

## Exposure to cats and dogs as risk factors for wheezing in preschool children: are their effects modified by removal?

*Exposición a perros y gatos como factores de riesgo para sibilancias en niños en edad escolar. ¿Se modifican los efectos tras la eliminación?*

*A exposição a cães e gatos como fatores de risco para sibilância em crianças em idade pré-escolar: são os seus efeitos modificados pela remoção?*

**Patricia Garcia-Marcos, Rosa Pacheco-Gonzalez, Manuel Sanchez-Solis, Luis Garcia-Marcos**

Servicio de Pediatría. Hospital Clínico Universitario "Virgen de la Arrixaca". Murcia

**Cita:** Garcia-Marcos P, Pacheco-Gonzalez R, Sanchez-Solis M, Garcia-Marcos L. Exposure to cats and dogs as risk factors for wheezing in preschool children: are their effects modified by removal?. Rev salud ambient. 2013;13(1):37-43.

**Recibido:** 29 de abril de 2013. **Aceptado:** 7 de mayo de 2013. **Publicado:** 28 de junio de 2013.

**Autor para correspondencia:** Prof. Luis Garcia-Marcos.

Correo e.: [lgmarcos@um.es](mailto:lgmarcos@um.es)

Pabellón Docente Universitario. Campus Ciencias de la Salud. Ctra. Madrid-Cartagena, s/n. 30120 El Palmar. Murcia. España. Tel.: +34868888129. Fax: +34868888127

**Financiación:** Ninguna.

**Declaración de conflicto de intereses:** Los autores declaran que no existen conflictos de intereses que hayan influido en la realización y la preparación de este trabajo.

### Abstract

**Objective:** To define the relationship between current wheezing in preschoolers and exposure to dogs and cats at home, and to find out to what extent their removal modifies the associations.

**Methods:** Previously validated questionnaires were completed by parents of 1784 preschoolers (mean age 4.08±0.8 years). Children were stratified according to the presence (20.0 %) or absence of wheezing in the previous year. Information regarding cat or dog exposure currently and during the first year of life was collected, as well as information about the removal of the pets.

**Results:** A higher proportion of families owning a cat in the first year of the child's life, as well as in the previous year, was found in the wheezing group. The proportion of families owning a dog was marginally higher in this group. Cat exposure was shown to be a significant risk factor when present in the first year of the child's life (Adjusted Odds Ratio [aOR] 1.73, 95 % CI 1.04-2.88), and an even higher association was found with current exposure (aOR 2.00, 95 % CI 1.22-3.26). The association was highest (aOR 2.68, 95 % CI 1.32-5.44) among the wheezing group for the subset of families that had removed a cat from the home. Dog exposure did not appear to be a significant risk factor, neither during the first year of life (aOR 1.24, 95 % CI 0.88-1.76) nor with current ownership (aOR 1.04, 95 % CI 0.73-1.50). However, a significant association was found in the group that had removed a dog from the home (aOR 5.88, 95 % CI 2.62-13.17).

**Conclusions:** Exposure to cat allergens is a risk factor for asthma, when exposure occurs during the first 12 months of life. However, this factor is of limited influence beyond the first year. It is likely that children who are prone to developing an allergy would benefit from control of environmental allergen exposure, including cat avoidance.

**Keywords:** Wheezing; cat; dog; preschool children; epidemiology; asthma; allergy.

### Resumen

**Objetivo:** Definir la relación entre sibilancias activas en niños en edad preescolar y su exposición a gatos y perros en el hogar, y mostrar hasta qué punto la retirada de los mismos modifica dicha asociación.

**Métodos:** Los padres de 1784 niños en edad preescolar (media de edad 4,08 ± 0,8) cumplieron los cuestionarios que previamente habían sido validados. Se realizó una estratificación de los niños en función de la presencia (20 %) o ausencia de sibilancias en el último año. Se recogió la información relacionada con la exposición actual a gatos o perros y durante el primer año de vida, además de información respecto a la retirada de las mascotas.

