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Pet ownership is associated with increased risk of non-atopic asthma and reduced risk of atopy in childhood: findings from a UK birth cohort

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Abstract

Background—Studies have shown an inverse association of pet ownership with allergy but inconclusive findings for asthma.

Objective—To investigate whether pet ownership during pregnancy and childhood was associated with asthma and atopy at age 7 years in a UK population-based birth cohort.

Methods—Data from the Avon Longitudinal Study of Parents and Children (ALSPAC) were used to investigate associations of pet ownership at six time-points from pregnancy to age 7 years with asthma, atopy (grass, house-dust mite, and cat skin prick test) and atopic *versus* non-atopic asthma at age 7 years using logistic regression models adjusted for child's sex, maternal history of asthma/atopy, maternal smoking during pregnancy and family adversity.

Results—3,768 children had complete data on pet ownership, asthma and atopy. Compared with non-ownership, continuous ownership of any pet (before and after age 3 years) was associated with 52% lower odds of atopic asthma (odds ratio [OR] 0.48, 95% CI 0.34–0.68). Pet ownership tended to be associated with increased risk of non-atopic asthma, particularly rabbits (OR 1.61, 1.04–2.51) and rodents (OR 1.86, 1.15–3.01), comparing continuous *versus* non-ownership. Pet ownership was consistently associated with lower odds of sensitization to grass, house-dust mite and cat allergens, but rodent ownership was associated with higher odds of sensitization to rodent allergen. Differential effects of pet ownership on atopic *versus* non-atopic asthma were evident for all pet types.

Conclusions—Pet ownership during pregnancy and childhood in this birth cohort was consistently associated with a reduced risk of aeroallergen sensitization and atopic asthma at age 7

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years, but tended to be associated (particularly for rabbits and rodents) with an increased risk of non-atopic asthma.

Clinical relevance—The opposing effects on atopy *versus* non-atopic asthma might be considered by parents when they are deciding whether to acquire a pet.

Keywords

pets; asthma; atopy; ALSPAC birth cohort

Introduction

Childhood asthma imposes a global burden of impaired quality-of-life and healthcare costs [1, 2]. Individual susceptibility to childhood asthma is likely to be determined by interacting heritable and environmental risk factors [3, 4]. Studies that have investigated putative environmental exposures have generated inconsistent and inconclusive findings, leaving us without a clear explanation for trends in asthma incidence and prevalence [5-7].

Household pet ownership has attracted considerable attention as an early-life environmental exposure which might play a role in the development of asthma and allergy. Pet ownership is common among households in countries where the incidence and prevalence of childhood asthma and allergies have changed substantially over the past few decades [8, 9]. Meta-analyses of pet ownership studies have indicated inverse associations with sensitization to aeroallergens and suggested positive associations with non-atopic asthma [10-12]. These results are consistent with the ‘hygiene hypothesis’ of allergy causation [13], and they warrant confirmation in population-based studies using measures of exposure at multiple time-points. Ideally, such studies would also differentiate effects of different types of pet and effects on atopic *versus* non-atopic asthma [14].

Here we use data from the Avon Longitudinal Study of Parents and Children (ALSPAC), a well-characterised UK-based birth cohort, to investigate associations of pet ownership (any pet and specific pet types) at six time points (from pregnancy to age 7 years) with asthma (current and ever-diagnosed), atopy (grass, house dust mite, and cat), atopic and non-atopic asthma at age 7 years, and bronchial response to methacholine challenge, at age 8 years.

Methods

Study population

The Avon Longitudinal Study of Parents and Children (ALSPAC) is a UK population-based study which aims to investigate environmental and genetic influences on the health and development of children [15]. Pregnant women residing in the former Avon Health Authority in south-west England who had an estimated date of delivery between 1 April 1991 and 31 December 1992 were invited to take part, resulting in a cohort of 14,541 pregnancies and 13,978 children alive at 12 months of age (excluding triplets and quads). The primary source of data collection was via self-completion questionnaires sent to mothers at four time points during pregnancy then at approximately annual intervals following birth. The representative nature of the ALSPAC sample has been investigated by

comparison with the 1991 National Census data of mothers with infants under 1 year of age who were residents in the county of Avon [16]. The ALSPAC sample had a slightly greater proportion of mothers who were married or cohabiting, who were owner-occupiers and who had a car in the household. The study had a smaller proportion of ethnic minority mothers, and 96.1% of children were white, compared with 86.5% in the general population [15]. The ALSPAC study website contains details of all the data that are available through a fully searchable data dictionary (www.bris.ac.uk/alspac/researchers/data-access/data-dictionary/).

Ethical approval

Ethical approval for this study was obtained from the ALSPAC Law and Ethics Committee and the Local Research Ethics Committees.

