosed asthma and also developed asthma sooner than children whose mothers were not exposed (adjusted HR 1.30 [95% CI, 1.06-1.60]). Children of nonsmoking mothers with home second-hand smoke exposure in pregnancy also had an increased risk of childhood asthma development (adjusted HR 1.34 [95% CI, 1.01-1.76]).

Strengths and limitations

This study was conducted in a population-based sample of children,¹ and the detailed longitudinal exposure and outcome data were collected by using a validated instrument. The absence of maternal home second-hand smoke exposure data among children who did not participate in phase 2 is a limitation of this study. Among children who participated in phase 2, only 7% had any changes in home second-hand smoke exposure between pregnancy and age 6 or 7 years. Given the small number of

children in the full phase 1 cohort for whom the current exposure might not reflect the exposure in pregnancy, we believed that the imputation was justified.

For mothers who did not smoke, imputing data regarding maternal second-hand smoke exposure in pregnancy based on child second-hand smoke exposure at age 6 or 7 years showed that 6.2% of mothers were nonsmokers with exposure to second-hand smoke in pregnancy. Among children who participated in phase 2, 12.6% of mothers reported to be nonsmokers and to have home second-hand smoke exposure in pregnancy. Maternal active smoking in pregnancy also was more common among children who participated in phase 2 (5.6% vs 5.0% among the full cohort). Therefore, there may have been an underestimation of maternal home second-hand smoke exposure in pregnancy among children who did not participate in phase 2. This exposure misclassification would likely have been nondifferential and would be expected to bias our results toward the null; hence, we may have underestimated the true association. Although phase 2 did not have sufficient statistical power to answer this question,

TABLE II. Association between age of physician-diagnosed incident asthma and maternal home second-hand smoke exposure during pregnancy*

	Adjusted HR of incident asthma (95% CI)		
	Maternal active and passive smoking (entire cohort, n = 4703)	Maternal active smoking (entire cohort, n = 4625)	Excluding children with maternal active smoking in pregnancy (n = 4384)
Home smoke (pregnancy)	1.30 (1.06-1.60)†	1.27 (0.95-1.69)	1.34 (1.01-1.76)†
Male sex	1.69 (1.45-1.96)‡	1.68 (1.44-1.95)‡	1.78 (1.51-2.08)‡
Preterm birth	1.64 (1.32-2.05)‡	1.61 (1.28-2.02)‡	1.55 (1.22-1.97)§
Maternal asthma	2.77 (2.33-3.30)‡	2.76 (2.31-3.29)‡	2.82 (2.34-3.40)‡
Breastfed for at least 6 mo	0.84 (0.72-0.98)†	0.83 (0.71-0.97)†	0.85 (0.73-1.00)†

*Results of Cox proportional hazard models.

†Significant associations, $P < .05$ level.

‡Significant associations, $P < .0001$ level.

§Significant associations, $P < .001$ level.

TABLE III. Association between age of physician-diagnosed incident asthma and maternal home second-hand smoke exposure during pregnancy, accounting for interaction between home second-hand smoke exposure in pregnancy and income adequacy*

	Adjusted HR of incident asthma (95% CI)
Home smoke (pregnancy) and high income adequacy	1.52 (1.17-1.99)†
Home smoke (pregnancy) and low income adequacy	0.99 (0.70-1.41)
No home smoke (pregnancy) and low income adequacy	1.10 (0.92-1.31)
Male sex	1.68 (1.43-1.96)‡
Preterm birth	1.63 (1.29-2.05)‡
Maternal asthma	2.80 (2.33-3.35)‡
Breastfed for at least 6 mo	0.85 (0.73-1.00)§

*Results of a Cox proportional hazard model; children without maternal home second-hand smoke exposure in pregnancy and of high-income adequacy are the reference group.

†Significant associations, $P < .01$ level.

‡Significant associations, $P < .0001$ level.

§Significant associations, $P < .05$ level.

the association between maternal home second-hand smoke exposure during pregnancy and incident childhood asthma was similar among the phase 2 participants ($n = 1327$; adjusted HR 1.24 [95% CI, 0.89-1.73]) compared with the full cohort.