**Resultados:** En el grupo con sibilancias se encontró una mayor proporción de familias que durante el primer año de vida del niño tuvieron un gato en casa. La proporción de familias con perro era ligeramente más alta en dicho grupo. La exposición a gatos

apareció como factor de riesgo significativo si el gato había estado presente en el hogar durante el primer año de vida del niño (Odds Ratio ajustada [aOR] 1,73, IC 95 % 1,04 – 2,88), y se encontró una asociación incluso más alta con la exposición actual (aOR 2, IC 95 % 1,22 – 3,26). La asociación más elevada (aOR 2,68, IC 95 % 1,32 – 5,44) se encontró en el subgrupo de familias que habían retirado el gato del hogar. La exposición a perros no se mostró como factor de riesgo significativo, ni durante el primer año de vida (aOR 1,24, IC 95 % 0,88 – 1,76), ni en el momento actual (aOR 1,04, IC 95 % 0,73 – 1,50). Sin embargo, en el grupo que había retirado el perro del hogar sí se encontró una asociación significativa (aOR 5,88, IC 95 % 2,62 – 13,17).

Conclusiones: La exposición a los alérgenos del gato es un factor de riesgo para el asma si dicha exposición tiene lugar en los primeros 12 meses de vida. Sin embargo este factor tiene una influencia limitada si ocurre más allá del primer año de vida. Es probable que los niños con tendencia a desarrollar alergias se beneficien del control de la exposición a alérgenos medioambientales, incluyendo evitar los gatos.

**Palabras clave:** sibilancias; gatos; perros; niños en edad preescolar; epidemiología; asma; alergia.

## Resumo

**Objetivo:** Definir a relação entre a sibilância em crianças em idade pré-escolar e a exposição doméstica a cães e gatos. Verificar até que ponto a remoção dos animais altera as associações.

**Metodologia:** Um questionário previamente validado foi respondido por pais de 1784 crianças em idade pré-escolar (média de idade 4.08±0.8 anos). As crianças foram estratificadas relativamente à presença (20.0 %) ou ausência de sibilância no ano anterior. Foi recolhida informação sobre a exposição a cães e gatos, atualmente e no primeiro ano de vida, bem como, informação sobre a remoção desses animais domésticos.

**Resultados:** A maior proporção de famílias que possuem um gato no primeiro ano de vida da criança, assim como no anterior ao estudo, foram encontradas no grupo de crianças com manifestações de sibilância. A proporção de famílias que possuem um cão foi ligeiramente superior neste grupo.

Verificou-se que a exposição a gatos no primeiro ano de vida é um fator de risco significativo (Odds Ration Ajustado [aOR] 1.73, 95 % CI 1.04-2.88), sendo a associação ainda mais forte para uma exposição atual (aOR 2.00, 95 % CI 1.22-3.26).

No grupo de crianças com sibilância a associação foi maior (aOR 2.68, 95 % CI 1.32-5.44) entre o subgrupo de famílias que removeram o gato da habitação.

A exposição a cães não pareceu ser um fator de risco significativo, nem para a exposição no primeiro ano de vida (aOR 1.24, 95 % CI 0.88-1.76) nem para a exposição atual (aOR 1.04, 95 % CI 0.73-1.50). Contudo, foi encontrada uma associação significativa no grupo que tinha retirado o cão da habitação (aOR 5.88, 95 % CI 2.62-13.17).

**Conclusões:** A exposição a alérgenos de gatos é um fator de risco para a asma, quando a exposição ocorre durante o primeiro ano de vida. Contudo, esse fator é de influência limitada além do primeiro ano.

É provável que as crianças que são propensas a desenvolver uma alergia beneficiem de um controlo da exposição ambiental a alérgenos, incluindo evitar o contato com gatos.