Outcomes

Asthma and atopy (primary outcomes)—At 7 years of age (median 91 months, range 90 to 111 months) mothers were asked in a “My son’s/daughter’s well-being” questionnaire to report if their child had asthma in the previous 12 months (current asthma), if a physician had ever told them that their child had asthma (ever had asthma), and if their child had used asthma medication in the previous 12 months. The atopic status of children was determined in ‘Focus@7’ research clinics at age 7 years (median 89, range 82 to 110 months). Skin prick test (SPT) responses were measured using a core panel of 6 common allergens (house dust mite (*Dermatophagoides pteronyssinus*), mixed grass pollens, cat fur, peanut, mixed tree nuts, and egg) plus 3 allergen panels rotated for 1 week at a time hence, each tested on approximately 1/3rd of clinic attendees: 1) other animal danders and soya (dog, horse, mouse, rabbit, guinea-pig, hamster, soya); 2) additional foods (cod, sesame seed, cashew nuts, almond, walnut, hazelnut, brazil nut, pecan nut); and 3) additional aeroallergens and food allergens (mixed tree pollens, *D. farinae*, *Alternaria alternata*, *Cladosporium herbarium*, *Aspergillus fumigatus*, cockroach, latex, milk) A positive response was defined as a mean weal diameter ≥ 2 mm with an absent response to negative control solution. For the purpose of our analysis, atopy was defined as a positive response to one or more of house dust mite, cat or grass pollen. These three allergens were tested on all children attending the clinic and positive reactions to one or more of them identified 95% of sensitized children in this population [17]. We investigated SPT positivity for dog, rabbit, and rodent (mice, guinea pigs and hamsters) allergens in relation to ownership of each of these pet types. Airway responsiveness to methacholine was measured in ‘Focus@8’ research clinics at age 8 years (median 103, range 89 to 127 months) using the method of Yan *et al* [18] and expressed for each subject as the log-transformed dose-response slope of FEV₁ (percentage decline from baseline) per mmol methacholine (slopes >0 were categorized into tertiles and slopes $=0$ were combined with the bottom tertile group).

Exposures

Pet ownership (primary exposure)—Pet ownership questions were asked (in questionnaires about the mother and her environment) during pregnancy (up to 28 weeks gestation) and at child ages of 8 months and 2, 3, 4, and 7 years. The carer of the child (usually the mother) was asked ‘do you have any pets’ and ‘how many of the following pets

do you have'. Pet types included cats, dogs, rabbits, rodents (mice, hamster, gerbil etc.), and birds. For the purpose of our study, we defined 4-level categorical variables to indicate whether a cat, dog, rabbit, rodent, bird, or any pet, had been owned/acquired as follows: "Never"; "At age 3 years or later, not before" (owned at age 33 months or at any time thereafter, but not at age 21 months or at any time before, including during pregnancy); "Before and after age 3 years" (owned at any time before age 33 months, including during pregnancy, and at any time thereafter, referred to as 'continuous' ownership); "Before but not after 3 years" (owned at any time before, including during pregnancy, but no longer owned at age 33 months or at any time thereafter). We chose age 3 years as a meaningful time point for the acquisition of pets because we wanted to isolate potential reverse-causality in associations of pet ownership with asthma and atopy, specifically, discontinuation of ownership due to the emergence of asthma or atopy during infancy or childhood. We also defined a binary exposure of "ever" or "never" having owned any pet and specific pet types.

Potential confounders

Family adversity and three factors previously reported to be associated with wheezing phenotypes in ALSPAC (sex of child, maternal history of asthma or allergy, and maternal smoking during pregnancy) [19] were investigated as potential confounders of the association between exposures and outcomes. Maternal history of asthma or allergy was a binary variable derived from responses to an antenatal (18 – 20 weeks gestation) questionnaire in which the mother was asked: a) "Have you ever had any of the following problems" with responses for "Asthma" of "Yes had it recently" or "Yes in past, not now" coded as '1'; and b) "Would you say that you were allergic to anything?", with affirmative responses to any of "cat", "pollen", "dust", "insect stings or bites", or "something else" coded as '1'. Maternal smoking during pregnancy was a binary variable derived from responses to questions put to the mother in an antenatal and a postnatal questionnaire, asking whether the mother had smoked in the first 3 months of the pregnancy, at the mid-point (18 – 20 weeks), or in the last 2 months of the pregnancy. In the ALSPAC dataset, maternal smoking during pregnancy is strongly correlated with subsequent maternal and household smoking behaviours (approximately 75% of children exposed to tobacco smoke *in utero* are also exposed to household tobacco smoke at age 7 years).

Family Adversity Index—The standard ALSPAC family adversity index (FAI) is derived from responses to questions asked during pregnancy about the following 10 factors, comprising 18 items in total: 1) age of mother at first pregnancy; 2) housing, comprising a) adequacy, b) basic amenities, c) defects, damp, infestation; 3) mother's and father's low educational attainment; 4) financial difficulties; 5) relationship with partner, comprising a) status, b) lack of affection, c) cruelty, d) lack of support; 6) family, comprising a) size, b) child in care, not with natural mother, on at-risk register; 7) social network, comprising a) lack of emotional support, b) lack of practical support; 8) substance abuse; 9) crime, comprising a) being in trouble with the police and b) convictions; and 10) psychopathology of the mother (anxiety, depression or suicide attempts). Each of the 18 items is assigned a value of 1 if an adversity is present and 0 if it is not present hence, the FAI has a theoretical range of 0 to 18. FAI scores are calculated where more than half of the items are valid, and non-adversity is assumed for any missing data hence, FAI scores are conservative.

