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Effect of Passive Smoking on the Growth of Pulmonary Function and Respiratory Symptoms in Schoolchildren

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ABSTRACT

Background: Environmental tobacco smoke affects the current and future health of children. **Objective:** To determine whether schoolchildren aged 8-17 years old residing at an altitude of 2,240 m and exposed to tobacco smoke at home presented a reduction in the growth of pulmonary function and a greater problem of respiratory symptoms and infections compared with non-exposed children. **Materials and Methods:** We followed, with questionnaires and spirometry, 1,632 boys and 1,555 girls from Mexico City and its metropolitan area (the Metropolitan Study to Evaluate the Chronic Effects of Pollution in School-age Children [EMPECE]) every six months for six years. The impact of passive smoking was estimated by mixed-effects models and Generalized Linear and Latent Mixed Models (GLLAMM), stratifying by gender and adjusting for age, height, weight, and ozone levels. **Results:** Passive smoking (reported by one-half of participants) was associated with reduced spirometric lung function (log transformed or as Z-scores) and a higher frequency of self-reported respiratory symptoms and respiratory infections. Levels of forced expiratory volume in 1 second and forced vital capacity in individuals exposed to passive smoking were 6.8 and 14.1 ml, respectively, below those of non-exposed children, and these values decreased with increasing number of smokers at home and higher ozone levels. **Conclusions:** Passive smoking in children is a significant risk factor for respiratory disease and reduced lung function growth, which are additive with levels of air pollution, asthma, and the presence of respiratory symptoms. (REV INVES CLIN. 2016;68:119-27)

Key words: Pulmonary function testing. Epidemiology. Passive smoking. Respiratory symptoms. Asthma.

INTRODUCTION

Environmental tobacco smoke is a world health problem and part of the tobacco epidemic which is suffered mostly by children and imposes risks for their current and future health, unfortunately mainly caused by their parents and close relatives. Environmental tobacco smoke contains thousands of chemical substances, many of which are toxic, irritating, or pharmacologically active, and over 40 of these cause cancer[1,2].

The 2009 report of the World Health Organization (WHO) indicates that 700 million children worldwide (about 40% of all children) are exposed to second-hand

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tobacco smoke (SHS) at home. Also, SHS is estimated to cause about 600,000 premature deaths each year worldwide. Of all deaths attributable to SHS, 31% occur among children[3]. Likewise, a study conducted in Scotland reported an association between salivary cotinine levels in children aged 2-12 years, the number of persons who smoke in the home, and the frequency with which they smoke[4]. The authors also found a positive association between passive smoking and respiratory problems in the children studied.

A decrease in pulmonary function has also been reported in children exposed to passive smoking[5], particularly in those with asthma[6] and those prenatally exposed[7,8]. Whether due to a direct exposure from their mothers or from environmental tobacco smoke, a reduction in birth weight has been observed, affecting the child's development and behavior[9,10], and increasing the risks for chronic obstructive pulmonary disease (COPD) or lung cancer at a mature age[11,12], as well as leukemias, lymphomas, and brain tumors during infancy[13]. In addition, boys exposed to tobacco smoke who reported wheezing and asthma showed greater functional deterioration than girls[14,15]. The SHS from parents and especially from the mother is associated with lower respiratory tract diseases in children[13].

In Mexico, surveys have shown that children's exposure to SHS is high[16], and smoking during pregnancy reduces the newborn's weight by 154 g and the size by 0.79 cm[17]. The 2002 National Drug Addictions Survey (ENA) in Mexico found that approximately 50% of the total population and up to 80% of those residing in urban areas were passive smokers[18].

The objective of the present study was to determine whether exposure to tobacco smoke at home in schoolchildren aged 8-17 years residing at 2,240 m above sea level is associated with a reduction in the growth of pulmonary function or with an increase in respiratory symptoms and infections, and whether there is a gender-related differential effect and an additive effect with air pollution.

MATERIALS AND METHODS

The Metropolitan Study to Evaluate the Chronic Effects of Pollution in School-age Children (EMPECE Study) was undertaken in Mexico City beginning on April 23, 1996, with children in third grade of primary school[19]. The protocol was approved by the Ethics Committee of the National Institute of Respiratory Diseases (INER) of Mexico. All parents provided written informed consent for their children to be study subjects.