**Palavras passe:** sibilância; gato; cão; crianças em idades pré escolar; epidemiologia; asma; alergia.

## INTRODUCTION

Causes of the worldwide asthma and allergy epidemic over recent decades remain uncertain. The prevalence of asthma varies considerably, but tends to be higher in developing countries<sup>1</sup>. In a similar way, pet exposure varies worldwide, and is most frequent in Western countries. It has been suggested that sensitization to pets may be a risk factor for asthma, and it has been assumed that pet ownership is a risk factor for atopic sensitization. Some epidemiological studies have failed to confirm this<sup>2</sup>. Whether cat or dog exposure should be considered a risk or a protective factor is still subject to debate. Previous case-control and cohort studies have shown heterogeneous results. Case-control studies assessing cat exposure have presented contrasting results, whereas cohort studies found cat ownership to be a protective factor for asthma. However, dog exposure

has been shown to be a risk factor for developing asthma both in case-control and cohort studies<sup>3</sup>. It should be stressed that pet avoidance behavior may modify the associations between pets and allergic diseases<sup>4,6</sup>, thereby explaining the lack of agreement between studies. The heterogeneity of results might also be explained by differences in the prevalence of pets in the community, as higher rates are found for this risk factor in communities where keeping pets at home is infrequent<sup>7</sup>. Moreover, climate may influence indoor versus outdoor pet keeping and its association with allergic outcomes<sup>8,9</sup>.

The aim of our study was to define the association between current wheezing in preschoolers and exposure to dogs and cats, and to find out to what extent cat and dog removal might modify that association.

## MATERIAL AND METHODS

Three- and four-year-old preschool children from the three major cities in the province of Murcia, Spain (Murcia, Cartagena and Lorca) were included in our study population. All parents whose children attended primary schools, including preschool education, were invited to participate in each city. Up to 1000 children per city were sampled from a number of schools selected at random until this sample size was reached. Within these schools, all classes in the 2 school grades were included. Teachers gave the questionnaires to the parents, who returned them filled in within one week.

The questionnaire distributed was the same that was used for the International Study of Asthma and Allergies in Childhood (ISAAC) phase III core and environmental questionnaires, and included questions about asthma, rhinoconjunctivitis and eczema, as well as questions directed to obtain demographic and environmental data. Demographic data included gender, age, race, current height and weight, type of delivery, preterm birth, weight at birth, maternal age, maternal education level, and number of older and younger siblings. Environmental data included: frequency of vigorous physical activity; hours spent watching television per day; fuel used for heating and cooking systems; antibiotic and acetaminophen consumption during the first year of life; acetaminophen administered by the mothers during the previous year; breast-feeding; livestock exposure (during pregnancy and currently); dogs and cats at home during the first year of the child's life (as well as in the previous year); dog and cat avoidance behavior; father's and mother's tobacco consumption (during pregnancy and currently); and truck traffic in front of the house.

Current wheezing was defined as when a positive answer was given to the question "Has your child had wheezing or whistling in the chest in the past 12 months?". Current rhinoconjunctivitis was defined as when a positive answer was given to the question "Has your child presented sneezing, a runny or blocked nose when he/she did not have a cold or the flu, accompanied by itchy, watery eyes in the past 12 months?". Current eczema was defined as when positive answers were given to 3 questions: "Has your child had an itchy rash that came and went in the past 6 months?"; "Has your child had this itchy rash in the past 12 months?"; and "Has this itchy rash affected these locations: elbow folds, behind the knees, ankles front, under the buttocks or around the neck, eyes or ears?".

The environmental questionnaire also included the following questions: were father/mother/siblings

affected by asthma; have allergy tests been carried out for the child, for the father/mother/siblings; and was there avoidance of cats or dogs at home because they were causing the child to develop any type of allergy.

The Ethics Committee of the University of Murcia approved this study. Full informed and signed consent was obtained from a parent of each participating child.