Statistical methods

Associations of pet ownership with asthma and atopy at age 7 years were investigated using logistic regression models adjusted for sex of child, maternal history of asthma or allergy, maternal smoking during pregnancy, and family adversity index. All analyses were based on subsets of children for whom complete outcome data, pet ownership data at all time points, and data for all confounders were available. We compared the results of complete-data analyses with results obtained using the maximum amount of available data (if this yielded additional observations) to determine possible influences of missing data. We used interaction terms (with $P \approx 0.1$ as a threshold for suspicion) to investigate whether any effects of pet ownership (using the binary ever/never owned exposure variable) were modified by sex of child, maternal history of asthma or allergy, maternal smoking during pregnancy, and family adversity index. Associations of pet ownership with atopic and non-atopic asthma *versus* no asthma were compared using multinomial logistic regression models adjusted for sex of child, maternal history of asthma or allergy, maternal smoking during pregnancy, and family adversity index. We investigated whether any effects of pet ownership on asthma and atopy were best described by an accumulation of exposure or by exposure occurring before or after age 3 years by comparing regression models following the method described by Mishra *et al* [20]. All analyses were performed using Stata version 12 (StataCorp, College Station, TX, USA).

Results

Of 13,978 children in ALSPAC, 8,190 (58.6%) had data on current asthma at age 7 years, 6,524 (46.7%) had skin prick test (SPT) data at age 7 years, and 6,700 children (47.9%) had pet ownership data up to age 7 years. 3,768 children (27.0%) had complete data on asthma, atopy, pet ownership, and confounders (maternal history of allergy/asthma, maternal smoking during pregnancy and family adversity index). Of these, 3,739 had data on ever having had asthma (doctor-diagnosed) and 3,749 on asthma medication use in the previous 12 months. Our analysis of bronchial response to methacholine was based on 2,822 children (20.2%). Children with complete data were similar to children with missing data, except children with complete data had mothers who were less likely to have smoked during pregnancy and lived in households with lower levels of adversity and less pet ownership (Table 1).

Of potential confounders, maternal smoking during pregnancy and family adversity were most strongly associated with pet ownership (Table S1). Asthma was more common in boys, among children of mothers who had a history of asthma or allergy or who smoked during pregnancy, and in households with a family adversity index above the median. Cat ownership was less common among mothers who reported allergy to cats, pollen, and dust (Table S2). Dog ownership was less common among mothers who reported allergy to cats and pollen, but was more common among mothers who reported a history of asthma. Rabbit and bird, but not rodent, ownership was less common among mothers who reported pollen allergy.

Pet ownership and asthma

Ownership of any pet before and after age 3 years ('continuous' ownership) was associated with 28% lower odds of asthma (OR=0.72; 95% CI 0.55–0.95) compared with never having owned a pet (Table 2, Table S3). This association was driven by a strong inverse association (OR=0.48; 95% CI 0.34–0.68) with atopic asthma, a pattern which was also evident for ownership of any pet at age 3 years or later but not beforehand. Compared with never having owned a pet, continuous cat and dog ownership was associated with 32% (OR=0.68; 95% CI 0.49–0.95) and 50% (OR=0.50; 95% CI 0.32–0.78) lower odds of atopic asthma, respectively. Ownership of rabbits and birds also appeared to have a protective effect against atopic asthma, but no association was evident for ownership of rodents. The effects on atopic asthma of ownership at any time *versus* non-ownership were: for any pet type, OR=0.52 (95% CI 0.38–0.72); for cats, OR=0.69 (95% CI 0.52–0.92); for dogs, OR=0.65 (95% CI 0.47–0.91); for rabbits, OR=0.72 (95% CI 0.52–1.01); for rodents, OR=1.01 (95% CI 0.76–1.35); and for birds, OR=0.49 (95% CI 0.29–0.85).

Pet ownership tended to be associated with higher odds of non-atopic asthma, an association that was most evident for continuous (before and after age 3 years) ownership of rabbits (OR=1.61; 95% CI 1.04–2.51) and rodents (OR=1.86; 95% CI 1.15–3.01) but which was of equal strength and magnitude for later (age 3 years or thereafter) dog ownership (OR=1.72; 95% CI 1.07–2.77). The odds ratios for continuous ownership of cats, dogs and birds were consistent with an increased risk of non-atopic asthma. The effects on non-atopic asthma of ownership at any time *versus* non-ownership were: for any pet type, OR=1.16 (95% CI 0.75–1.80); for cats, OR=1.19 (95% CI 0.89–1.59); for dogs, OR=1.24 (95% CI 0.91–1.68); for rabbits, OR=1.27 (95% CI 0.93–1.73); for rodents, OR=1.36 (95% CI 1.02–1.83); and for birds, OR=1.21 (95% CI 0.81–1.81).

