



In utero exposure to pets is associated with asthma and wheezing in Mexican American children

Kamal Eldeirawi PhD, Colin Kunzweiler MS, Angela M. T. Combs MSN, MPH & Victoria W. Persky MD

To cite this article: Kamal Eldeirawi PhD, Colin Kunzweiler MS, Angela M. T. Combs MSN, MPH & Victoria W. Persky MD (2016): In utero exposure to pets is associated with asthma and wheezing in Mexican American children, Journal of Asthma, DOI: [10.3109/02770903.2015.1104693](https://doi.org/10.3109/02770903.2015.1104693)

To link to this article: <http://dx.doi.org/10.3109/02770903.2015.1104693>



Published online: 21 Jan 2016.



Submit your article to this journal [↗](#)



Article views: 60



View related articles [↗](#)



View Crossmark data [↗](#)



ORIGINAL ARTICLE

***In utero* exposure to pets is associated with asthma and wheezing in Mexican American children**Kamal Eldeirawi, PhD¹, Colin Kunzweiler, MS², Angela M. T. Combs, MSN, MPH¹, and Victoria W. Persky, MD²¹Department of Health Systems Science, College of Nursing and ²Division of Epidemiology and Biostatistics, School of Public Health, University of Illinois at Chicago, Chicago, IL, USA**Abstract**

Objective: To examine the associations of *in utero* and early life exposure to cats/dogs and birds with the risk of lifetime doctor-diagnosed asthma and other respiratory conditions in a sample of Mexican American (MA) children 4–18 years of age. **Methods:** This study is a population-based cross-sectional investigation of 1816 MA children. We conducted multiple logistic models examining the relationship of asthma and wheezing with exposures to cats/dogs and birds *in utero*, infancy and at the time of the survey adjusted for country of birth, family history of asthma/allergies, antibiotics use in infancy and other covariates. **Results:** In adjusted analyses, *in utero* exposure to cats/dogs and birds jointly was associated with increased odds of asthma (adjusted odds ratio (aOR): 2.89; 95% confidence interval (CI): 1.34–6.23), ever wheezing (aOR: 1.96; 95% CI: 1.11–3.46) and current exercise-induced wheezing (aOR: 3.16; 95% CI: 1.27–7.85) compared to children not exposed to these pets *in utero*. Children who were exposed to both cats/dogs and birds *in utero* had an elevated, albeit statistically non-significant, odds of current wheezing. Exposures in infancy and at the time of the survey to cats/dogs and birds were not associated with asthma or wheezing. **Conclusions:** *In utero* exposure to pets might be associated with an increased risk of asthma and respiratory conditions in a sample of non-affluent MA children.

Keywords

Asthma, birds, cats/dogs, children, Mexican Americans, pets, pregnancy, wheezing

History

Received 2 July 2015

Revised 18 September 2015

Accepted 3 October 2015

Published online 21 January 2016

Introduction

Several studies found inverse associations of living on a farm as well as exposure to farm animals and pets with the risk of respiratory and allergic conditions [1,2]. However, most of these studies were conducted in Europe and affluent western populations. Limited studies from non-affluent societies demonstrated positive [3–7] associations of exposure to pets or farm animals with the risk of asthma. For example, Brunekreef et al. [8] examined data based on the International Study of Asthma and Allergies in Children (ISAAC) and found that exposures to farm animals during pregnancy as well as in the first year of life were positively associated with increased symptoms of asthma, rhinoconjunctivitis and eczema in children aged 6–7 years living in low- and middle-income, but not in high-income, countries. In another analysis of ISAAC data, Brunekreef et al. [9] found that exposure to cats in the first year of life was associated with an increased risk of current symptoms of asthma, wheeze, rhinoconjunctivitis and eczema, in children 6–7 years of age, especially those from less-affluent countries. Similarly, a

positive relationship between exposure to farm animals during pregnancy and cumulative asthma was observed in boys 6–7 years of age in Mexico City [10]. Other studies from China [11], Saudi Arabia [12,13], the United Arab Emirates [14], Brazil [15] and Turkey [16] also suggested that exposure to pets is positively associated with the risk of respiratory conditions. However, Lodrup et al. [17] conducted a pooled analysis of 11 European birth cohorts and concluded that pet ownership in early life was not associated with the risk of asthma or allergic rhinitis symptoms. These mixed findings suggest that the relationship of exposure to pets and farm animals with the risk of asthma and other related conditions might not be uniform across all populations [8,18].

Mexican Americans (MAs) in the US represent an economically disadvantaged group. Previously, we documented that US-born MA children were more likely to have asthma [19–21] and other respiratory conditions [19–21] as well as to be sensitized [21] to various allergens than their peers born in Mexico. We also found the risk of asthma in MA children to be associated with acculturation [22], longer residence in the US [19], immigrating in early childhood [19], ear infections [23] and antibiotic use in infancy [24]. Yet, risk and protective factors of asthma and respiratory conditions in MAs remain poorly understood.

The purpose of the current study was to examine the associations of *in utero* exposure to cats/dogs and birds with

Correspondence: Kamal Eldeirawi, PhD, Associate Professor, Department of Health Systems Science, College of Nursing, University of Illinois at Chicago, 845 S Damen Avenue, M/C 802, Room 956, Chicago, IL 60612, USA. Tel: +1 312-413-9792. Fax: +1 312-996-7725. E-mail: keldei1@uic.edu

the risk of asthma and other respiratory outcomes in children of Mexican origin living in an inner city community; a non-affluent population residing in an affluent country.