## STATISTICAL ANALYSIS

Statistical analyses of the differences between the current wheezing and non-current wheezing groups were performed using the  $\chi^2$  test. Odds ratios (ORs) and 95 % confidence intervals (CIs) were also calculated. A multivariate logistic regression model was built using current wheezing and cat or dog exposure in the first year of life and current cat or dog exposure as the dependent variables. Cat and dog removal was considered as an independent variable. Adjusted Odds Ratios (aORs) and 95 % CIs were calculated from the logistic regression model. In the present study, associations were adjusted for gender, preterm birth, breast-feeding, paternal and maternal asthma, and current maternal smoking. All analyses were performed using Stata 7.0 statistical software (Stata Corp, College Station, TX).

## RESULTS

A total of 1784 children completed the questionnaire, out of the 2922 children invited to participate (61 % participation rate). The question about current wheezing status was answered by 1757 children (mean age  $4.08 \pm 0.8$  years; 48.8 % male). In this group, the prevalence of current wheezing was 20.0 % ( $n=351$ ). There were no significant gender differences between wheezing and non-wheezing children. In the current wheezing group, there was a slightly lower number of children who were breast-fed beyond 6 months of age. It was statistically significant ( $p=0.022$ ) that more children in the wheezing group were never breast-fed. Parental asthma showed significantly higher prevalence in the wheezing group ( $p=0.004$ ). This higher prevalence was also seen for maternal asthma ( $p=0.002$ ). The proportion of wheezing children was significantly higher among those born preterm ( $p<0.001$ ). A significant number of children presenting current wheezing were from this preterm population. Finally, maternal current smoking was also higher in this group (Table I).

Table I. Prevalence of factors significantly associated with current wheezing

		Current wheezing (n=351)	Current non-wheezing (n=1406)	P-value
Male		186/351	718/1406	0.519
Breast-feeding (in months)	Never	91/341	288/1375	0.022
	1-3	114/341	467/1375	0.852
	4-6	75/341	296/1375	0.851
	7-9	33/341	153/1375	0.441
	10-12	8/341	77/1375	0.013
	>12	20/341	94/1375	0.519
Maternal current smoking		171/351	555/1400	0.002
Maternal asthma		28/350	56/1400	0.002
Paternal asthma		22/347	43/1349	0.004
Preterm birth		61/317	122/1287	<0.001
Cat ownership during the 1st year of life		27/317	65/1401	0.006
Cat ownership currently		33/346	65/1393	<0.001
Dog ownership during the 1st year of life		62/346	195/1397	0.06
Dog ownership currently		54/344	202/1395	0.568

In the wheezing group, there was a higher proportion of families owning a cat in the first year of the child's life and in the previous year. The proportion of families owning a dog was marginally higher in the wheezing group. Crude and adjusted ORs were calculated (Table II) for factors related to cat and dog ownership in the wheezing group. Regarding cat exposure, this was shown to be a significant risk factor when present in the first year of child's life (aOR 1.73, 95 % CI 1.04-2.8), and an even higher association was found with current exposure (aOR 2.00, 95 % CI 1.22-3.26). In the group that removed a

cat from the home, the association rate was highest (aOR 2.68, 95 % CI 1.32-5.44). Dog exposure did not appear to be a significant risk factor, either during the first year of life or with current ownership (aOR 1.24, 95 % CI 0.88-1.76 and aOR 1.045, 95 % CI 0.728-1.500, respectively). However, a significant association was found in the group that removed a dog from the home (aOR 5.88, 95 % CI 2.62-13.17).

In the subset where no cat removal had occurred, currently having a cat (n=1520) was a significant risk factor (aOR 1.97, 95 % CI 1.18-3.26). Yet, in this subgroup, cat ownership during the first year of life (n=1525) was neither a risk nor a protective factor (aOR 1.40, 95 % CI 0.79-2.47) (Figure 1).

Associations were not significant in the other subset, where removal of a cat (n=35) took place at some point: aOR 2.74, 95 % CI 0.50-14.98 during the first year of life and aOR 1.86, 95 % CI 0.18-19.20 currently.