Differential effects of pet ownership on atopic *versus* non-atopic asthma were apparent for all pet types. Multinomial logistic regression provided strong evidence of heterogeneity of odds ratios for atopic (OR<1) *versus* non-atopic (OR>1) asthma for continuous ownership of any pet type (P=0.001) and for continuous ownership of cats (P=0.004), dogs (P=0.002), rabbits (P=0.01), and birds (P=0.03) but less so for continuous ownership of rodents (P=0.10). Estimates for the associations of pet ownership with asthma were minimally attenuated by adjustment for child's sex, maternal history of asthma or atopy, maternal smoking during pregnancy, family adversity or ownership of other pet types. Associations of pet ownership with asthma as indicated by use of asthma medications in the previous 12 months were very similar to those estimated for parental report of episodes of asthma (data not shown). There were no interactions of pet ownership (any or specific pet types) with sex of child, maternal history of asthma or allergy, maternal smoking during pregnancy, or family adversity index in relation to any of the asthma outcomes. Pet ownership was not associated with bronchial response to methacholine challenge among all children (Table S4) or among atopic and non-atopic children when analysed as separate groups, or when we excluded children who were reported to have used medication during the 12-month period which defined 'current' asthma, or when we excluded children who reported use of asthma medication at the time of their clinic attendance (data not shown).

Pet ownership and atopy

Continuous pet ownership, particularly of cats and dogs, was consistently associated with lower odds of specific types of atopy and of atopy overall, compared with non-ownership (Table 3, Table S5). Continuous ownership of any pet was associated with 43% lower odds of atopy (OR=0.57; 95% CI 0.46–0.70), compared with non-ownership. Although an inverse association tended to be less evident for ownership before but not after, or after but not before, age 3 years, the majority of the point estimates for these patterns of ownership were <1.

The protective effects against any atopy of ownership at any time *versus* non-ownership were: for any pet type, OR=0.62 (95% CI 0.50–0.76); for cats, OR=0.71 (95% CI 0.60–0.84); for dogs, OR=0.65 (95% CI 0.54–0.79); for rabbits, OR=0.75 (95% CI 0.63–0.91); for rodents, OR=0.86 (95% CI 0.73–1.02); and for birds, OR=0.67 (95% CI 0.51–0.87). As with the asthma outcomes, there was little or no attenuation of effect estimates after adjustment for child's sex, maternal history of asthma or atopy, maternal smoking during pregnancy, family adversity or ownership of other pet types, and no interactions of pet ownership with child's sex, maternal history of asthma or atopy, maternal smoking during pregnancy, or family adversity.

Cat ownership (at any time *versus* non-ownership) was inversely associated with sensitization to cat allergen (OR=0.76 (95% CI 0.60, 0.96), N=5,146). Rabbit and dog ownership were not associated with rabbit allergen SPT positivity (OR=1.22 (95% CI 0.57–2.61), N=1,761) or dog allergen SPT positivity (OR=1.10 (95% CI 0.69, 1.76), N=1,859), respectively. Rodent ownership was strongly positively associated with sensitization to rodent (mouse, hamster or guinea pig) allergen (OR=2.88 (95% CI 1.34, 6.18), N=1,764).

Critical periods

We compared the log likelihoods of 3 separate models containing terms only for i) early exposure (pregnancy to age 2), ii) later exposure (age 3 onwards), and iii) cumulative exposure (total number of time points at which exposure occurred) with the log likelihood of a 'saturated' model containing all of these terms plus an interaction term for early $\times$ late exposure. Inspection of P-values derived from these statistical tests (Table 4, Table S6) did not indicate any critical period effects other than later exposure (from age 3 onwards) driving the association of any pet ownership with atopic asthma and of dog ownership with non-atopic asthma and atopy. Also, early exposure (pregnancy to age 3) appeared to drive the association of bird ownership with atopic asthma and atopy. The effect of any pet ownership on atopy appeared to be a cumulative effect, as did the effect of rodent ownership on non-atopic asthma.

Discussion

Pet ownership during childhood in this birth cohort was consistently associated with a reduced overall risk of aeroallergen sensitization and atopic asthma, but tended to be associated (particularly for rabbits and rodents) with an increased risk of non-atopic asthma at age 7 years. This pattern was evident for all pet types, although for rodents the increased

risk of non-atopic asthma was not offset by a reduced risk of atopic asthma. Rodent ownership showed a strong positive association with sensitization to rodent allergens, whereas cat ownership was inversely associated with sensitization to cat allergen, and rabbit and dog ownership were not associated with their respective allergens. There was no convincing evidence of critical period effects, although the inverse associations of exposure to any pet type with atopic asthma and atopy appeared to be later-childhood (after age 3 years) and cumulative effects, respectively. We found no associations of pet ownership with bronchial response to methacholine challenge at age 8 years.