Methods

Design and data collection

The current study, Study of Asthma in Children of Mexican Descent [SACMD] [19,23], was a population-based cross-sectional study which targeted parents of children who responded to the asthma screener of the Chicago Asthma School Study [20] between January and May of 2004. In that period, completed surveys were received from parents of 6896 children of Mexican origin enrolled in 15 public schools in Chicago. For SACMD, parents of all Mexico-born (1366) and a random sample of US-born (1485) children were invited to complete a questionnaire or a telephone interview between August 2004 and April 2005. Of these potential participants, 2233 had valid contact information and 2023 completed the study questionnaire by mail (199) or telephone (1824). Approximately 91% of the participants completed the study questionnaire in Spanish. To minimize potential biases related to the language of the survey, we restricted this analysis to participants who completed the questionnaire in Spanish ($n = 1816$).

Definition of variables

Doctor-diagnosed asthma was assessed by the question: “Has a doctor ever said that your child has asthma?” Ever wheezing was assessed by the question: “Has your child ever had wheezing or whistling in the chest at any time in the past?” Current wheezing was assessed by: “Has your child had wheezing or whistling in the chest in the last 12 months?” Current exercise-induced wheezing was determined by the question: “In the last 12 months, has your child’s chest sounded wheezy during or after exercise?” *In utero* exposure to pets/animals was determined by the question: “During pregnancy with your child, did the mother of this child have regular contact (spent time around feeding or taking care of the animals more than once a week) with the following animals or pets?” The list included cats or dogs, poultry, birds, sheep or goats, pigs and cattle. Parents were presented with the same list and were asked to indicate whether the child had regular contact (spent time around or played with more than once a week) with each of the animals in the first year of the child’s life. Unfortunately, the questions were not specific enough to capture whether this contact with the animals was in or outside the home. For current exposure, parents were asked to indicate the number (1, 2 or ≥ 3) of animals (cats, dogs and birds) they had at home at the time of the survey. A small percentage of children were exposed to more than one animal of the same type. Therefore, we combined responses and treated current exposure as a dichotomous variable (yes versus no). In the current study, the main exposure variables included exposure to cats/dogs and birds in pregnancy. Due to the high association between, and overlap among, these two variables, we combined responses into a four-level nominal variable: exposure to both cats/dogs and birds, exposure to cats/dogs but not birds,

exposure to birds but not cats/dogs and no exposure to cats/dogs or birds in pregnancy. Using children who were not exposed to any birds or animals, including livestock, *in utero* as the reference category did not appreciably change the observed associations.

Statistical analysis

Statistical analyses were completed using SAS version 9.3 (SAS Institute, Cary, NC). Statistical significance was set at $p < 0.05$. We used Pearson Chi-square statistics to compare proportions. The final multiple logistic regression models were adjusted for gender, age group (4–7; 8–11; 12–18 years old), country of birth (US versus Mexico), family history of asthma or allergies (in parents or siblings), ever daycare or pre-school attendance, exposure to environmental tobacco smoke (ETS) at birth, current exposure to ETS, having access to a regular doctor or clinic, breast feeding, antibiotic use in infancy, history of ear infections in infancy, history of viral infections in infancy and number of siblings (0, 1, ≥ 2). These covariates were included because they have been linked with asthma in previous investigations but only family history of asthma or allergies, country of birth and antibiotics use in infancy confounded the associations examined in the current analysis as assessed by the change-in-estimate method; a change of $>10\%$ was considered evidence for confounding. A small percentage, 1.66%, of the participants reported maternal smoking during pregnancy. In multiple logistic regression, smoking during pregnancy made no difference in the association of exposure to cats or dogs/birds *in utero* with asthma, ever wheezing and current wheezing. We were not able to assess for the confounding effect of maternal smoking during pregnancy on current exercise induced wheeze due to the small number of women who smoked during pregnancy.

We combined exposures to sheep, goats, pigs or cattle into an exposure to livestock variable. The additional adjustment for exposure to poultry and livestock in pregnancy did not change the associations of exposure to cats/dogs/birds with asthma, ever wheezing or current wheezing appreciably. The associations of those additional exposure variables with the outcome variables were unstable, and therefore are not a focus of the current analysis. The further adjustment for place of birth (farm or rural versus not) with country of birth in the same models made almost no difference in the estimated odd ratios for the associations of exposure to cats/dogs and/or birds with respiratory conditions.

Results

Participant characteristics are provided in Table 1. This analysis was based on data from 1816 children 4–18 years of age, of whom 51.5% were female, 49.1% were born in Mexico (versus US), 22.5% were born on a farm or in a village or rural area and 13.1% reported a family history of asthma or allergies.

Of participants, 16.1, 4.6 and 12.6% were exposed to cats/dogs during pregnancy, in infancy and at the time of survey, respectively; 10.0, 3.3 and 10.0% were exposed to birds during pregnancy, in infancy and at the time of the survey, respectively. Of the participants who were exposed to cats/dogs during pregnancy, 18.1% were also exposed to cats/dogs

Table 1. Distribution of characteristics for the study population by exposure to cats and dogs during pregnancy and to birds during pregnancy.