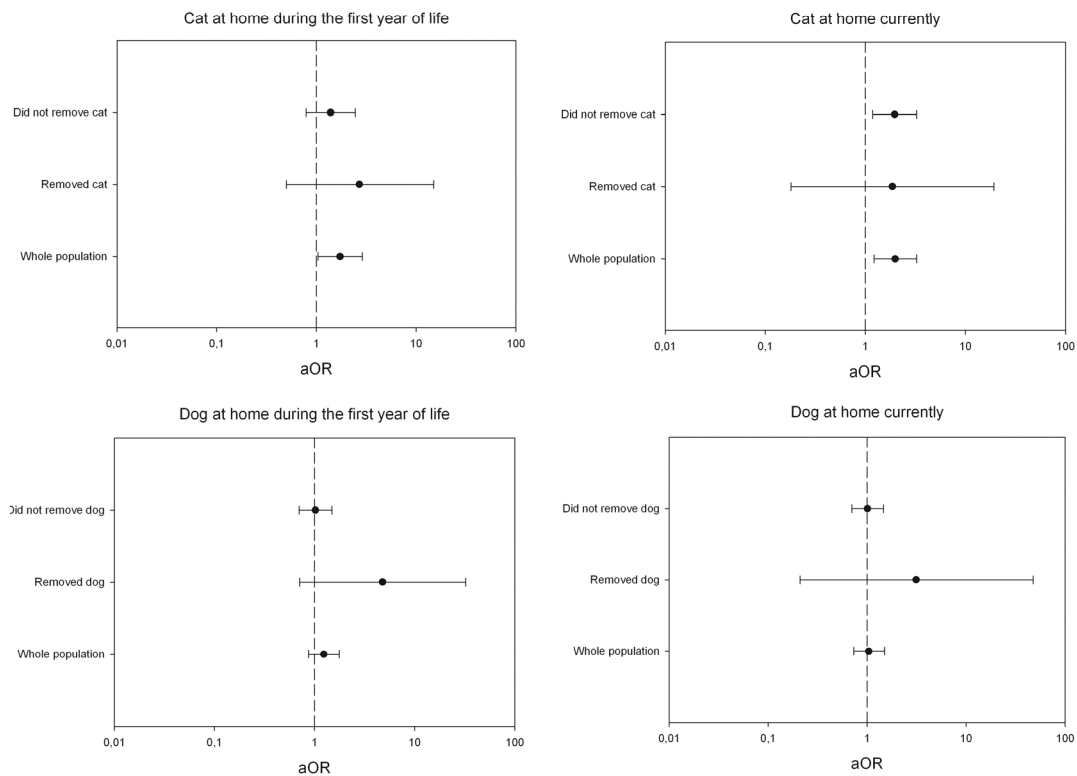
Regarding dog ownership, the results showed no significant association (aOR 1.01, 95 % CI 0.70-1.46) in both the subset that did not remove a dog, and in the subset of families that did remove a dog from the home (aOR 3.13, 95 % CI 0.21-47.51). Similar results were obtained when the dog was present during the first year of the child's life: no evidence of association was found either when a dog was removed from the home (n=23; aOR 1.02, 95 % CI 0.70-1.49) or when a dog was not removed (n=1535; aOR 4.78, 95 % CI 0.709-32.263).

Table II. Associations (crude and adjusted Odds Ratios) of factors related to cat and dog ownership

	cOR	(95 % CI)	aOR*	(95 % CI)
Cat ownership during the first year of life	1.75	1.10-2.79	1.73	1.04-2.88
Cat ownership currently	2.15	1.39-3.33	2.00	1.22-3.26
Cat removal at any time	3.25	1.73-6.09	2.68	1.32-5.44
Dog ownership during the first year of life	1.34	0.98-1.84	1.24	0.88-1.76
Dog ownership currently	1.10	0.79-1.52	1.04	0.73-1.50
Dog removal at any time	6.45	2.99-13.91	5.88	2.62-13.17

\*Adjusted for gender, preterm birth, breast-feeding three or more months, paternal and maternal asthma, and maternal current smoking.