Strengths and limitations

ALSPAC is a well-characterized birth cohort which has provided data for several studies into *in utero* and childhood factors in relation to childhood asthma, wheezing and atopy [19, 21-25]. A key strength of our study was the availability of exposure measures derived from identical questionnaire items for specific pet types at multiple time points, from pregnancy through to age 7 years, plus data for potential confounders. We also had two outcome measures for asthma (current and doctor-diagnosed) and clinic-derived data on atopy and bronchial response to methacholine.

The main limitations of our study, as with any birth cohort, relate to losses to follow-up. Our analysis was based on less than one-third of the original cohort. In particular, the effect of higher rates of attrition among children from less affluent families [15]. Given that these children were more likely to be exposed to household pets and have asthma, we would tend to under-estimate associations between pet ownership and asthma. We found that crude associations of pet ownership with asthma and atopy were not much changed when adjusted for family adversity or potential confounding factors such as smoking during pregnancy, and the results of complete-data analyses were similar to results obtained using the maximum amount of available data. This suggests that our results would not be substantially biased by higher losses to follow-up in the lower social strata. We defined atopic asthma as a combination of current asthma (in the 12 months prior to '91 months' questionnaire) and SPT positivity at a 'Focus@7' clinic, with a median interval of only 2 months between the questionnaire and the clinic. However, we are relying on maternal report of child's asthma, which has some potential [unquantified in this dataset] for misclassification, as does the mother's report of her own history of asthma and allergy [26, 27]. Ever-diagnosed asthma may also be susceptible to misclassification bias if transient wheezing caused by exposure to pets was misdiagnosed as asthma [28].

We found that the inclusion of potential confounders made little or no difference to our point estimates, but our results may be confounded by variables such as number of siblings, sibling history of asthma and allergy, time spent outdoors, physical activity, etc, which we did not include. We verified that estimates adjusted for maternal history of asthma and allergy as a composite variable were similar to estimates adjusted for maternal asthma and specific allergies as separate variables. We also verified that paternal history of asthma and allergy did not confound or modify any of the associations, although inclusion of this co-variable reduced the size of the dataset by approximately 800 observations. ALSPAC is a predominantly urban cohort and, although a small number of partners were engaged in farm

work, this would not necessarily mean that the family lived on a farm. Hence, we did not include this in our analysis. Neither did we have data which could have been used to adjust for exposure to particularly high levels of urban air pollution.

The inclusion of atopics in our reference (non-asthmatic) group (rather than excluding atopics or stratifying our analysis by presence/absence of atopy) [29] was a valid approach, given our research questions, namely: “What are the overall associations between pet ownership and a) all asthma; b) atopic asthma; and c) non-atopic asthma?”. Also, given i) the association between pets and atopy, ii) the possibility of unmeasured confounders associated with asthma and allergy (but not with pet ownership), and iii) a probable link between allergy and asthma, then conditioning on atopic status would induce a spurious association between pet ownership and asthma [30].

Our dataset did not include factors which might alter some of our observed associations, in particular whether pets were kept indoors or outdoors, type of dog owned (e.g. moulting *versus* non-moulting), and the frequency and type of contact between children and pets. In the present analysis, we did not investigate dose-response effects in terms of the number and variety of pets owned. There were also gaps in our recording of pet ownership, from mid-gestation to 8 months, >8 months to 2 yrs, and 21 to 33 months of age.

The null finding for bronchial response to methacholine challenge may be attributable to the sample size in our analysis and/or to it being both a measure of atopic asthma and non-atopic asthma (hence, the inverse and positive associations of pet ownership with the outcome cancel each other out, as we observed for ‘all asthma’) or to it being an insensitive measure of asthma in this cohort [31]. Analysis of this outcome excluding children who had used asthma medication during the 12-month period which defined ‘current’ asthma (who, if still using medication to control their asthma might be expected not to respond to methacholine challenge) or who reported having used an inhaler at the time of the challenge, also failed to demonstrate any associations.

Our findings in the context of other studies

Pet ownership during pregnancy and childhood in this birth cohort was associated with a reduced risk of sensitization to three common allergens and with an increased risk of non-atopic asthma at age 7 years. The first of these findings reinforces the results of a recent meta-analysis of data from ten European birth cohorts, which showed that exposure to cats, dogs and rodents in childhood protected against sensitization to aeroallergens [12]. Meta-analysis of data from the same cohorts did not indicate evidence of associations of pet ownership with atopic or with non-atopic asthma, although the pooled estimates for associations of dog, rodent and bird ownership with non-atopic asthma were positive, and results from the two cohorts with data on concurrent cat and dog ownership indicated almost 4-fold higher odds of non-atopic asthma compared with no pet ownership. These discrepancies with our findings could be a consequence of the meta-analysis being restricted to exposure to pets during the first two years of the child's life, and to analysing exclusive ownership of each pet type.

Our investigation of critical periods suggested cumulative effects of pet ownership on atopy, and a later effect of dog ownership on non-atopic asthma, although it should be noted that some of the underlying frequencies are quite small. In relation to a cumulative effect against atopy, studies have indicated that there might be an 'optimal' level of exposure to cat allergen which induces the lowest risk of sensitization (or the highest level of tolerance) [32]. Indeed, we found inverse associations of cat ownership with sensitization to cat allergen. This 'cat paradox' [33] is related to the observation that children are exposed to cat allergen in public places and in homes without cats [34].