Characteristics	Total % (n/N)	Cats/Dogs – Yes % (n/N)	Cats/Dogs – No % (n/N)	p	Birds – Yes % (n/N)	Birds – No % (n/N)	p
Male (versus female)	48.5 (881/1816)	49.1 (143/291)	48.3 (731/1512)	0.804	52.8 (95/180)	47.9 (772/1613)	0.211
Age (years)							
<8	22.7 (413/1816)	18.9 (55/291)	23.7 (358/1512)	0.137	21.1 (38/180)	23.1 (372/1613)	0.382
8–11	44.5 (809/1816)	44.7 (130/291)	44.4 (672/1512)		43.3 (78/180)	44.5 (718/1613)	
12+	32.7 (594/1816)	36.4 (106/291)	31.9 (482/1512)		35.6 (64/180)	32.4 (523/1613)	
Born in Mexico (versus US)	49.1 (892/1815)	79.7 (232/291)	43.1 (652/1512)	<0.001	78.3 (141/180)	45.9 (740/1613)	<0.001
Born or lived during infancy on Farm or rural (versus city, town or urban)	22.5 (408/1815)	46.4 (135/291)	17.9 (271/1512)	<0.001	56.7 (102/180)	18.7 (301/1613)	<0.001
Family history of asthma or allergies ^a	13.1 (237/1813)	18.9 (55/291)	11.9 (179/1510)	0.001	19.4 (35/180)	12.1 (195/1611)	0.005
Day care/pre-school attendance ^a	48.7 (881/1808)	45.2 (131/290)	49.1 (739/1505)	0.22	37.2 (67/180)	49.7 (798/1606)	0.002
Has a regular doctor or clinic ^a	79.7 (1444/1811)	72.7 (210/289)	81.3 (1227/1510)	0.001	77.2 (139/180)	80.2 (1292/1610)	0.336
Presence of a smoker at home at birth ^a	15.0 (268/1781)	25.1 (71/283)	12.9 (191/1486)	<0.001	23.6 (42/178)	13.6 (216/1584)	<0.001
Current presence of a smoker at home ^a	10.1 (183/1812)	16.6 (48/290)	8.6 (130/1509)	<0.001	15.1 (27/179)	9.2 (148/1610)	0.012
Exposure to cats/dogs during pregnancy ^a	16.1 (291/1803)	–	–	–	66.3 (118/178)	9.9 (159/1609)	<0.001
Exposure to cats/dogs during 1st year ^a	4.6 (82/1801)	18.1 (52/287)	1.9 (29/1507)	<0.001	16.9 (30/177)	3.0 (49/1608)	<0.001
Current exposure to cats or dogs ^a	12.6 (227/1798)	17.1 (49/287)	11.8 (177/1504)	0.013	15.8 (28/177)	12.0 (193/1604)	0.147
Exposure to birds during pregnancy ^a	10.0 (180/1793)	42.6 (118/277)	4.0 (60/1510)	<0.001	–	–	–
Exposure to birds during first year of life ^a	3.3 (58/1782)	11.6 (32/276)	1.7 (26/1498)	<0.001	21.1 (37/175)	1.3 (21/1600)	<0.001
Current exposure to birds ^a	10.0 (178/1786)	11.1 (31/280)	9.5 (142/1497)	0.411	17.9 (32/179)	9.0 (143/1595)	
Was your child ever fed breast milk? ^a	71.1 (1290/1814)	77.6 (225/290)	69.9 (1057/1512)	0.008	76.0 (136/179)	70.6 (1138/1613)	0.129
Received antibiotics in the 1st year of life ^a	39.3 (711/1807)	42.9 (124/289)	38.6 (582/1506)	0.175	44.4 (79/178)	38.6 (620/1608)	0.131
Number of siblings							
2+	72.0 (1304/1811)	71.5 (208/291)	72.1 (1087/1508)	0.907	68.9 (124/180)	72.3 (1164/1609)	0.455
1	23.6 (427/1811)	24.4 (71/291)	23.4 (353/1508)		27.2 (49/180)	23.1 (372/1609)	
None	4.4 (80/1811)	4.1 (12/291)	4.5 (68/1508)		3.9 (7/180)	4.5 (73/1609)	

^aYes versus no response.

in infancy and 17.1% were exposed at the time of the survey. Only 7 and 6 participants were exposed to cats/dogs and birds, respectively, in all three time periods and, therefore, we were not able to examine the effect of the continuous exposure on respiratory conditions. Of those exposed to cats/dogs during pregnancy, almost 43% were also exposed to birds during the same period.

Table 1 shows the bivariate associations of exposure to cats/dogs and birds with other covariates. Children who were exposed to cats/dogs during pregnancy were significantly less likely to have access to a regular doctor or clinic but more likely to be born in Mexico, be born on a farm or rural area, be breastfed, have a family history of asthma or allergies, have a smoker in the home at birth, and have a smoker in the home at the time of the survey than children who were not exposed to cats/dogs. Similarly, children who were exposed to birds during pregnancy were less likely to attend daycare, but were more likely to be born in Mexico, be born on a farm or rural area, have a family history of asthma or allergies, have a smoker in the home at birth and have a smoker in the home at the time of the survey than their peers who were not exposed to birds.

Most children who reported exposure to animals during pregnancy were born on a farm or in a rural area or village or were Mexico-born. Interestingly, we did not find significant differences in the risk of asthma and any of the other respiratory conditions examined in this study by place of birth (rural versus urban) or farm versus not farm among Mexico-born children (not shown in tables). As shown in Table 2, children who were exposed, relative to those who were not, to cats/dogs during pregnancy were more likely to have ever wheezing ($p=0.002$), current wheezing ($p=0.021$), current exercise-induced wheezing ($p=0.002$) and asthma ($p=0.069$). Similarly, *in utero* exposure to birds was

significantly associated with a higher prevalence of the four respiratory outcomes.

In multiple logistic regression models (Table 3), children who were exposed *in utero* to cats/dogs and birds were significantly more likely to have asthma (aOR: 2.89; 95% CI: 1.34–6.23), ever wheezing (aOR: 1.96; 95% CI: 1.11–3.46), and current exercise-induced wheezing (aOR: 3.16; 95% CI: 1.27–7.85) than children who were not exposed to these pets/animals. The odds for current wheeze was also elevated but did not reach statistical significance in children who were, compared to those who were not, exposed *in utero* to cats/dogs and birds (aOR: 2.09; 95% CI: 0.91–4.78). Exposure to cats/dogs but not birds in pregnancy increased the odds of the four respiratory conditions by approximately 100–200% (Table 3). Exposure to birds but not cats/dogs *in utero* seems to exert a greater influence with the odds of asthma (aOR: 3.02; 95% CI: 1.15–7.93), ever wheezing (aOR: 2.66; 95% CI: 1.42–5.00), current wheezing (aOR: 3.97; 95% CI: 1.72–9.18) and current exercise induced wheezing (aOR: 4.82; 95% CI: 1.53–15.15) significantly increasing (Table 3). These associations were independent of exposure to cats/dogs/birds in infancy and at the time of the survey.