Figure 1. Associations between cat and dog ownership and wheezing at 4 years of age in the whole study population and stratified for cat removal



A. Cat ownership during the first year of life; B. Cat Ownership at the time of the survey; C. Dog ownership during the first year of life; D. Dog Ownership at the time of the survey

## DISCUSSION

When all children were included, early and current cat keeping were significant risk factors for wheezing in the present cohort. Conversely, dog exposure at any time did not appear to be a significant risk factor, again when including the whole study population. The difference in the effects between exposure to a dog and that to a cat may have several explanations. Cat allergens are ubiquitous and may be found in environments where cats are absent, as they can be carried on clothes. Moreover, Fel d 1, the major cat allergen belongs to the group of secretoglobins, whereas Can f 1, the major dog allergen, belongs to the family of lipocalins with significantly lower allergenic power.

The fact that the aORs for wheezing were markedly higher in the subsets where pet removal occurred, led us to decide to carry out a separate analysis to eliminate this possible confounding factor.

Once this separate analysis was performed, it was found that the subset of families who had owned a pet

during the first year of life of the child, and had removed the pet from their house at some time point, had higher aORs than the remaining families in the sample. Although these subsets were small in number they seem to modify the strength of the association found in the whole population. This influence was sufficient to increase the aOR to a level that reached statistical significance in the case of cat exposure during the first year of the child's life. Nevertheless, this influence was not clear when exposure to pets occurred in the last 12 months, as the aOR rates in the subset, where pet removal occurred, were not sufficiently strong to modify the aOR for the whole population. These findings support the view that sensitization to pet allergens occurs early in life<sup>10</sup>.

Strachan et al. suggest that exposure to furred pets in general is an independent risk factor for the more severe forms of wheeze in adolescence<sup>11</sup>. Early pet exposure was no more influential than current exposure, allowing for pet avoidance. Brunekreef et al. found the lowest prevalence of pet allergy in children, who currently (but not previously) had a pet at home, whereas the highest prevalence was found in families without pets

at present, but who had previously owned pets<sup>5</sup>. Kuehr et al. reported similar findings for skin prick tests, the prevalence of sensitization to cats was significantly higher in children whose families had owned cats in the past, but not among current cat owners<sup>12</sup>.

Inconsistencies between studies could be explained through a tendency of removing pets from the home after the child or other family members has/have developed allergic complaints. In our study, children with allergic predisposition were mainly represented in the subset that removed a pet from the house. This predisposition would explain the strong influence of this small subset on the average aOR.

Among the studies that found exposure to furry pets has a preventive effect on asthma, many consider that this effect could be a result of confounding factors. Moraes et al. showed that cat exposure behaves as a protective factor against asthma. In their study, the question regarding duration of exposure to pets referred to the 12 months prior to the interview, and not prior to the onset of symptoms. In this sense, the asthmatic children in their population were already being followed up. This indicates that a routine preventive orientation regarding hygiene at home for the reduction of exposure to allergens, including distancing the patient from pets, was already being carried out; therefore, pet exposure was lower in the asthmatic group<sup>13</sup>. Similarly, Smedje et al. found that the incidence of asthma diagnosis and self-reported pollen allergy was less common among those keeping a cat at the beginning of the study period. The possibility of selection bias was also included in the discussion, with health-motivated avoidance of pets present among those prone to develop allergies<sup>14</sup>. Only de Meer et al. suggested the "hygiene hypothesis" as an explanation for this inverse relationship. Microbial exposure in early life might protect against atopic disease by shifting the immature immune response of a Th2 type toward a non-allergic Th1 type. Another model of tolerance could occur under high exposure, with a Th2 response expressed as IgG4 rather than specific IgE. Selective avoidance of pets, because of previously diagnosed allergic disease, is dismissed after excluding subjects with childhood asthma at enrollment. However, they finally could not completely exclude this as a source of bias, as there was no information on if parents did avoid acquiring a cat (or removed an existing cat) because their child or one of the parents had asthma<sup>15</sup>.