We selected 10 fixed-site air-monitoring stations in Mexico City and randomly selected 39 elementary schools from among those located within a 2 km radius of the stations. The study cohort consisted of students at the selected schools who were eight years of age at the beginning of the study and whose parents had signed a letter of informed consent. Children could enter or leave the cohort during the course of the study. At baseline, a questionnaire was completed by the parents of 1,819 children, and a spirometric test was administered to each child (Phase 1). The subsequent evaluations (a total of six) were done every six months during the spring and autumn of each year until the end of the children's primary school education in 1999. Children remaining in the same school to study secondary level were followed for three additional years until 2002; thus, we collected information for a total of 12 evaluations[9,20,21]. A health questionnaire and written informed consent were filled out by parents and returned the day before each evaluation; it included self-reported diseases (asthma, respiratory infections, vaccination, previous pneumonias, ear infections, allergies, previous tonsillectomy, hyperactivity, neurologic diseases, heart diseases, gastroesophageal reflux, and obesity), and chronic respiratory symptoms (cough, wheezing, phlegm, and dyspnea). We also analyzed the reported frequency of respiratory infections (common cold, sore throat, and bronchitis). Exposure to SHS in children was evaluated with the most common questions, all bearing an independent association with cotinine levels in children[22]: Does the father smoke inside the house? Does the mother smoke inside the house? Do other persons smoke inside the house? During the last evaluation in secondary school (Phase 12), a question of direct smoking was included: Have you smoked a cigarette in the last month?

Spirometry tests were conducted using identical computerized dry-rolling seal spirometers (922 Spirometer; SensorMedics, USA) that were calibrated each morning prior to data collection with a 3 l syringe (SensorMedics). We recorded only the expiratory part of forced expiratory maneuvers and analyzed forced expiratory volume

Table 1. Description of variables by gender and phase of the study

		Exposed to passive smoking	Age (years)	Height (cm)	BMI
Girls	Phase*	n/total (%)	Mean (SD)	Mean (SD)	Mean (SD)
	1	406/929 (43.7)	8.7 (0.8)	130.6 (6.5)	17.2 (3.0)
	2	509/944 (53.9)	9.1 (0.8)	133.3 (6.5)	17.5 (3.0)
	3	637/1,161 (54.9)	9.6 (0.8)	137.3 (7.0)	18.2 (3.4)
	4	598/1,117 (53.5)	10.2 (0.8)	140.5 (7.5)	18.8 (3.6)
	5	515/942 (54.7)	10.6 (0.8)	143.4 (7.3)	19.2 (3.7)
	6	595/1,112 (53.5)	11.1 (0.8)	146.3 (7.1)	19.9 (3.8)
	7	573/1,115 (51.4)	11.7 (0.8)	149.1 (6.7)	20.1 (3.9)
	8	202/462 (43.7)	12.6 (0.7)	152.8 (5.9)	21.8 (4.4)
	9	186/426 (43.7)	13.1 (0.6)	154.2 (5.7)	22.0 (4.2)
	10	161/403 (40.0)	13.5 (0.6)	155.0 (5.5)	22.4 (4.2)
	11	141/350 (40.3)	14.0 (0.6)	155.7 (5.5)	22.7 (4.1)
	12	149/355 (42.0)	14.4 (0.7)	156.2 (5.6)	22.7 (4.2)
Boys	Phase	n/total (%)	Mean (SD)	Mean (SD)	Mean (SD)
	1	342/890 (42.9)	8.7 (0.8)	131.0 (6.2)	17.4 (3.1)
	2	540/962 (56.1)	9.2 (0.8)	133.7 (6.7)	17.8 (3.3)
	3	648/1,160 (55.9)	9.7 (0.8)	136.8 (6.8)	18.3 (3.6)
	4	546/1,087 (54.8)	10.2 (0.8)	139.8 (7.4)	19.0 (3.9)
	5	503/917 (54.9)	10.7 (0.8)	142.8 (7.6)	19.2 (3.9)
	6	598/1,105 (54.1)	11.2 (0.8)	145.5 (8.0)	19.6 (3.9)
	7	585/1,103 (53.0)	11.7 (0.8)	148.7 (8.1)	19.8 (4.1)
	8	185/466 (39.7)	12.6 (0.7)	155.1 (8.3)	21.0 (4.5)
	9	159/407 (39.1)	13.1 (0.6)	158.1 (8.2)	21.0 (4.3)
	10	141/389 (36.3)	13.5 (0.6)	160.7 (7.8)	21.3 (4.4)
	11	124/330 (37.6)	14.1 (0.6)	163.1 (7.4)	21.7 (4.4)
	12	148/343 (43.2)	14.5 (0.6)	164.9 (7.3)	22.0 (4.6)

*Study phase: 12 study evaluations, one every six months.
BMI: body mass index; SD: standard deviation.

in 1 second (FEV_1), forced vital capacity (FVC), and their ratio (FEV_1/FVC): forced expiratory flow (FEF) between 25-75% of the FVC ($FEF_{25-75\%}$).

Tests were performed at the school during morning and early afternoon hours. As many as eight maneuvers were conducted for each child to obtain three acceptable tests according to 1994 American Thoracic Society (ATS) criteria[23]. Additional details on spirometry methodology, including sustained quality control along the study, longitudinal variability, reference values and impact of socioeconomic status, were described in previous reports[17,18,24,25].