Exposure to cats/dogs or birds during infancy, as well as exposure at the time of the survey, were not significantly associated with the odds of any of the four respiratory conditions examined in this study (Table 3). Children who were exposed to cats/dogs in infancy were almost two times as likely to have asthma and over three times more likely to have current exercise-induced wheezing than their peers who were not exposed to cats/dogs in infancy. However, these associations were not statistically significant.

We found no evidence for interaction between exposure to cats/dogs/birds with country of birth, gender and family history of asthma or allergies. Because almost all the students

Table 2. Prevalence of health conditions by exposure to cats and dogs during pregnancy and to birds during pregnancy.

Health Conditions (yes versus no)	Total % (n/N)	Cats/Dogs – Yes % (n/N)	Cats/Dogs – No % (n/N)	p	Birds – Yes % (n/N)	Birds – No % (n/N)	p
Child had ear infection in 1st year of life	18.6 (337/1807)	17.9 (52/291)	18.8 (283/1504)	0.704	21.2 (38/179)	18.2 (292/1606)	0.319
Child had viral infection in 1st year of life	18.7 (339/1814)	21.3 (62/291)	18.1 (273/1511)	0.194	18.3 (33/180)	18.5 (298/1612)	0.960
Ever wheezing	16.3 (295/1812)	22.3 (65/291)	15.0 (226/1509)	0.002	24.0 (43/179)	15.5 (249/1610)	0.003
Current wheezing	5.5 (99/1812)	8.2 (24/291)	4.9 (74/1510)	0.021	9.4 (17/180)	4.5 (81/1811)	0.014
Current exercise-induced wheezing	3.0 (55/1808)	5.8 (17/291)	2.4 (36/1505)	0.002	5.6 (10/180)	2.7 (43/1607)	0.031
Lifetime doctor-diagnosed asthma	6.4 (116/1808)	8.7 (25/288)	5.8 (88/1507)	0.069	10.7 (19/178)	6.0 (96/1608)	0.015

Table 3. Adjusted associations of exposure to cats, dogs and/or birds with lifetime doctor-diagnosed asthma, ever wheezing, current wheezing and current exercise-induced wheezing.

Parameters	Ever Asthma OR (95% CI)	Ever Wheezing OR (95% CI)	Current Wheezing OR (95% CI)	Current Exercise- induced wheezing OR (95% CI)
<i>In utero</i> exposure				
Cats/dogs and birds (level 1)	2.89 (1.34–6.23)	1.96 (1.11–3.46)	2.09 (0.91–4.78)	3.16 (1.27–7.85)
Cats/dogs but not birds (level 2)	2.09 (1.02–4.27)	2.29 (1.45–3.62)	2.53 (1.26–5.09)	3.07 (1.43–6.59)
Birds but not cats or dogs (level 3)	3.02 (1.15–7.93)	2.66 (1.42–5.00)	3.97 (1.72–9.18)	4.82 (1.53–15.15)
No exposure to cats, dogs or birds	1	1	1	1
Exposure to cats or dogs in infancy (Yes versus No)	2.07 (0.64–6.67)	0.75 (0.27–2.08)	1.03 (0.30–3.51)	3.27 (0.89–12.02)
Current exposure to cats or dogs (Yes versus No)	1.03 (0.55–1.91)	0.94 (0.62–1.43)	0.77 (0.38–1.58)	0.95 (0.37–2.45)
Exposure to birds in infancy (Yes versus No)	0.35 (0.08–1.46)	1.25 (0.47–3.37)	1.63 (0.52–5.14)	0.17 (0.03–1.07)
Current exposure to birds (Yes versus No)	0.95 (0.48–1.89)	0.80 (0.50–1.30)	1.02 (0.52–1.99)	1.00 (0.38–2.61)

Adjusted for gender, age group, country of birth, family history of asthma or allergies, daycare attendance, exposure to environmental tobacco smoke (ETS) at birth, exposure to ETS at time of survey, having access to a regular doctor or clinic, breast feeding, antibiotic use in infancy, history of ear infections in infancy, history of viral infections in infancy and number of siblings in addition to the other variables in the models.

who were born in a farm or rural area were Mexico-born, we were not able to assess the interaction between the exposure to pets and rural residence. In sensitivity analyses, we stratified the analysis by country of birth, but several of the models did not converge and some estimates became imprecise and unstable due to sample size limitations.

Discussion

In a sample of underserved and less acculturated MAs living in an urban, inner city community, we found that children’s *in utero* exposure to cats/dogs and birds jointly or independently increase the odds of lifetime doctor-diagnosed asthma, ever wheezing and current exercise induced wheeze, while *in utero* exposure to cats/dogs and birds were independently, but not jointly, associated with an increased risk of current wheeze. These findings were independent of exposures to the same types of pets in infancy or at the time of the survey, which were not associated with any of the respiratory conditions examined in the current investigation. Interestingly, *in utero* exposure to birds seems to exert a more pronounced effect on the odds of the four respiratory conditions examined in this study as compared to the exposure to cats/dogs.