Implications for clinical practice and future research

The consistency of our findings across different pet types suggests a common underlying mechanism (or mechanisms) for non-specific desensitization to aeroallergens and causation or exacerbation of non-atopic asthma. Whether apparent differences in effects, such as the stronger positive associations of rabbit and rodent ownership with non-atopic asthma, are real differences which reflect between-pet variation in allergens, danders, endotoxins and other immunological agents [35-38] or variation in pet keeping and handling practices is a question for future research. That the 'cat paradox' might not be applicable to all pet types is strongly indicated by the positive association of rodent ownership with sensitization to rodent allergens and the absence of associations of dog and rabbit ownership with their respective allergens, in stark contrast with the inverse association of cat ownership with sensitization to cat allergens.

Deciding whether a potentiating effect of pet ownership on the development of non-atopic asthma outweighs a protective effect against atopies and atopic asthma requires the consideration of other factors. These opposing effects were not modified by maternal history of asthma and allergy but, in the presence of factors known to pre-dispose a child to non-atopic asthma, avoidance of pet ownership might be a sensible precaution. This is particularly so for rodents, for which the positive associations with non-atopic asthma was not offset by an inverse association with atopic asthma. Unfortunately, some of the factors associated jointly with pet ownership and with childhood asthma, for example, maternal smoking and family adversity, suggest that parents of children at highest risk of non-atopic asthma might not be receptive to public health advice regarding pet ownership. The potential physical and psychological benefits of pet ownership must also be taken into account [39]. Future research is needed to explore whether the effects of pet ownership are modified by genetic variants which pre-dispose children to asthma or atopy [4, 40].

Conclusion

Cumulative family ownership of domestic pets during early life, including the pre-natal period, was associated with lower odds of aeroallergen sensitization and atopic asthma by mid-childhood compared with no pet ownership, confirming findings from previous studies. Pet ownership, particularly of rabbits and rodents, was associated with higher odds of non-atopic asthma in this population, but whether this reflects a causal effect or trigger mechanism remains unclear.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1
Characteristics of children in our analysis compared with children who had missing data on asthma, atopy, and pet ownership

	Children with complete data (n=3,768 unless otherwise shown), frequency (%) or mean (SD)	Children with missing data (n=10,210 unless otherwise shown), frequency (%) or mean (SD)	P-value *
Sex (male)	1,891 (50.2%)	5,329 (52.2%)	0.04
Exact age at time of '91-month' follow-up questionnaire (months)	91.7 (1.4), n=3,738 median 91 (range 91 – 108)	92.1 (1.9), n=4,424 median 91 (range 90 – 111)	<0.001
Exact age at time of 'Focus @ 8' follow-up clinic (months)	102.9 (2.51), n=3,433 median 102 (range 94 – 123)	104.1 (4.0), n=3,737 median 103 (range 89 – 126)	<0.001
Maternal history of asthma or allergy (yes)	1,811 (48.1%)	3,243/7,175 (45.2%)	0.004
Maternal smoking during pregnancy (yes)	637 (16.9%)	2,214/7,291 (30.4%)	<0.001
Family adversity index (range 0 – 10)	0.90 (1.27)	1.37 (1.62), n=6,368	<0.001
Current asthma (past 12 months)	415 (11.0%)	536/4,422 (12.1%)	0.13
Atopy (any skin prick test positivity)	774 (20.5%)	575/2,756 (20.9%)	0.73
Ever had asthma (doctor-diagnosed)	714/3,739 (19.1%)	946/4,392 (21.5%)	0.007
Any pet owned/acquired **			
Never	582 (15.5%)	425/5,499 (7.7%)	<0.001
Age 3 years or later, not before	738 (19.6%)	789/5,499 (14.4%)	
Before and after age 3 years	2,307 (61.2%)	4,120/5,499 (74.9%)	
Before but not after 3 years	141 (3.7%)	165/5,499 (3.0%)	

* Chi-squared test for proportions, Student's *t* test for means

** "Age 3 years or later, not before" = owned at or after age 33 months but not at any time before; "Before and after age 3 years" = owned at any time before age 33 months and at any time thereafter; "Before but not after 3 years" = owned at any time before, but not owned at or at any time after, age 33 months