The impact of several air pollutants on the lung function of the cohort was previously reported[16]. As an indicator of air pollution, we included in the present analysis ambient ozone (O_3) from 10 government air-monitoring stations, assigning for each child data from the station closest to his/her school. We calculated 8 hour O_3 means (parts per billion, ppb, between 10 a.m. and 6 p.m.), whereas long-term exposure for each day of the study period was estimated as the average over the previous six months of the daily O_3 8 h mean[19].

Statistical analysis

We fitted multilevel mixed-effects linear models adjusted for age and gender to determine the association of SHS (the presence of any parent or person smoking inside the home) with spirometry variables (log-transformed FEV_1 and FVC) along time with and without height, and ozone concentrations (average over the previous six months of the daily O_3 8 h mean, as a general indicator of air pollution). Levels considered

in the models were the city zone (air pollution monitors) and repeated measurements. We also explored lung function (FEV_1 and FVC) expressed as the Z-score of height-, age-, and gender-predicted values[25] in models adjusted for ozone, presence of asthma, presence of respiratory symptoms, and frequent respiratory infections. Three-level Generalized Linear and Latent Mixed Models (GLLAMM) were fitted for dichotomous responses (yes/no) such as the presence of respiratory symptoms and the reported frequency of respiratory infections as a function of secondhand smoking. The order of levels included was as follows: the observations, the children, and the pollutant monitors reflecting the geographical area of Mexico City. Repeatability of passive smoking questions was estimated by the Kappa coefficient[26]. Secondhand smoking was included as adjustment variable in a previous report on the impact of socioeconomic status on lung function[24].

Analyses were conducted using STATA v.13 statistical software (Stata Corp., College Station, TX, USA).

RESULTS

We included a total of 1,819 participants (929 girls and 890 boys) in the first study phase; the number of children studied in each phase is described in table 1 as well as the proportion of passive smoking and anthropometric variables by gender. Kappa coefficient for multiple observations of passive smoking questions (up to a maximum of 12 evaluations) were for the father 0.520 (95% CI: 0.496-0.533), for the mother 0.605 (95% CI: 0.595-0.607), and for "other persons smoking at home" 0.477 (95% CI: 0.463-0.486), concordance classified usually between moderate and considerable[26]. The proportion of passive smoking ranged from 40.0 to 54.9% in girls and from 36.3 to 56.1% in boys in the repeated questionnaires applied, with no significant difference secondary to reported income or parents' education level. Reports of respiratory infections in the previous three months (bronchitis, common cold, and sore throat) in Phase 1 were as high as 69.6% in girls and 66.3% in boys.

Passive smoking, measured as the number of persons smoking inside the home and as dichotomous variable (yes/no), was associated significantly with respiratory symptoms and respiratory infections. For age-, height-, weight-, and ozone-level-adjusted GLLAMM models, we observed odds ratios (OR) of between 1.4 and 2.3 predicting respiratory symptoms in those exposed to passive smoking, exhibiting a trend to increase with the number of persons smoking inside the home both in boys and in girls; for recent respiratory infections, OR were between 1.2 and 1.5 in both boys and girls (Table 2).

Table 2. Multilevel linear logistic models by gender and the number of persons who smoked inside home

Number of persons smoking inside home	Girls				Boys			
	Crude		Adjusted*		Crude		Adjusted	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Respiratory symptoms (cough, wheezing, phlegm and dyspnea)								
One	1.6†	(1.21-2.05)	1.4†	(1.08-1.89)	1.4†	(10.07-10.83)	1.3	(0.94-1.66)
Two	1.6†	(1.18-2.20)	1.7†	(1.23-2.38)	1.6†	(1.18-2.18)	1.7†	(1.22-2.36)
Three	1.7‡	(1.09-2.72)	1.8†	(1.10-2.87)	2.2†	(1.41-3.42)	2.3†	(1.41-3.64)
Ozone			1.0	(0.98-1.01)			1.0	(0.97-0.99)
Respiratory infections (common cold, sore throat and bronchitis)								
One	1.4†	(1.21-1.54)	1.3†	(1.12-1.44)	1.3†	(1.14-1.45)	1.2‡	(1.03-1.33)
Two	1.3†	(1.17-1.54)	1.3†	(1.16-1.55)	1.5†	(1.32-1.74)	1.5†	(1.28-1.71)
Three	1.5†	(1.24-1.88)	1.5†	(1.19-1.83)	1.4†	(1.11-1.72)	1.4‡	(1.06-1.68)
Ozone			1.04†	(1.03-1.05)			1.04†	(1.04-1.05)

*Models adjusted for age, height, weight, and ozone levels; †$p < 0.01$; ‡$p < 0.05$.
OR: odds ratio; 95% CI: 95% confidence interval.