Our findings are consistent with several investigations, especially those conducted in non-affluent communities showing positive associations of pet or animal exposure with the risk of asthma and other respiratory conditions [8,10]. For example, recent examinations of pooled data from the third phase of the International Study of Asthma and Allergies in Childhood (ISAAC), demonstrated positive associations of exposure to farm animals during pregnancy with current wheeze among children living in non-affluent

countries, but not in children living in more affluent societies [8]. In another investigation from Mexico City, researchers reported that exposure to farm animals during pregnancy was positively associated with ever asthma among boys [10]. In a cross-sectional study of infants 12–15 months old in southern Brazil, Chong et al. [15] reported that exposure to pets in the home during pregnancy was associated with increased prevalence of wheezing in first year of life. Furthermore, in a high-risk birth cohort from Canada, Carlsten et al. [25] showed that dog ownership prior to birth is positively associated with asthma with a nearly three-fold increase in risk. In a study of 12 910 elementary school children in China, exposure to any pets (including cats, dogs, birds, farm animals and other animals) during pregnancy, in infancy and at the time of the study increased the odds of doctor-diagnosed asthma and other respiratory outcomes [26]. In another study with a large, multi-center sample of Chinese children 2–13 years of age, current pet exposure was associated with an increased risk of doctor-diagnosed asthma, ever wheezing and other respiratory conditions such as persistent cough and persistent phlegm [27]. Similarly, in Northeast China, Dong et al. [11] noted that in pre-school and elementary school children without a family history of allergy or asthma, exposure to pets during pregnancy, in infancy and at the time of the study were independently associated with increased odds of doctor-diagnosed asthma and current wheeze. In children with a family history of allergy or asthma, exposure to pets *in utero* and in infancy increased the risk of current wheeze but was not associated with doctor-diagnosed asthma [11].

While little research has been done that explicitly identifies the role of exposure to birds during pregnancy

and childhood respiratory conditions, one study from southern Brazil reported that exposure to pets, including birds, during pregnancy was associated with wheezing in children [15]. Another study by Dong et al. [27] found that current exposure to birds was not associated with asthma but was associated with a tendency to increase the odds of wheezing (OR: 1.31, 95% CI, 0.96–1.78). Several studies reported negative or mixed associations between exposure to cats and asthma or other respiratory conditions [1,28], and a recent study by Gaffin et al. [29] found a protective effect of cats during pregnancy and early life. In a longitudinal prospective cohort study in the US, Gaffin et al. [29] showed that children exposed to cats between birth and age 3 or 4 were more than 80% less likely to develop asthma compared to children who were not exposed. A study using ISAAC methodology in two cities in Russia and Finland reported positive associations of indoor dog keeping ever exposure with self-reported allergic asthma in Russian children (aOR: 4.56; 95% CI: 1.10–18.91) but noted inverse association in children from Finland (aOR: 0.35; 95% CI: 0.13–0.95) [6]. In both countries, the risk of asthma was elevated, but not significantly, in children who were exposed to farm animals during pregnancy (Finland: aOR: 1.95; 95% CI: 0.69–5.50; Russia: aOR: 1.90; 95% CI: 0.70–5.17) [6].

These inconsistent findings in the literature show that the effect of pet or animal exposure on the risk of asthma and respiratory conditions is not uniform across all populations. Our findings and those of other investigations [8,9] might suggest that the hygiene hypothesis may be useful in explaining the increase in prevalence of allergic diseases in affluent, but not in less affluent, communities [8], such as those examined in the current study, where almost half of the participants were born in Mexico with a large percent of those born in rural areas in Mexico. Most studies showing protective effects of exposure to farms or farm animals and providing support for the hygiene hypothesis were conducted with populations in Europe where exposure to farm animals has been characterized as intense and continuous as animals live in barns attached or in close proximity to houses of participants. Hugg et al. [6] suggested that effects of exposure to farm animals or pets on the risk of asthma and respiratory conditions might depend on the intensity and/or frequency of the exposure as well as on the level of microbial burden already present, with intermittent or occasional, rather than continuous or intense, contact with the animals and their microbes not being high enough to confer protection. Brunekreef et al. [8] agreed with this argument stating that most children enrolled in the ISAAC study were from urban or semi-urban areas where exposure to farm animals may have been occasional, as opposed to continuous, relative to children from farming communities. As further evidence, Brunekreef et al. [8] stated that equal proportions of children in their analyses were exposed to farm animals during pregnancy or during the first year of life, compared with children exposed during both periods, suggesting that exposure patterns to farm animals within urban areas may be heterogeneous and non-continuous. In our study, very few participants had continuous exposure *in utero*, infancy and currently. In addition, maternal regular contact with the animals during pregnancy as stated in our questionnaire might

not reflect continuous nor intense exposure. This might partially explain the similarity of our findings to those observed with other non-affluent communities.

In the current study, the percentage of exposure to pets in infancy was significantly less than the percentage of the exposure to pets during pregnancy. The difference in pet exposure between the *in utero* and infancy periods might be due, in part, to how we defined regular contact in the two periods and/or pet avoidance by parents. In the prenatal period, regular contact was defined for the mothers as “spending time around feeding or taking care of the animals more than once a week”. However, regular contact in the infancy period was defined as “spending time around or playing with more than once a week”. In addition, the wording of the questions suggests that some of the *in utero* exposure might have been outdoors but we did not specifically ask whether the exposure to the animals was indoor or outdoor. Another possibility is pet avoidance behavior by parents. In the current study, only 18% of the children who were exposed to cats/dogs *in utero* were also exposed to cats/dogs in infancy. Similarly, around 21% of the children who were exposed to birds *in utero* were also exposed to birds in infancy. This might reflect some parents deciding to avoid exposing the infant to these animals in infancy due to parental history of allergies. This is supported by the finding in our study that the prevalence of exposure to cats/dogs in infancy was 1.85% and exposure to birds in infancy was 2% for the infants with, but 4.63 and 3.3%, respectively than in those without, a parental history of asthma or allergies, differences, however, that were not statistically significant (data not shown).

