University of Cincinnati

Date: 1/15/2014

I, Gang Cheng, hereby submit this original work as part of the requirements for the degree of Master of Science in Clinical and Translational Research.

It is entitled:
Duration of Year One Daycare Attendance Predicts Asthma at Age Seven: The Cincinnati Childhood Allergy and Air Pollution Study (CCAAPS)

Student’s name: Gang Cheng

This work and its defense approved by:

Committee chair: Erin Nicole Haynes, Ph.D.
Committee member: David Bernstein, M.D.
Committee member: Linda Levin, Ph.D.
Duration of year one daycare attendance predicts asthma at age seven: The Cincinnati Childhood Allergy and Air Pollution Study (CCAAPS)

A thesis submitted to the
Graduate School
of the University of Cincinnati
in partial fulfillment of the
requirements for the degree of
Master of Science
in Clinical & Translational Research
In the Department of Environmental Health
Division of Epidemiology & Biostatistics
of the College of Medicine
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By

Gang Cheng
Ph.D., Dokkyo University School of Medicine, April 2002
M.D., Harbin Medical University, July 1995

Committee Chair: Erin Haynes, Ph.D.
Abstract

Background: Studies vary in the reported effects impact of daycare attendance on childhood asthma. The objective is to evaluate the independent and combined effects of daycare attendance and respiratory infections on the development of asthma at age 7 in a high-risk birth cohort (The Cincinnati Childhood Allergy and Air Pollution Study).

Method: At age 7 years, 589 children had complete data out of 762 enrolled at birth. Daycare hours and the number of respiratory infections were reported in follow-up questionnaires through age four. Asthma was diagnosed in 95 children (16%) at age 7, based on pre-defined symptoms criteria confirmed by either 12% reversibility in FEV1 after bronchodilator or a positive methacholine test (PC20≤4mg/ml). Logistic regression was used to investigate the relationships between asthma at age 7, cumulative hours of daycare attendance and reported respiratory infections at ages 1 to 4.

Results: In the univariate analyses, daycare attendance at 12 months was associated with an increased risk of asthma (Odds ratio[OR]=1.8, 95% Confidence Interval[CI]=1.1-3.0). Both upper and lower respiratory infections at 12 months also increased the likelihood of asthma (OR=2.4 [1.4-4.1]; OR=2.3 [1.5-3.7], respectively). After adjustment for potential confounders, higher cumulative hours of daycare attendance and the number of lower respiratory infections at 12 months were associated with asthma (OR=1.2 [1.1-1.5]; OR=1.4 [1.2-1.7], respectively). In contrast, attending daycare ≥ 37.5 hours per week on average was associated with a lower risk of asthma (OR=0.6 [0.4-0.9]).
Conclusion: Depending on duration of attendance, daycare during the first 12 months can either increase or reduce risk of asthma at age 7.
ACKNOWLEDGMENTS

I would like to express my special gratitude to my mentor Dr. David Bernstein, who encouraged and helped me throughout my years at University of Cincinnati. I am also very grateful to my committee members, Dr. Linda Levin and Dr. Erin Haynes. Without their enormous support and insightful comments, this thesis would not have been possible.

I also would like to warmly acknowledge T32 grant for its general financial support for my graduate research.

My thesis research also benefited greatly from discussions with other allergy fellows and faculty members at University of Cincinnati. It is a pleasure to express my appreciation to all those who have helped me. In addition, I would like to thank Ms. Aimee Nance and Mr. Greg Taulbee for their kind assistance. Finally, I am indebted to my family for everything they have done for me in the past several years. I greatly appreciate their endless love and support.
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INTRODUCTION