Table 3. Multilevel linear regression models of mixed effects by gender

Dependent variable	Girls		Boys	
Log-lung function models	β	**95% CI**	β	**95% CI**
	Number of persons who reported smoking within the home			
Ln(FEV_1)	−0.00412†	−0.0069, −0.0014	−0.00173	−0.0044, 0.0009
Ln(FVC)	−0.00757†	−0.0101, −0.0050	−0.00280‡	−0.0052, −0.0004
Ln(FEV_1/FVC)	0.00359†	0.0020, 0.0052	0.00106	−0.0006, 0.0027
	Ozone effect			
Ln(FEV_1)	−0.00096†	−0.0012, −0.0008	−0.00110†	−0.0013, −0.0009
Ln(FVC)	−0.00056†	−0.0008, −0.0004	−0.00065†	−0.0008, −0.0005
Ln(FEV_1/FVC)	−0.00039†	−0.0005, −0.0003	−0.00045†	−0.0006, −0.0003
Z score models	β	**95% CI**	β	**95% CI**
	Number of persons who reported smoking within the home			
FEV_1 (Z-score)	−0.04174†	−0.0629, −0.0206	−0.04076†	−0.0620, −0.0196
FVC (Z-score)	−0.07171†	−0.0920, −0.0514	−0.05016†	−0.0709, −0.0294
FEV_1/FVC (Z-score)	0.04488†	0.0233, 0.0665	0.00895	−0.0120, 0.0299
	Ozone effect			
FEV_1 (Z-score)	−0.01032†	−0.0118, −0.0088	−0.01016†	−0.0117, −0.0087
FVC (Z-score)	−0.00662†	−0.0081, −0.0052	−0.00660†	−0.0081, −0.0051
FEV_1/FVC (Z-score)	−0.00707†	−0.0086, −0.0055	−0.00593†	−0.0074, −0.0045

Lung function models: each model was adjusted for age, age squared, height, weight, ozone levels, asthma, respiratory symptoms, and respiratory infections. Z-score models were adjusted for age, height, and weight according to Martínez-Briseño, et al.[20] predicting equations. Each model was additionally adjusted for ozone levels, asthma, respiratory symptoms, and respiratory infections.
†$p < 0.01$; ‡$p < 0.05$.
β: coefficients; 95% CI: 95% confidence interval; Ln: lung; FEV_1: forced expiratory volume in 1 second; FVC: forced vital capacity.

We also observed a decrease in log-lung function (log-FEV_1 and logFVC) according to the number of persons smoking at home in multilevel models adjusted for age, height, weight, and ozone levels in girls, and of logFVC in boys (Table 3), whereas both were decreased significantly in both genders if lung function was expressed as a Z-score. The average impact of passive smoking on an individual of mean age and height for each person smoking indoors was a decrease in FEV_1 of 0.30% (6.8 ml) for all individuals, 0.41% (9.2 ml) for girls, and 0.17% (4.1 ml) for boys. For FVC, the average drop was of 0.53% (14.1 ml) for all participants, 0.75% (19.4 ml) for girls, and 0.28% (7.8 ml) for boys. We did not observe a worse adverse effect of secondhand smoking in children with a diagnosis of asthma than in the remainder.

In the models, we tested other possible predictors: reported allergies, degree of physical activity, distance from school to home, and exposure to fuel smoke at home, but no significant association was observed with the outcome variables. Exposure to increased levels of ozone was associated with a decrease in lung function, as reported previously[19]. Tables 2 and 3 show that individuals in the higher quartile of ozone exposure had 3.3% (78.9 ml) less FEV_1 and 2.3% (62.8 ml) less FVC than individuals in the lower air pollution quartile (see online table 1 for the full model). Also, a reported physician's diagnosis of asthma was associated with a significant average drop in FEV_1 of 3.5% (82.7 ml), but without a relevant change in FVC. These effects were additive to those due to second-hand smoking. We found no significant impact of active smoking in lung function or symptoms in the 274 acknowledged direct smokers.

DISCUSSION

In this study, we showed that in the cohort of primary- and secondary-level students (aged 8-17 years) residing in metropolitan Mexico City, secondhand smoking

was associated with an increase in respiratory symptoms, in the frequency of self-reported respiratory infections (common cold, sore throat, and bronchitis), and with a reduction of spirometric pulmonary function. Second-hand smoking was homogeneous across different strata of reported income or parents' education.

Exposure to tobacco smoke prenatally and during infancy is associated with a reduction in the growth of pulmonary function and a greater risk for the development of asthma[27,28], as well as for respiratory symptoms and/or respiratory infections[29,30]. The placenta allows the penetration of smoke products into the fetus[31], likely affecting the development and growth of the forming lungs, with a possible drop in the spirometry indices[6,32].

In our study, an adverse effect on lung function was observed in children exposed to passive smoking, proportional to the number of smokers at home. Although this appears small in magnitude (5-15 ml of FEV_1 or FVC per smoker inside the home), it is also associated with respiratory symptoms, implying persistent inflammation, and is additive to other insults such as air pollution[19], as observed in models depicted in tables 2 and 3. For example, if an individual simultaneously reported respiratory symptoms, frequent respiratory infections, asthma, passive smoking, and residing in an area with ozone levels in the upper quartile, the estimated lung function decrease was 7.6% (183.3 ml) in FEV_1 and 2.9% (78.1 ml) in FVC, which may possibly lead to permanent deficits in lung function.