The discrepancy in the wording along with pet avoidance behavior might explain the lack of association of exposure to cats/dogs and birds in infancy with the risk of any of the four conditions examined in the study. There might be a greater variation in the level of the maternal exposure “feeding or taking care of” than the exposure of an infant “spending time around or playing with”. The nature of the exposure might be related to the country of birth. In our study, US-born children were significantly less likely to be exposed *in utero* and in infancy to cats/dogs, livestock, poultry and birds than their Mexico born peers. This suggests that exposure in Mexico might be mostly to outdoor animals to which an infant will be less likely than his/her mother to spend time around or play with. This might be also suggested by the very small percentage of children born in the US who were exposed to animals in infancy where exposure to outdoor animals in the inner city is limited. Pet avoidance behavior has been cited in the literature as one of the possible explanations of the inverse associations of pets with allergic conditions. This could have diluted the associations of pets with respiratory conditions observed in our study.

As microbial burden in underdeveloped communities might be already high, the added exposure to animals might have detrimental effects on respiratory conditions. Dong et al. [26] suggested that the protective effect of exposure to animals/pets in affluent societies might be due to reduced levels of microbial stimulation related to increased hygiene. However, in less affluent settings where microbial burden in early life may be high regardless of pets, a protective effect of animal/pet exposure may not be observed [26].

The exact mechanisms through which exposure to animals in pregnancy might increase the risk of asthma are unclear but the associations are biologically plausible. Allergen and microbial pressures during pregnancy may skew the development of the child's immune response system towards an allergic phenotype [30–33]. Higher levels of endotoxins have been reported in homes with pets [34,35], stables and barns [36] and in homes with no pets but where exposure to farm animals is ubiquitous [32]. The role of endotoxins in the etiology of asthma is not clear. Although it has been suggested that exposure to high levels of endotoxins might exert a protective effect against asthma and respiratory conditions, other studies demonstrated positive associations of endotoxins with respiratory outcomes. Smit et al. [37] conducted a review of the health effects of occupational exposure to endotoxins and concluded that inhalation of endotoxins may lead to airway inflammation, respiratory symptoms and non-allergic asthma. In another study, Smit et al. [38] documented that occupational exposure to high levels of endotoxins in farmers increased the risk of non-atopic bronchial hyper-responsiveness and current wheeze. Endotoxin was also associated with an elevated risk of non-atopic wheeze in farm children in Germany, Switzerland and Austria [34]. In a US longitudinal study of inner city children [35], endotoxin exposure in early life increased the risk of any wheeze between ages 1 and 7 years, although endotoxin was associated with a reduced risk of atopy. Although the mechanisms through which endotoxins increase the risk of respiratory conditions need further investigation, there is evidence suggesting that endotoxin exposure activates neutrophils in the bloodstream and subsequent airway exposure to an allergen is met with an amplified inflammatory response [39]. Celedon et al. [35] suggest that increased risk for wheeze after exposure to endotoxin is due to increased production of inflammatory cytokines (i.e. $\text{TNF-}\alpha$) which lead to airway constriction.

The role of exposure to birds in the etiology of asthma remains poorly defined [40]. Among studies that examined birds as a separate exposure, conflicting associations were reported. Among nearly 7000 six to seven years old children participating in ISAAC phase I and III cross-sectional surveys in Munich, Germany, Behrens et al. [41] reported that only during the first year of life was bird ownership positively associated with asthma. Svanes et al. [42] reported that respiratory symptoms were more common among individuals who owned birds during childhood, but the authors only assessed the association of childhood bird ownership with asthma during adulthood.

It is well documented that sensitization has been found to increase the risk of asthma and respiratory conditions. Unfortunately, we did not collect information on participants' history of sensitization and whether it varies by exposure levels. The impact of exposure to pets in pregnancy or in early life on the risk of early sensitization is not fully understood, with studies showing both inverse [32,34,43] and positive [8] associations with risk of sensitization. It has been suggested that exposure to multiple species of animal may contribute to exposure to intense microbial diversity leading to pressures, especially during pregnancy, that may influence the development of the child's immune response system [33].

However, it must be noted that farm animal contact and the farming environment experienced in non-affluent societies may be dramatically different from that experience in affluent societies [44]. Another possibility is that in non-affluent or rural communities there is increased exposure to helminths, a parasite found more frequently in the excrement of farm-based cats and dogs versus domestic cats and dogs [8]. Helminth sensitization has been associated with respiratory conditions such as wheezing and adult asthma [8,45].

Limitations

There are several limitations associated with this study. This study represents a cross-sectional analysis and data regarding pet/animal exposure and health outcomes were collected retrospectively and relied on parental recall. Therefore, these results may be prone to recall bias. In this study, we assessed the exposure dichotomously: having close contact (i.e. feeding or caring for) with animals more than once a week or not. There was inconsistency in the wording of the questions for the *in utero* versus the infancy periods. In addition, our question on the *in utero* exposure might not have captured the outdoor exposure and we did not collect data on *in utero* or early life exposure to pets/animals in the home. While other studies have utilized this same or similar definition or classification, this definition does not reflect gradations in exposure and may not capture "regular" exposure. Therefore, our study might not have sufficient information on the intensity nor the continuity. In addition, we did not measure the concentration of pet allergens in the homes of the children to better quantify the exposure. Furthermore, we asked about maternal exposure to cats/dogs during pregnancy in the same question and it was not possible to separate the effect of exposure to cats from the exposure to dogs. Moreover, the study did not assess the level of pet ownership within the communities where participants lived. Studies have demonstrated that cat allergens are ubiquitous throughout a community and can be found in non-cat owners' homes [7]. Future efforts should attempt to collect data on community-level exposure to pets.