We did not have information about the number of smokers present in the household or about pack-years of exposure. In the reported adjusted models, missing breastfeeding duration was imputed as fewer than 6 months, reasoning that mothers who breastfed for at least 6 months would be more likely to remember and report the duration. A sensitivity analysis showed similar results when missing breastfeeding duration was imputed as at least 6 months and when breastfeeding duration was not imputed. As with any observational study, the possibility of residual confounding by variables not included in the final model remains an inherent limitation.

Selection bias in the Toronto Child Health Evaluation Questionnaire data has been evaluated by comparison with data from the Census and the National Longitudinal Survey of Children and Youth; the populations were found to be similar with respect to demographic characteristics and the primary

study outcomes.¹ The risk of recall bias due to retrospective data collection was minimized by the method of data collection, which focused on the home addresses and on recall of exposures within each home. Under-reporting of second-hand smoke exposure due to the stigma of smoking is possible, but the proportion of children with reported exposure to second-hand smoke in this 2006 cohort was similar to national data collected in the 2006 Canadian Tobacco Use Monitoring Survey (9%).³ Although laboratory measures of current smoking were not obtained, reporting of second-hand smoke among 6- to 11-year-old children in the 2007-2009 Canadian Health Measures Survey has been shown to accurately reflect exposure measured by cotinine levels, with a mean cotinine of 69.6 ng/mL (95% CI, 58.4-78.9 ng/mL) among children with reported second-hand smoke exposure and 7.7 ng/mL (95% CI, 5.6-10.3 ng/mL) among children reported to have no exposure.²¹ Similar associations with prevalent asthma in toddlers also have been shown for reported smoking versus measured cotinine levels.⁷

Interpretation

Our findings are consistent with previous cross-sectional analyses that showed associations between maternal smoking in pregnancy and childhood asthma development.^{6-8,11,15,17} Our findings also corroborate a longitudinal study that used 1996-1999 National Longitudinal Survey of Children and Youth data, which demonstrated an association between maternal smoking of more than 5 cigarettes per day during pregnancy and asthma development up to age 5 years (adjusted HR 1.29 [95% CI, 1.07-1.57]).¹⁸ The proportion of mothers who reported smoking during pregnancy (18.8%)¹⁸ was higher than reported in the current study, consistent with higher overall exposure to second-hand smoke among Canadian children in the 2000 Canadian Tobacco Use Monitoring Survey compared with 2006.³

Two longitudinal studies found associations between parental smoking in the first 3 months of life and asthma development,²²⁻²⁴ but in one of these studies, the association was present only until age 2 years (adjusted HR 1.34 [95% CI, 1.24-1.45]) and disappeared after age 2 years (adjusted HR 1.00 [95% CI, 0.84-1.17]);²² neither study evaluated exposure during pregnancy, and these early life exposures also may have reflected continued exposure from pregnancy. These results differed slightly from our study, which did not distinguish home second-hand smoke exposure in the first 3 months of life from exposure

TABLE IV. Association between age of physician-diagnosed incident asthma and maternal home second-hand smoke exposure during pregnancy, accounting for the interaction between home second-hand smoke exposure in pregnancy and a history of maternal asthma*

	Adjusted HR of incident asthma (95% CI)
Home smoke (pregnancy) and no maternal asthma	1.49 (1.17-1.89) [†]
Home smoke (pregnancy) and maternal asthma	2.76 (1.88-4.06) [‡]
No home smoke (pregnancy) and maternal asthma	3.03 (2.50-3.66) [‡]
Male sex	1.69 (1.45-1.96) [‡]
Preterm birth	1.64 (1.31-2.05) [‡]
Breastfed for at least 6 mo	0.83 (0.72-0.96) [§]

*Results of a Cox proportional hazard model; children without maternal home second-hand smoke exposure in pregnancy or maternal asthma are the reference group.

[†]Significant associations, $P < .01$ level.

[‡]Significant associations, $P < .0001$ level.