A decrease in FEV_1 associated with passive smoking was reported in another study as being worse if the exposure was through the mother and in individuals with wheezing[15]. A reduction in FEV_1 and FVC was worse in asthmatic children exposed to SHS compared with exposed children without asthma[33]. However, in our study, previous asthma and wheezing did not predict a more important decrease in lung function with passive smoking, although we were unable to analyze whether children with asthma had more symptoms or a more difficult control if exposed to SHS than those without exposure. Passive smoking was not associated with asthma in a cross-sectional study performed in Mexican children[34].

Respiratory symptoms in children of mothers who smoke during pregnancy may also be worse: of 313 schoolchildren between the ages of 5 and 13 years, 18% were exposed to SHS during pregnancy and had an OR of a 2.2-times greater risk of having cough in comparison with children of non-smoking mothers[35]. Additionally, in our study we did not know whether the mothers smoked during pregnancy, but 23% of mothers acknowledged smoking and some of them could have been smokers during pregnancy[36].

Exposure to air pollution including second-hand smoking is of higher concern in children because ventilation per size is higher than in adults[37], an effect more relevant in Mexico City, with altitude-induced hyperventilation. In addition, the infant's immunological system is immature and more susceptible to respiratory infections, and environmental toxins or infections may interfere with lung growth and development during key periods.

Additional study limitations

We based the assessment of passive smoking on the report of the parents, but lacked measurements of cotinine; were unaware of how many cigarettes they smoked inside the home, which was relevant for adverse effects in previous studies[38,39]; and whether the mothers smoked during pregnancy. Children were studied before attaining final growth, and we do not know whether functional deficits in those exposed to SHS were or were not permanent. In addition, the report of respiratory symptoms and infections was obtained from the questionnaires and may be affected by recall. On the other hand, the study represents a well-characterized cohort of children studied repeatedly with high-quality spirometry measurements, with respiratory symptoms (cough, phlegm, and wheezing) assessed by standard questions utilized in respiratory epidemiology. In other studies, as in ours, the simple parental report of passive smoking was a predictor of symptoms and altered pulmonary function, and questions about smoking at home by the mother, the father and other persons correlated with cotinine levels in children[22].

We found more respiratory symptoms, more frequent respiratory infections, and lower spirometry function in schoolchildren exposed to tobacco smoke at home, with the risk increasing if more persons smoked within the home. This information supports international efforts to eliminate passive smoking in children.