One important limitation of this present study is that no information about the precise moment of pet removal is available. Results could have been modified if this information had been collected. Another limitation of the study is the potential recall bias as the information

was collected from a questionnaire that enquired about past events.

In summary, our study supports the concept that exposure to cat allergens is a risk factor for asthma when exposure occurs during the first 12 months of life, while the influence seems to be limited beyond the first year of life. It is likely that children who are prone to developing an allergy would benefit from control of environmental cat allergen exposure.

## REFERENCES

1. Simpson A, Custovic A. Early pet exposure: friend or foe? *Curr Opin Allergy Clin Immunol.* 2003;3:7-14.
2. Worldwide variations in the prevalence of asthma symptoms: the International Study of Asthma and Allergies in Childhood (ISAAC) *Eur Respir J.* 1998;2:315-35.
3. Takkouche B, González-Barcala FJ, Etminan M, Fitzgerald M. Exposure to furry pets and the risk of asthma and allergic rhinitis: a meta-analysis. *Allergy* 2008;63:857-64.
4. Bornehag CG, Sundell J, Hagerhed L, Janson S, DBH Study Group. Pet-keeping in early childhood and airway, nose and skin symptoms later in life. *Allergy* 2003;9:939-44.
5. Brunekreef B, Groot B, Hoek G. Pets, allergy and respiratory symptoms in children. *Int J Epidemiol.* 1992;2:338-42.
6. Svanes C, Zock JP, Antó J, Dharmage S, Norbäck D, et al. Do asthma and allergy influence subsequent pet keeping? An analysis of childhood and adulthood. *J Allergy Clin Immunol.* 2006;3:691-8.
7. Eller E, Roll S, Chen CM, Herbarth O, Wichmann HE et al. Meta-analysis of determinants for pet ownership in 12 European birth cohorts on asthma and allergies: a GALEN initiative. *Allergy.* 2008;11:1491-8.
8. Al-Mousawi MS, Lovel H, Behbehani N, Arifhodzic N, Woodcock A, Custovic A. Asthma and sensitization in a community with low indoor allergen levels and low pet-keeping frequency. *J Allergy Clin Immunol.* 2004;6:1389-94.
9. Woodcock A, Addo-Yobo EO, Taggart SC, Craven M, Custovic A. Pet allergen levels in homes in Ghana and the United Kingdom. *J Allergy Clin Immunol.* 2001;3:463-5.
10. Medjo B, Atanaskovic-Markovic M, Nikolic D, Spasojevic-Dimitrijeva B, Ivanovski P, Djukic S. Association between pet keeping and asthma in school children. *Pediatr Int.* 2013 Feb 20. doi: 10.1111/ped.12071.
11. Strachan D, Carey IM. Home environment and severe asthma in adolescence: a population based case-control study *BMJ* 1995;311:1053-6.
12. Kuehr J, Frischer T, Karmaus W, Meinert R, Barth R, Herrman-Kunz E, et al. Early childhood risk factors for sensitization at school age. *J Allergy Clin Immunol.* 1992;90:358-63.

- 
13. Moraes LSL, Barros MD, Takano OA, Assami NMC. Fatores de risco, aspectos clínicos e laboratoriais da asma em crianças. *J Pediatr (Rio J)* 2001;77(6):447-54.
  14. Smedje G, Norbäck D. Incidence of asthma diagnosis and self-reported allergy in relation to the school environment-a four-year follow-up study in schoolchildren. *Int J Tuberc Lung Dis.* 2001;11:1059-66.
  15. Gea de Meer, Toelle BG, Ng K, Tovey E, Marks GB. Presence and timing of cat ownership by age 18 and the effect on atopy and asthma at age 28. *J Allergy Clin Immunol.* 2004;3:433-8.