Table 2
Associations of pet ownership with asthma at age 7 years

	Asthma (in past 12 months) n=3,768 of whom 415 asthmatic	Atopic asthma (SPT positive) n=3,572 of whom 219 asthmatic	Non-atopic asthma (SPT negative) n=3,549 of whom 196 asthmatic	Doctor has ever diagnosed asthma n=3,739 of whom 714 asthmatic
Any pet owned/acquired*				
Never	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Age 3 years or later, not before	0.67 (0.47, 0.94)	0.55 (0.36, 0.84)	0.93 (0.54, 1.60)	0.85 (0.64, 1.13)
Before and after age 3 years	0.72 (0.55, 0.95)	0.48 (0.34, 0.68)	1.25 (0.81, 1.95)	0.94 (0.74, 1.18)
Before but not after 3 years	1.07 (0.63, 1.81)	1.12 (0.61, 2.07)	0.95 (0.38, 2.38)	1.54 (1.00, 2.36)
Cat owned/acquired*				
Never	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Age 3 years or later, not before	0.83 (0.55, 1.25)	0.55 (0.29, 1.03)	1.21 (0.72, 2.04)	0.98 (0.72, 1.34)
Before and after age 3 years	0.94 (0.75, 1.19)	0.68 (0.49, 0.95)	1.31 (0.96, 1.80)	0.97 (0.81, 1.17)
Before but not after 3 years	0.75 (0.45, 1.24)	0.94 (0.52, 1.70)	0.49 (0.20, 1.22)	1.07 (0.74, 1.53)
Dog owned/acquired*				
Never	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Age 3 years or later, not before	1.18 (0.81, 1.73)	0.78 (0.43, 1.39)	1.72 (1.07, 2.77)	1.33 (0.98, 1.80)
Before and after age 3 years	0.81 (0.61, 1.08)	0.50 (0.32, 0.78)	1.22 (0.85, 1.75)	1.04 (0.84, 1.30)
Before but not after 3 years	0.87 (0.53, 1.43)	1.07 (0.59, 1.95)	0.64 (0.28, 1.48)	1.47 (1.03, 2.09)
Rabbit owned/acquired*				
Never	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Age 3 years or later, not before	0.86 (0.63, 1.17)	0.74 (0.48, 1.13)	1.02 (0.67, 1.57)	1.08 (0.85, 1.36)
Before and after age 3 years	1.08 (0.76, 1.54)	0.68 (0.39, 1.19)	1.61 (1.04, 2.51)	1.26 (0.96, 1.67)
Before but not after 3 years	1.05 (0.64, 1.72)	0.77 (0.37, 1.60)	1.39 (0.73, 2.64)	1.12 (0.75, 1.67)
Rodent owned/acquired*				
Never	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Age 3 years or later, not before	1.08 (0.85, 1.37)	0.98 (0.71, 1.36)	1.21 (0.87, 1.69)	1.20 (1.00, 1.45)
Before and after age 3 years	1.40 (0.96, 2.04)	1.04 (0.60, 1.80)	1.86 (1.15, 3.01)	1.62 (1.20, 2.18)
Before but not after 3 years	1.41 (0.78, 2.53)	1.29 (0.58, 2.86)	1.58 (0.71, 3.52)	1.58 (0.98, 2.54)
Bird owned/acquired*				
Never	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Age 3 years or later, not before	0.93 (0.56, 1.54)	0.76 (0.37, 1.58)	1.13 (0.58, 2.19)	0.98 (0.66, 1.45)
Before and after age 3 years	0.92 (0.55, 1.52)	0.48 (0.19, 1.18)	1.45 (0.80, 2.62)	0.92 (0.61, 1.38)
Before but not after 3 years	0.58 (0.30, 1.11)	0.21 (0.05, 0.88)	1.01 (0.49, 2.12)	0.86 (0.55, 1.35)

* "Age 3 years or later, not before" = owned at or after age 33 months but not at any time before; "Before and after age 3 years" = owned at any time before age 33 months and at any time thereafter; "Before but not after 3 years" = owned at any time before, but not owned at or at any time after, age 33 months; odds ratios adjusted for sex of child, maternal history of asthma or allergy, maternal smoking during pregnancy, and family adversity index

Table 3
Associations of pet ownership with atopy as indicated by skin prick test (SPT) positivity