REFERENCES

1. Ash Research Report: Action on smoking and health [Internet]. 2006. Secondhand Smoke: the impact on children. Available from: http://www.ash.org.uk/files/documents/ASH_temp_bed8.pdf (Accessed Oct 30, 2015).
2. Samet JM. [Risks of active and passive smoking]. Salud Pública de México. 2002;44:S144-60.
3. Report on the Global Tobacco Epidemic. 2009. World Health Organization [Internet]. Available from: http://www.who.int/tobacco/mpower/2009/c_gtcr_protect_people_tobacco_smoke.pdf (Accessed Nov 03, 2015).
4. Irvine L, Crombie IL, Clark RA, et al. What determines levels of passive smoking in children with asthma? Thorax. 1997;52:766-9.
5. Cook DG, Strachan DP, Carey IM. Parental smoking and spirometric indices in children. Thorax. 1998;53:884-93.
6. Mallol J. Childhood asthma in developing countries. Low income aspects and related matters. Allergol Immunopathol. 2000;28:283-6.
7. Li Y, Gilliland FD, Berhane K, et al. Effects of *in utero* and environmental tobacco smoke exposure on lung function in boys and girls with and without asthma. Am J Respir Crit Care Med. 2000;162:2097-104.
8. Stick SM, Burton PR, Gurrin L. Effects of maternal smoking during pregnancy and a family history of asthma on respiratory function in newborn infants. Lancet. 1996;348:1060-4.
9. Eskenazi B, Castorina R. Association of prenatal maternal or postnatal child environmental tobacco smoke exposure and neurodevelopmental and behavioral problems in children. Environ Health Perspect. 1999;107:991-1000.
10. Lodrup Carlesen KC, Jaakkola JJ, Nafstad P. In utero exposure to cigarette smoking influences lung function at birth. Eur Respir J. 1997;10:1774-9.
11. Environmental Protection Agency. Respiratory Health Effects of Passive Smoking: Lung Cancer and Other Disorders. Washington, D.C., USA: Environmental Protection Agency (EPA); 1992. Available at: file:///Users/Admin/Downloads/PASSIVE_SMOKE.PDF
12. Gilliland FD, Berhane K, McConnell R, et al. Maternal smoking during pregnancy, environmental tobacco smoke exposure and childhood lung function. Thorax. 2000;55:271-6.
13. The Health Consequences of Involuntary Exposure to Tobacco Smoke: A Report of the Surgeon General. U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, Coordinating Center for Health Promotion, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 2006. Available at: http://www.surgeongeneral.gov/library/reports/secondhandsmoke/fullreport.pdf
14. Rizzi M, Sergi M, Andreoli A, Pecis M, Bruschi C, Fanfulla F. Environmental tobacco smoke may induce early lung damage in healthy male adolescents. Chest. 2004;125:1387-93.
15. Sherrill DL, Martínez FD, Lebowitz MD, et al. Longitudinal effects of passive smoking on pulmonary function in New Zealand children. Am Rev Respir Dis. 1992;145:1136-41.
16. Barrientos GT, Reynales SL, Ávila TE, Wipfli H, Lazcano PE. [Environmental tobacco smoke exposure in homes of Mexico City: analysis of environmental samples and children and women hair]. Salud Publica Mex. 2007;49:2:S224-32.
17. Sánchez ZL, Téllez RM, Hernández AM. [Effect of smoking during pregnancy on anthropometric characteristics at birth]. Salud Publica Mex. 2004;46:529-33.
18. Encuesta Nacional de Adicciones [Internet]. 2002. Available at: http://www.inegi.gob.mx/prod_serv/contenidos/espanol/bvinegi/productos/continuas/sociales/salud/2004/Ena02.pdf Accessed Nov 03, 2015).
19. Rojas MR, Pérez PR, Olaiz FG, et al. Lung function growth in children with long-term exposure to air pollutants in Mexico City. Am J Respir Crit Care Med. 2007;15:176:377-84.
20. Pérez-Padilla R, Regalado PJ, Mendoza AL, et al. Spirometric variability in a longitudinal study of school-age children. Chest. 2003;123:1090-5.
21. Pérez-Padilla R, Regalado PJ, Rojas M, et al. Spirometric function in children of Mexico City compared to Mexican-American children. Pediatr Pulmonol. 2003;35:177-83.
22. Jarvis MJ. Children's exposure to passive smoking: survey methodology and monitoring trends. WHO/NCD/TLF/99.11:130-47. Available at: http://www.who.int/tobacco/media/en/jarvis.pdf.
23. American Thoracic Society. Standardization of Spirometry. Am J Respir Crit Care Med. 1995;152:1107-36.
24. Martínez BD, Fernández PR, Gochicoa RL, et al. Socioeconomic status and longitudinal lung function of healthy Mexican children. PLoS One. 2015;10:e0136935.
25. Martínez BD, Fernández PR, Gochicoa RL, et al. Longitudinal lung function growth of Mexican children compared with international studies. PLoS One. 2013;8:e77403.
26. Cerda LJ, Villarroel PL. Evaluación de la concordancia inter-observador en investigación pediátrica: Coeficiente de Kappa. Rev Chil Pediatr. 2008;79:54-8.
27. Tager IB, Ngo L, Hanrahan JP. Maternal smoking during pregnancy: effects on lung function during the first 18 months of life. Am J Respir Crit Care Med. 1995;152:977-83.
28. Xepapadaki P, Manios Y, Liarigkovinos T, et al. Association of passive exposure of pregnant women to environmental tobacco smoke with asthma symptoms in children. Pediatr Allergy Immunol. 2009;20:423-9.
29. Chinn S, Rona RJ. Quantifying health aspects of passive smoking in British children aged 5-11 years. J Epidemiol Community Health. 1991;45:188-94.
30. Britton J. Passive smoking damages children's health. Practitioner. 2010;254:27-30.
31. Cheraghi M, Salvi S. Environmental tobacco smoke (ETS) and respiratory health in children. Eur J Pediatr. 2009;168:897-905.
32. Rosewich M, Adler S, Zielen S. Effects of active and passive smoking on the health of children and adolescents. Pneumologie. 2008;62:423-9.
33. Hernández AE, Alba RG, Muñoz CB, et al. Passive smoking induces leukotriene production in children: influence of asthma. J Asthma. 2013;50:347-53.
34. Bedolla BM, Barrera ZA, López ZJ, Morales RJ. Asthma in Mexican school-age children is not associated with passive smoking or obesity. Asia Pac Allergy. 2013;3:42-9.
35. Constant C, Sampaio I, Negreiro F, et al. Environmental tobacco smoke (ETS) exposure and respiratory morbidity in school age children. Rev Port Pneumol. 2011;17:20-6.
36. Ligna CA, Soddard JJ. Tobacco and children. An economic evaluation of the medical effects of parental smoking. Arch Pediatr Adolesc Med. 1997;151:648-53.
37. [Second-Hand Smoke: Children's Health]. Office of Environmental Health Hazard Assessment, California Environmental Protection Agency [Internet]. 2006. Available at: http://www.oehha.ca.gov/air/environmental_tobacco/pdf/smoke2final_span.pdf Accessed Nov 03, 2015).
38. Venners SA, Wang X, Chen C, et al. Exposure-response relationship between paternal smoking and children's pulmonary function. Am J Respir Crit Care Med. 2001;164:973-6.
39. Valsamis C, Krishnan S, Dozor AJ. The effects of low-level environmental tobacco smoke exposure on pulmonary function tests in preschool children with asthma. J Asthma. 2014;51:685-90.