Conclusion/key findings

Our results suggest that *in utero* exposure to cats/dogs and birds jointly or independently may increase the risk of asthma and wheezing in an underserved sample of MA children. Our study adds to the evidence suggesting a differential effect of pet exposure by population characteristics. We showed detrimental effects of prenatal exposure to pets on the risk of asthma in MA children currently living in inner city communities in the US. Therefore, our study provides additional support for the need for conducting more research and analyses with subgroups to identify other genetic and environmental factors that may modify the associations of pet exposure with the risk of asthma and other respiratory conditions. In addition, our findings call for more research focused on a better assessment of the frequency, timing and intensity of the exposures to different types of pets and effects of these various measures on the risk of asthma and other respiratory conditions.

Declaration of interest

The authors report no conflict of interest. The authors alone are responsible for the content and writing of this paper. This study was supported by the University of Illinois at Chicago's Provost's Award for Graduate Research. Time for data analysis and manuscript preparation is supported by the Robert Wood Johnson Foundation Nurse Faculty Scholar Program (Grant # 71249).

References

- Dagoye D, Bekele Z, Woldemichael K, Nida H, Yimam M, Venn AJ, Hall A, et al. Domestic risk factors for wheeze in urban and rural Ethiopian children. *Q J Med* 2004;97:489–498.
- Karimi M, Mirzaei M, Baghiani Moghadam B, Fotouhi E, Zare Mehrjardi A. Pet exposure and the symptoms of asthma, allergic rhinitis and eczema in 6–7 years old children. *Iran J Allergy Asthma Immunol* 2011;10:123–127.
- Apelberg BJ, Aoki Y, Jaakkola JJ. Systematic review: exposure to pets and risk of asthma and asthma-like symptoms. *J Allergy Clin Immunol* 2001;107:455–460.
- Chen C-M, Tischer C, Schnappinger M, Heinrich J. The role of cats and dogs in asthma and allergy—a systematic review. *Int J Hyg Environ Health* 2010;213:1–31.
- Chen H, Yu H, Wei L, ZhiJun Z, Jan S. Pet-keeping and its impact on asthma and allergies among preschool children in Shanghai, China. *Chin Sci Bull* 2013;58:4203–4210.
- Hugg TT, Jaakkola MS, Ruotsalainen R, Pushkarev V, Jaakkola JJK. Exposure to animals and the risk of allergic asthma: a population-based cross-sectional study in Finnish and Russian children. *Environ Health* 2008;7:28.
- Schäfer T, Steiger B, Polzius R, Krauspe A. Associations between cat keeping, allergen exposure, allergic sensitization and atopic diseases: results from the Children of Lübeck Allergy and Environment Study (KLAUS). *Pediatr Allergy Immunol* 2009;20:353–357.
- Brunekreef B, Von Mutius E, Wong GK, Odhiambo JA, Clayton TO. Early life exposure to farm animals and symptoms of asthma, rhinoconjunctivitis and eczema: an ISAAC Phase Three Study. *Int J Epidemiol*. 2012;41:753–761.
- Brunekreef B, Von Mutius E, Wong G, Odhiambo J, Garcia-Marcos L, Foliaki S. Exposure to cats and dogs, and symptoms of asthma, rhinoconjunctivitis, and eczema. *Epidemiology*. 2012;23:742–750.
- Del-Rio-Navarro B, Berber A, Blandon-Vijil V, Ramirez-Aguilar M, Romieu I, Ramirez-Chanona N, Heras-Acevedo S, et al. Identification of asthma risk factors in Mexico City in an International Study of Asthma and Allergy in Childhood survey. *Allergy Asthma Proc*. 2006;27:325–333.
- Dong G-H, Wang J, Liu M-M, Wang D, Lee YL, Zhao Y-D. Allergic predisposition modifies the effects of pet exposure on respiratory disease in boys and girls: the seven northeast cities of China (SNECC) study. *Environ Health* 2012;11:50.
- Al-Dawood KM. Epidemiology of bronchial asthma among school boys in Al-Khobar city, Saudi Arabia. *Saudi Med J* 2001;22:61–66.
- Alshehri MA, Abolfotouh MA, Sadeg A, Al Najjar YM, Asindi AA, Al Harthi AM, et al. Screening for asthma and associated risk factors among urban school boys in Abha city. *Saudi Med J* 2000;21:1048–1053.
- Abdulrazzaq YM, Bener A, DeBuse P. Pet ownership in the UAE: its effect on allergy and respiratory symptoms. *J Asthma* 1995;32:117–124.
- Chong Neto HJ, Rosario NA, Grupo Curitiba EISL. Risk factors for wheezing in the first year of life. *J Pediatr (Rio J)* 2008;84:495–502.
- Kalyoncu AF, Selcuk ZT, Karakoca Y, Emri AS, Coplu L, Sahin AA, Bariş YI. Prevalence of childhood asthma and allergic diseases in Ankara, Turkey. *Allergy* 1994;49:485–488.
- Lodrup Carlsen KC, Roll S, Carlsen K-Hk, Mowinkel P, Wijga AH, Brunekreef B, Torrent M, et al. Does pet ownership in infancy lead to asthma or allergy at school age? Pooled analysis of individual participant data from 11 European birth cohorts. *PLoS One* 2012;7:e43214.
- Fretzayas A, Kotzia D, Moustaki M. Controversial role of pets in the development of atopy in children. *World J Pediatr* 2013;9:112–119.
- Eldeirawi K, McConnell R, Furner S, Freels S, Stayner L, Hernandez E, Amoroso L, et al. Associations of doctor-diagnosed asthma with immigration status, age at immigration, and length of residence in the United States in a sample of Mexican American School Children in Chicago. *J Asthma* 2009;46:796–802.
- Eldeirawi KM, Persky VW. Associations of physician-diagnosed asthma with country of residence in the first year of life and other immigration-related factors: Chicago asthma school study. *Ann Allergy Asthma Immunol* 2007;99:236–243.
- Eldeirawi K, McConnell R, Freels S, Persky VW. Associations of place of birth with asthma and wheezing in Mexican American children. *J Allergy Clin Immunol* 2005;116:42–48.
- Eldeirawi KM, Persky VW. Associations of acculturation and country of birth with asthma and wheezing in Mexican American youths. *J Asthma* 2006;43:279–286.
- Eldeirawi K, McConnell R, Furner S, Freels S, Stayner L, Hernandez E, Amoroso L, et al. Frequent ear infections in infancy and the risk of asthma in Mexican American children. *J Asthma* 2010;47:473–477.
- Eldeirawi KM, Kunzweiler C, Atek A, Persky VW. Antibiotic use in infancy and the risk of asthma in Mexican American children. *J Asthma* 2015;52:707–714.
- Carlsten C, Brauer M, Dimich-Ward H, Dybuncio A, Becker aB, Chan-Yeung M. Combined exposure to dog and indoor pollution: incident asthma in a high-risk birth cohort. *Eur Respir J* 2011;37:324–330.
- Dong GH, Ma YN, Ding HL, Jin J, Cao Y, Zhao YD, He QC. Pets keeping in home, parental atopy, asthma, and asthma-related symptoms in 12,910 elementary school children from northeast China. *Indoor Air* 2009;19:166–173.
- Dong G-H, Ding H-L, Ma Y-N, Jin J, Cao Y, Zhao Y-D, He Q-C. Asthma and asthma-related symptoms in 16 789 Chinese children in relation to pet keeping and parental atopy. *J Investig Allergol Clin Immunol* 2008;18:207–213.
- Perzanowski MS, Chew GL, Divjan A, Johnson A, Goldstein IF, Garfinkel RS, Hoepner LA, et al. Cat ownership is a risk factor for the development of anti-cat IgE but not current wheeze at age 5 years in an inner-city cohort. *J Allergy Clin Immunol* 2008;121:1047–1052.
- Gaffin JM, Spergel JM, Boguniewicz M, Eichenfield LF, Paller AS, Fowler JF, Dinulos JG, et al. Effect of cat and daycare exposures on the risk of asthma in children with atopic dermatitis. *Allergy Asthma Proc* 2012;33:282–288.
- Bufford JD, Gangnon R, Lemanske RF, Gern JE, Reardon CL, Li Z, Liu AH, et al. Effects of dog ownership in early childhood on immune development and atopic diseases: effects of dog ownership in early childhood. *Clin Exp Allergy* 2008;38:1635–1643.
- Ownby DR, Johnson CC, Peterson EL. Exposure to dogs and cats in the first year of life and risk of allergic sensitization at 6 to 7 years of age. *JAMA* 2002;288:963–972.
- von Mutius E. Infection: friend or foe in the development of atopy and asthma? The epidemiological evidence. *Eur Respir J* 2001;18:872–881.
- von Mutius E, Vercelli D. Farm living: effects on childhood asthma and allergy. *Nat Rev Immunol* 2010;10:861–868.
- Braun-Fahrlander C, Riedler J, Herz U, Eder W, Waser M, Grize L, Maisch S, et al. Environmental exposure to endotoxin and its relation to asthma in school-age children. *N Engl J Med* 2002;347:869–877.
- Celedon JC, Milton DK, Ramsey CD, Litonjua AA, Ryan L, Platts-Mills TA, Gold DR. Exposure to dust mite allergen and endotoxin in early life and asthma and atopy in childhood. *J Allergy Clin Immunol* 2007;120:144–149.
- von Mutius E, Braun-Fahrlander C, Schierl R, Riedler J, Ehlermann S, Maisch S, Waser M, Nowak D. Exposure to endotoxin or other bacterial components might protect against the development of atopy. *Clin Exp Allergy* 2000;30:1230–1234.
- Smit LA, Wouters IM, Heederik D, Douwes J. Health effects of occupational endotoxin exposure: a review and relevance to veterinary practice. *Tijdschr Diergeneeskde* 2009;134:840–846.