[§]Significant associations, $P < .05$ level.

at any time during the first year of life. Our results were consistent with other longitudinal studies that evaluated current exposure in children at or above age 6 years and did not show an association between second-hand smoke exposure later in childhood and asthma development.^{25,26}

This study extends the results of published longitudinal studies by determining that maternal home second-hand smoke exposure during pregnancy is associated with childhood asthma development, even if the mother is not an active smoker during pregnancy. The risks of active maternal smoking during pregnancy have been described,¹⁸ but longitudinal associations between asthma development and maternal home second-hand smoke exposure from household smokers in the absence of active maternal smoking during pregnancy have not been previously demonstrated.

We found evidence of statistical interaction between maternal home second-hand smoke exposure in pregnancy and several of the confounding variables. Among children without a history of maternal asthma, only children from families with higher income adequacy had an increased risk of incident childhood asthma associated with maternal home second-hand smoke exposure (adjusted HR 1.81 [95% CI, 1.34-2.44]). One possible explanation for this finding is that other harmful exposures not measured in this study, such as chronic family²⁷ and maternal²⁸ stress, community crime,²⁹ proximity to major roads,³⁰ and poor outdoor³¹ or indoor^{32,33} air quality may be more common exposures among mothers of lower income adequacy and may mask the additional effect of second-hand smoke exposure in their children. Associations have been shown between chronic lower socioeconomic status and asthma development in other studies,²⁷ but the associations between income adequacy and incident asthma remain under investigation; additional studies will be needed to confirm the presence or absence of a true biologic interaction.

Our findings also suggest a slightly lower risk of incident asthma for children with a history of maternal asthma if they also were exposed to maternal home second-hand smoke during pregnancy (adjusted HR 2.76 [95% CI, 1.88-4.06]) compared with those who were not exposed (adjusted HR 3.03 [95% CI, 2.50-3.66]). This finding may be due to the small number

($n = 87$ [1.5%]) of children with home second-hand smoke exposure and a history of maternal asthma. Once again, additional studies will be needed to confirm or refute a true biologic interaction. Maternal asthma is a well-established risk factor for childhood asthma development¹⁸ and remained associated with incident childhood asthma in all the models.

The stronger association between maternal home second-hand smoke exposure in pregnancy and incident asthma among children without breastfeeding for at least 6 months and in male children may represent interaction or additive effects of risk factors. Recent studies of breastfeeding and childhood asthma development have shown variable associations.^{10,18,34-43} The stronger association between maternal home second-hand smoke exposure in pregnancy and incident asthma among children without breastfeeding for at least 6 months (adjusted HR 1.45 [95% CI, 1.13-1.87]) may also reflect children being held and fed by smokers living in the home, rather than by the nonsmoking mother. Male children generally have been shown to have an increased risk of asthma compared with female children;^{8,10,18} smaller airways in male children may increase susceptibility to the effects of smoking as well as increasing the inherent risk of asthma.

Generalizability

The demographic,¹ outcome,¹ and exposure³ variables in this cohort were similar to national data, which suggests that these results should be generalizable to other urban centers in Canada. Some communities in Canada have much higher rates of maternal smoking and exposure to home second-hand smoke than the national average.⁴⁴ Our results may not be generalizable to children who live in these communities.

CONCLUSION

Children whose mothers have home second-hand smoke exposure during pregnancy are more likely to develop physician-diagnosed asthma and to develop asthma sooner, even if the mother does not smoke actively during pregnancy. This study highlights the continued importance of reducing children's exposure to home second-hand smoke and suggests that childhood asthma prevention programs should include strategies for smoking cessation targeted toward smokers living in the homes of smoking and nonsmoking pregnant women as well as women who smoke actively in pregnancy. Maternal smoking during pregnancy has decreased over time,^{1,18} which suggests that messages regarding the dangers of maternal smoking during pregnancy have had a positive effect. We suggest that messages that recommend smoking cessation for pregnant women should also advise smoking cessation for household contacts of all smoking and nonsmoking pregnant women.