SUPPLEMENTAL MATERIAL

Table 1. Multilevel linear regression models of mixed effects by gender

	GIRLS			BOYS		
Ln (FEV_1)	**β**	**p value**	**95% CI**	**β**	**p value**	**95% CI**
Age (years)	0.03499	0.000	(0.02, 0.05)	−0.07287	0.000	(−0.08, −0.06)
Age^2	−0.00011	0.708	(−0.00, 0.00)	0.00432	0.000	(0.00, 0.01)
Height (cm)	0.01354	0.000	(0.01, 0.01)	0.01543	0.000	(0.01, 0.02)
Weight (kg)	0.00350	0.000	(0.00, 0.00)	0.00154	0.000	(0.00, 0.00)
Exposed to passive smoking	−0.00412	0.003	(−0.01, −0.00)	−0.00173	0.197	(−0.00, 0.00)
Ozone	−0.00096	0.000	(−0.00, −0.00)	−0.00110	0.000	(−0.00, −0.00)
Asthma	−0.04563	0.005	(−0.08, −0.01)	−0.02532	0.110	(−0.06, 0.01)
Respiratory symptoms	0.00195	0.179	(−0.00, 0.00)	−0.00120	0.423	(−0.00, 0.00)
Respiratory infections	−0.00408	0.049	(−0.01, −0.00)	−0.00524	0.010	(−0.01, −0.00)
Constant	−1.55347	0.000	(−1.62, −1.48)	−1.06199	0.000	(−1.14, −0.98)
Ln (FVC)	**β**	**p value**	**95% CI**	**β**	**p value**	**95% CI**
Age (years)	0.01353	0.036	(0.00, 0.03)	−0.07368	0.000	(−0.08, −0.06)
Age^2	0.00070	0.008	(0.00, 0.00)	0.00423	0.000	(0.00, 0.00)
Height (cm)	0.01204	0.000	(0.01, 0.01)	0.01418	0.000	(0.01, 0.01)
Weight (kg)	0.00446	0.000	(0.00, 0.01)	0.00258	0.000	(0.00, 0.00)
Exposed to passive smoking	−0.00757	0.000	(−0.01, −0.01)	−0.00280	0.024	(−0.01, −0.00)
Ozone	−0.00056	0.000	(−0.00, −0.00)	−0.00065	0.000	(−0.00, −0.00)
Asthma	0.00726	0.646	(−0.02, 0.04)	0.00498	0.740	(−0.02, 0.03)
Respiratory symptoms	0.00346	0.009	(0.00, 0.01)	0.00156	0.256	(−0.00, 0.00)
Respiratory infections	−0.00406	0.033	(−0.01, −0.00)	−0.00466	0.012	(−0.01, −0.00)
Constant	−1.15742	0.000	(−1.22, −1.09)	−0.79747	0.000	(−0.87, −0.73)
Ln (FEV_1/FVC)	**β**	**p value**	**95% CI**	**β**	**p value**	**95% CI**
Age (years)	0.02187	0.000	(0.01, 0.03)	0.00075	0.833	(−0.01, 0.01)
Age^2	−0.00080	0.000	(−0.00, −0.00)	0.00009	0.545	(−0.00, 0.00)
Height (cm)	0.00154	0.000	(0.00, 0.00)	0.00125	0.000	(0.00, 0.00)
Weight (kg)	−0.00113	0.000	(−0.00, −0.00)	−0.00106	0.000	(−0.00, −0.00)
Exposed to passive smoking	0.00359	0.000	(0.00, 0.01)	0.00106	0.204	(−0.00, 0.00)
Ozone	−0.00039	0.000	(−0.00, −0.00)	−0.00044	0.000	(−0.00, −0.00)
Asthma	−0.05216	0.000	(−0.07, −0.04)	−0.03005	0.002	(−0.05, −0.01)
Respiratory symptoms	−0.00160	0.066	(−0.00, 0.00)	−0.00285	0.002	(−0.01, −0.00)
Respiratory infections	0.00010	0.935	(−0.00, 0.00)	−0.00056	0.657	(−0.00, 0.00)
Constant	−0.40146	0.000	(−0.44, −0.36)	−0.26367	0.000	(−0.31, −0.22)

Ln: lung: FEV1: forced expiratory volume in 1 second; FVC: forced vital capacity.