	Grass SPT-positive n=3,768 of whom 450 (11.9%) atopic	House dust mite SPT- positive n=3,768 of whom 462 (12.3%) atopic	Cat SPT-positive n=3,768 of whom 264 (7.0%) atopic	Any atopy (grass, house dust mite or cat SPT positive) n=3,768 of whom 774 (20.5%) atopic
Any pet owned/acquired*				
Never	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Age 3 years or later, not before	0.70 (0.52, 0.95)	0.79 (0.58, 1.07)	0.57 (0.38, 0.84)	0.72 (0.55, 0.92)
Before and after age 3 years	0.52 (0.40, 0.67)	0.57 (0.44, 0.73)	0.51 (0.37, 0.69)	0.57 (0.46, 0.70)
Before but not after 3 years	0.79 (0.47, 1.33)	1.03 (0.63, 1.68)	0.68 (0.35, 1.33)	0.94 (0.62, 1.44)
Cat owned/acquired*				
Never	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Age 3 years or later, not before	0.55 (0.35, 0.86)	0.50 (0.31, 0.79)	0.46 (0.25, 0.86)	0.52 (0.36, 0.75)
Before and after age 3 years	0.72 (0.57, 0.90)	0.71 (0.56, 0.89)	0.70 (0.52, 0.95)	0.73 (0.61, 0.88)
Before but not after 3 years	0.86 (0.55, 1.35)	0.99 (0.65, 1.52)	1.01 (0.59, 1.73)	0.89 (0.62, 1.28)
Dog owned/acquired*				
Never	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Age 3 years or later, not before	0.75 (0.49, 1.13)	0.69 (0.44, 1.06)	0.57 (0.31, 1.03)	0.59 (0.41, 0.84)
Before and after age 3 years	0.45 (0.33, 0.63)	0.71 (0.54, 0.94)	0.55 (0.37, 0.81)	0.60 (0.48, 0.76)
Before but not after 3 years	0.76 (0.46, 1.24)	1.35 (0.89, 2.03)	1.16 (0.68, 1.99)	0.98 (0.68, 1.42)
Rabbit owned/acquired*				
Never	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Age 3 years or later, not before	0.77 (0.57, 1.05)	0.87 (0.65, 1.17)	0.72 (0.49, 1.08)	0.80 (0.63, 1.02)
Before and after age 3 years	0.86 (0.59, 1.23)	0.67 (0.45, 0.99)	0.50 (0.28, 0.88)	0.68 (0.50, 0.93)
Before but not after 3 years	0.82 (0.49, 1.37)	0.62 (0.35, 1.09)	1.08 (0.60, 1.94)	0.74 (0.49, 1.13)
Rodent owned/acquired				
Never	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Age 3 years or later, not before	0.99 (0.79, 1.25)	0.83 (0.65, 1.05)	1.02 (0.76, 1.37)	0.85 (0.70, 1.03)
Before and after age 3 years	0.78 (0.50, 1.20)	0.82 (0.54, 1.24)	0.81 (0.47, 1.40)	0.79 (0.57, 1.11)
Before but not after 3 years	1.12 (0.60, 2.09)	1.22 (0.68, 2.20)	1.06 (0.48, 2.33)	1.24 (0.76, 2.02)
Bird owned/acquired*				
Never	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Age 3 years or later, not before	0.72 (0.42, 1.21)	1.00 (0.63, 1.59)	0.90 (0.48, 1.69)	0.87 (0.59, 1.29)
Before and after age 3 years	0.55 (0.30, 1.00)	0.48 (0.26, 0.89)	0.47 (0.21, 1.08)	0.56 (0.35, 0.88)
Before but not after 3 years	0.59 (0.31, 1.10)	0.35 (0.16, 0.75)	0.47 (0.19, 1.16)	0.56 (0.34, 0.92)

* "Age 3 years or later, not before" = owned at or after age 33 months but not at any time before; "Before and after age 3 years" = owned at any time before age 33 months and at any time thereafter; "Before but not after 3 years" = owned at any time before, but not owned at or at any time after, age 33 months; odds ratios adjusted for sex of child, maternal history of asthma or allergy, maternal smoking during pregnancy, and family adversity index

Table 4
P-values from likelihood ratio tests comparing models for no effect, early effect, late effect, and cumulative effect of exposure to household pets on asthma and atopy*

	Effect	Asthma	Atopic asthma	Non-atopic asthma	Atopy	Bronchial response to methacholine
Any pet	None	0.070	0.000	0.507	0.000	0.177
	Early	0.046	0.001	0.841	0.001	0.375
	Late	0.891	0.458	0.463	0.026	0.113
	Cumulative	0.144	0.082	0.940	0.358	0.211
Cat	None	0.432	0.036	0.028	0.000	0.353
	Early	0.575	0.068	0.018	0.000	0.900
	Late	0.294	0.451	0.078	0.036	0.744
	Cumulative	0.312	0.316	0.021	0.005	0.801
Dog	None	0.459	0.022	0.138	0.000	0.908
	Early	0.841	0.175	0.074	0.000	0.807
	Late	0.372	0.675	0.426	0.231	0.826
	Cumulative	0.628	0.673	0.119	0.086	0.804
Rabbit	None	0.759	0.325	0.293	0.044	0.360
	Early	0.678	0.406	0.968	0.321	0.377
	Late	0.654	0.715	0.314	0.438	0.246
	Cumulative	0.638	0.437	0.826	0.568	0.270
Rodent	None	0.053	0.531	0.040	0.246	0.298
	Early	0.120	0.397	0.209	0.155	0.621
	Late	0.043	0.369	0.080	0.827	0.181
	Cumulative	0.488	0.478	0.910	0.394	0.314
Bird	None	0.432	0.026	0.736	0.013	0.605
	Early	0.575	0.646	0.739	0.905	0.487
	Late	0.294	0.036	0.835	0.041	0.876
	Cumulative	0.312	0.126	0.981	0.247	0.763

* Early effect = "exposure to pet at any time up to and including age 2 years"; Late effect = "exposure to pet at any time from age 3 years onwards"; Cumulative = "total number of time points (pregnancy, 8, 21, 33, 47, and 85 months) at which child was exposed to pet (range 0 – 6)". P-values indicate whether any of the four models provide a fit as good as that for the saturated model. Small model P values provide evidence that the modelled effect alone does not sufficiently account for the overall association. Bronchial response to methacholine challenge is based on 3rd compared with 1st tertile.