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TABLE E1. Association between age of physician-diagnosed incident asthma and home second-hand smoke exposure during pregnancy and childhood (n = 5590)*

	Adjusted odds ratio of incident asthma (95% CI)		
	Imputation for children with the same exposure in the first and current years (n = 3436)†	Further imputation for children with different exposure in the first and current years (n = 657)	
		Imputed no exposure from ages 1-5 y	Imputed full exposure from ages 1-5 y
Home smoke (pregnancy)	1.58 (1.10-2.27)‡	1.39 (1.04-1.87)‡	1.40 (1.01-1.94)‡
Home second-hand smoke (birth to 7 y)	0.85 (0.58-1.26)	0.94 (0.67-1.31)	0.95 (0.69-1.31)
Male sex	1.70 (1.45-2.00)§	1.69 (1.44-1.97)§	1.69 (1.44-1.97)§
Preterm birth	1.59 (1.24-2.02)	1.56 (1.22-1.97)	1.56 (1.23-1.98)
Maternal asthma	2.88 (2.38-3.48)§	2.99 (2.49-3.60)§	2.99 (2.48-3.59)§
Breastfed for at least 6 months	0.84 (0.72-0.99)‡	0.82 (0.70-0.96)‡	0.82 (0.70-0.96)‡

*Results of discrete-time hazard models; all discrete-time hazard models use the full sample because all the children had data for home second-hand smoke exposure in pregnancy and the first and current years; the association between home smoke exposure in pregnancy and asthma development persists after adjustment for second-hand smoke exposure from birth to age 7 y; relative effects of second-hand smoke exposure in pregnancy and from birth to age 7 y cannot be determined due to collinearity.

†Children exposed in the first and current years were assumed to be exposed in all years and those unexposed in the first and current years were assumed to be unexposed in all years.

‡Significant associations, $P < .05$ level.

§Significant associations, $P < .0001$ level.

||Significant associations, $P < .001$ level.

TABLE E2. Association between age of physician-diagnosed incident asthma and maternal home second-hand smoke exposure during pregnancy, accounting for interaction between home second-hand smoke exposure in pregnancy, income adequacy and history of maternal asthma*

	Adjusted HR of incident asthma (95% CI)
No home smoke (pregnancy), no maternal asthma, low income adequacy	0.98 (0.81-1.20)
No home smoke (pregnancy), maternal asthma, high income adequacy	2.59 (2.04-3.29)†
No home smoke (pregnancy), maternal asthma, low income adequacy	4.65 (3.37-6.42)†
Home smoke (pregnancy), no maternal asthma, high income adequacy	1.81 (1.34-2.44)‡
Home smoke (pregnancy), no maternal asthma, low income adequacy	1.02 (0.66-1.56)
Home smoke (pregnancy), maternal asthma, high income adequacy	2.49 (1.42-4.34)§
Home smoke (pregnancy), maternal asthma, low income adequacy	2.48 (1.36-4.55)§
Male sex	1.67 (1.43-1.95)†
Preterm birth	1.64 (1.30-2.06)†
Breastfed for at least 6 mo	0.85 (0.73-0.99)

*Results of a Cox proportional hazard model; children without maternal home second-hand smoke exposure in pregnancy, without maternal asthma and of high-income adequacy are the reference group.

†Significant associations, $P < .0001$ level.

‡Significant associations, $P < .001$ level.

§Significant associations, $P < .01$ level.

||Significant associations, $P < .05$ level.

TABLE E3. Association between age of physician-diagnosed incident asthma and maternal home second-hand smoke exposure during pregnancy, accounting for the interaction between home second-hand smoke exposure in pregnancy and the history of being breastfed for at least 6 months*

	Adjusted HR of incident asthma (95% CI)
Home smoke (pregnancy) and breastfed for at least 6 mo	0.92 (0.63-1.34)
Home smoke (pregnancy) and breastfed for less than 6 mo	1.45 (1.13-1.87)†
No home smoke (pregnancy) and breastfed for at least 6 mo	0.88 (0.75-1.03)
Male sex	1.68 (1.45-1.96)‡
Preterm birth	1.64 (1.31-2.04)‡
Maternal asthma	2.74 (2.30-3.27)‡

*Results of a Cox proportional hazard model; children without maternal home second-hand smoke exposure in pregnancy and breastfed for less than 6 mo are the reference group.

†Significant associations, $P < .01$ level.