38. Smit LA, Heederik D, Doekes G, Lammers JW, Wouters IM. Occupational endotoxin exposure reduces the risk of atopic sensitization but increases the risk of bronchial hyperresponsiveness. *Int Arch Allergy Immunol* 2010;152:151–158.
39. Michel O. Role of lipopolysaccharide (LPS) in asthma and other pulmonary conditions. *J Endotoxin Res* 2003;9:293–300.
40. Gorman J, Cook A, Ferguson C, van Buynder P, Fenwick S, Weinstein P. Pet birds and risks of respiratory disease in Australia: a review. *Aust N Z J Public Health* 2009;33:167–172.
41. Behrens T, Maziak W, Weiland SK, Rzehak P, Siebert E, Keil U. Symptoms of asthma and the home environment. The ISAAC I and III Cross-Sectional Surveys in Münster, Germany. *Int Arch Allergy Immunol* 2005;137:53–61.
42. Svanes C, Heinrich J, Jarvis D, Chinn S, Omenaas E, Gulsvik A, Künzli N, Burney P. Pet-keeping in childhood and adult asthma and hay fever: European community respiratory health survey. *J Allergy Clinical Immunol* 2003;112:289–300.
43. Riedler J, Braun-Fahrlander C, Eder W, Schreuer M, Waser M, Maisch S, Carr D, et al. Exposure to farming in early life and development of asthma and allergy: a cross-sectional survey. *Lancet* 2001;358:1129–1133.
44. Svanes C. Commentary: a step towards understanding asthma in low- and middle-income countries. *Int J Epidemiol* 2012;41:761–763.
45. Kuk S, Özel E, Oğuztürk H, Kirkil G, Kaplan M. Seroprevalence of Toxocara antibodies in patients with adult asthma. *South Med J* 2006;99:719–722.