Table 2. Multilevel linear regression models of mixed effects by gender

	GIRLS			BOYS		
FEV_1 Z-score	**β**	**p value**	**95% CI**	**β**	**p value**	**95% CI**
Exposed to passive smoking	–0.04174	0.000	(–0.06, –0.02)	–0.04076	0.000	(–0.06, –0.02)
Ozone	–0.01032	0.000	(–0.01, –0.01)	–0.01016	0.000	(–0.01, –0.01)
Asthma	–0.34549	0.005	(–0.59, –0.10)	–0.22725	0.074	(–0.48, 0.02)
Respiratory symptoms	0.03225	0.004	(0.01, 0.05)	–0.00129	0.916	(–0.03, 0.02)
Respiratory infections	–0.08591	0.000	(–0.12, –0.06)	–0.08903	0.000	(–0.12, –0.06)
Constant	0.89761	0.000	(0.78, 1.01)	0.74864	0.000	(0.64, 0.86)
FVC Z-score	**β**	**p value**	**95% CI**	**β**	**p value**	**95% CI**
Exposed to passive smoking	–0.07171	0.000	(–0.09, –0.05)	–0.05017	0.000	(–0.07, –0.03)
Ozone	–0.00662	0.000	(–0.01, –0.01)	–0.00660	0.000	(–0.01, –0.01)
Asthma	0.05933	0.636	(–0.19, 0.31)	0.00212	0.987	(–0.25, 0.25)
Respiratory symptoms	0.04155	0.000	(0.02, 0.06)	0.02060	0.084	(–0.00, 0.04)
Respiratory infections	–0.07791	0.000	(–0.11, –0.05)	–0.08134	0.000	(–0.11, –0.05)
Constant	0.58562	0.000	(0.48, 0.69)	0.43609	0.000	(0.33, 0.55)
FEV_1/FVC Z-score	**β**	**p value**	**95% CI**	**β**	**p value**	**95% CI**
Exposed to passive smoking	0.04488	0.000	(0.02, 0.07)	0.00895	0.401	(–0.01, 0.03)
Ozone	–0.00707	0.000	(–0.01, –0.01)	–0.00593	0.000	(–0.01, –0.00)
Asthma	–0.70136	0.000	(–0.93, –0.47)	–0.38995	0.002	(–0.64, –0.14)
Respiratory symptoms	–0.00957	0.410	(–0.03, 0.01)	–0.03850	0.001	(–0.06, –0.01)
Respiratory infections	–0.03360	0.034	(–0.06, –0.00)	–0.01663	0.286	(–0.05, 0.01)
Constant	0.72584	0.000	(0.61, 0.84)	0.46292	0.000	(0.35, 0.57)

FEV_1: forced expiratory volume in 1 second; FVC: forced vital capacity.

Table 3. Multilevel linear logistic models predicting symptoms by gender

	GIRLS			BOYS		
Respiratory symptoms	**OR**	**p value**	**95% CI**	**OR**	**p value**	**95% CI**
One person smokes indoors	1.43	0.013	(1.08, 1.89)	1.25	0.130	(0.94, 1.66)
Two people smoking indoors	1.71	0.001	(1.23, 2.38)	1.70	0.002	(1.22, 2.36)
Three people smoking indoors	1.78	0.019	(1.10, 2.87)	2.26	0.001	(1.41, 3.64)
Age	0.70	0.000	(0.62, 0.80)	0.59	0.000	(0.51, 0.67)
Height (cm)	0.97	0.010	(0.95, 0.99)	0.99	0.472	(0.97, 1.01)
Weight (kg)	1.01	0.428	(0.99, 1.03)	1.01	0.335	(0.99, 1.03)
Ozone	0.99	0.230	(0.98, 1.01)	0.98	0.000	(0.97, 0.99)
Constant	125.93	0.000	(9.90, 1,601.4)	81.06	0.001	(6.78, 969.42)
Respiratory infections	**OR**	**p value**	**95% CI**	**OR**	**p value**	**95% CI**
One person smokes indoors	1.27	0.000	(1.12, 1.44)	1.17	0.018	(1.03, 1.33)
Two people smoking indoors	1.34	0.000	(1.16, 1.55)	1.48	0.000	(1.28, 1.71)
Three people smoking indoors	1.48	0.000	(1.19, 1.83)	1.34	0.012	(1.06, 1.68)
Age	0.61	0.000	(0.58, 0.65)	0.72	0.000	(0.68, 0.76)
Height (cm)	1.04	0.000	(1.03, 1.05)	1.00	0.393	(0.98, 1.00)
Weight (kg)	0.98	0.000	(0.98, 0.99)	1.00	0.215	(0.99, 1.00)
Ozone	1.04	0.000	(1.03, 1.05)	1.04	0.000	(1.04, 1.05)
Constant	0.08	0.000	(0.02, 0.25)	2.52	0.121	(0.78, 8.09)