‡Significant associations, $P < .0001$ level.

TABLE E4. Association between age of physician-diagnosed incident asthma and maternal home second-hand smoke exposure during pregnancy, accounting for interaction between home second-hand smoke exposure in pregnancy and sex*

	Adjusted HR of incident asthma (95% CI)
Home smoke (pregnancy) and male children	1.96 (1.45-2.64)†
Home smoke (pregnancy) and female children	1.62 (1.20-2.18)‡
No home smoke (pregnancy) and male children	1.80 (1.52-2.12)†
Preterm birth	1.64 (1.32-2.05)†
Maternal asthma	2.77 (2.33-3.30)†
Breastfed for at least 6 mo	0.84 (0.72-0.97)§

*Results of a Cox proportional hazard model; female children without maternal home second-hand smoke exposure in pregnancy are the reference group.

†Significant associations, $P < .0001$ level.

‡Significant associations, $P < .01$ level.

§Significant associations, $P < .05$ level.

TABLE E5. Association between age of physician-diagnosed incident asthma and child's home second-hand smoke exposure during the first year of life*

	Adjusted HR of incident asthma (95% CI)		
	Home smoke exposure in pregnancy and first year (n = 4679)	Home smoke exposure in first year of life (n = 4714)	Home smoke exposure in first year (no pregnancy exposure) (n = 4028)
Home smoke (pregnancy)	1.78 (1.16-2.75)†	-	-
Home smoke (first year)	0.69 (0.45-1.05)	1.14 (0.93-1.39)	0.90 (0.55-1.46)
Male sex	1.68 (1.44-1.95)‡	1.69 (1.46-1.97)‡	1.79 (1.51-2.12)‡
Preterm birth	1.65 (1.32-2.06)‡	1.62 (1.30-2.03)‡	1.63 (1.27-2.10)§
Maternal asthma	2.79 (2.34-3.32)‡	2.79 (2.35-3.33)‡	3.09 (2.55-3.74)‡
Breastfed for at least 6 mo	0.84 (0.72-0.98)	0.82 (0.71-0.96)	-
Parental university education		-	1.21 (1.03-1.43)

*Results of Cox proportional hazard models; the association between home smoke exposure in pregnancy and asthma development persists after adjustment for second-hand smoke exposure in the first year of life; relative effects of second-hand smoke exposure in pregnancy and the first year cannot be determined due to collinearity.

†Significant associations, $P < .01$ level.

‡Significant associations, $P < .0001$ level.

§Significant associations, $P < .001$ level.

||Significant associations, $P < .05$ level.

TABLE E6. Association between age of physician-diagnosed incident asthma and home second-hand smoke exposure during childhood (n = 5590)*

	Adjusted odds ratio of incident asthma (95% CI)		
	Imputation for children with same exposure in the first and current years (n = 3436)†	Further imputation for children with different exposure in the first and current years (n = 657)	
		Imputed no exposure from ages 1-5 y	Imputed full exposure from ages 1-5 y
Home second-hand smoke (birth to 7 y)	1.21 (0.95-1.55)	1.18 (0.92-1.51)	1.14 (0.94-1.39)
Male sex	1.71 (1.45-2.00)‡	1.69 (1.45-1.97)‡	1.69 (1.45-1.97)‡
Preterm birth	1.57 (1.23-2.01)§	1.50 (1.19-1.90)§	1.50 (1.19-1.90)§
Maternal asthma	2.87 (2.37-3.47)‡	3.08 (2.57-3.69)‡	3.10 (2.59-3.71)‡
Breastfed for at least 6 mo	0.83 (0.71-0.97)	0.80 (0.69-0.93)¶	0.80 (0.69-0.93)¶

*Results of discrete-time hazard models; all discrete-time hazard models use the full sample because all children had data for home second-hand smoke exposure in pregnancy and the first and current years.

†Children exposed in the first and current years were assumed to be exposed in all years, and those unexposed in the first and current years were assumed to be unexposed in all years.

‡Significant associations, $P < .0001$ level.

§Significant associations, $P < .001$ level.

||Significant associations, $P < .05$ level.

¶Significant associations, $P < .01$ level.

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