Asthma prevalence has increased in the United States during the last 20 years, and is the most common chronic disorder in children[1]. Numerous host and environmental factors have been suspected as playing causative roles[2]. Several hypotheses have been proposed to explain the increasing prevalence of allergic disorders and asthma during childhood[3]. The hygiene hypothesis, for example, proposes that a general decline in the frequency of early infections and reduced exposure to microbial products during infancy may alter the maturation of the immune system favoring Th2 biased allergic responses during infancy and childhood[4]. Altered exposures to environmental microbial flora (e.g., via alterations in the intestinal microbiome) unique to westernized lifestyles have been postulated to account for the increasing prevalence of asthma and other allergic diseases[5]. This theory is bolstered by epidemiological observations that the risk of asthma is reduced among children living with farm animals, thereby enhancing the opportunities for greater exposure to environmental sources of microbial contaminants in early childhood[6]. If this were true, children attending day care with ample opportunities for daily exposure to microbial contaminants from other children may be less likely to develop asthma and other allergic disorders including asthma. However, the results of cross sectional and longitudinal studies examining the effect of attendance at day care on the development of asthma are conflicting.

In some reports, day care attendance is inversely associated with asthma
It is known that children attending day care contract more respiratory tract infections than children living at home [13, 14]. In a birth cohort study of children born to atopic parents, Jackson et al. demonstrated that early rhinovirus infections are associated with a greater likelihood of asthma at age 6 [15]. Thus uncertainty persists as to whether or not early exposure to the daycare milieu during infancy and early childhood enhances or reduces the risk of asthma. To address these questions, we hypothesized that early exposure to daycare and occurrence of early respiratory infections were likely to independently increase the risk for later development of childhood asthma. Using longitudinal data from the Cincinnati Childhood Allergy and Air Pollution Study (CCAAPS) birth cohort, we investigated the association between duration and timing of daycare attendance, reported respiratory infections during the first four years of life, and the development of asthma objectively confirmed at age 7.

METHODS

The CCAAPS birth cohort study has been described in our previously published studies. Infants born in the Greater Cincinnati and Northern Kentucky area were identified from birth records and recruited between 2001 and 2003[16, 17]. The hypothesis of the CCAAPS study was that early life exposure to traffic pollutants increased risk for allergic sensitization and development of allergic rhinitis and asthma during childhood. Parents living either within 400 meters or greater than 1500 meters of a major road were invited to a screening visit at one
of clinical study sites. At that initial visit, parents received informed consent, were administered medical and environmental questionnaire, and received skin prick testing to a panel of 15 aeroallergens and two food allergens (egg white, milk). Infants were eligible for participation if one or both parents reported rhinitis, eczema, or asthma and exhibited a positive skin prick test (SPT) to at least 1 aeroallergen. The study protocol and informed consent statement were approved by the University of Cincinnati Institutional Review Board. Children enrolled in CCAAPS received annual evaluations at ages 1, 2, 3, 4 years, and follow up at 7 years.

**Clinical evaluation**

Upper or lower respiratory infections

Upper Respiratory Infection (URI) was defined as a positive parental response to the question "In the past 12 months, has your child had any of the following: ear infections, sinus infections and respiratory flu". Lower Respiratory Infection (LRI) was defined as a positive parental response to the question "In the past 12 months, has your child had any of the following: croup, pneumonia, bronchitis and viral infection"[18]. Both URI and LRI were captured by validated questionnaire items adapted from the validated International Study of Asthma and Allergies in Childhood questionnaire[19].

Asthma evaluation at age 7

Asthma symptoms were defined as at least one of the following: (1) a tight or clogged chest or throat in the past 12 months, (2) difficulty breathing or wheezing after exercise, (3) wheezing or whistling in the chest in the previous 12
months, or (4) a previous physician diagnosis of asthma. All children in the study underwent baseline spirometry performed by trained technicians using methods recommended by American Thoracic Society[20]. Those children underwent evaluation for reversibility in FEV₁ and methacholine testing (if reversibility was not demonstrated) with one of the following features: 1) there was a parental report of asthma symptoms in the previous 12 months, 2) predicted FEV₁ of less than 90%, 3) exhaled nitric oxide level of 20 ppb or greater. Airway reversibility was assessed 15 minutes after administration of 2.5 mg of nebulized levalbuterol.

Children with less than 12% increase in FEV₁ after administration of bronchodilator were tested for bronchial hyperresponsiveness by methacholine challenge testing (MCCT) at a follow-up clinic visit. A modified 4-dose ATS methacholine challenge protocol was used with sequential methacholine concentrations of 0.0625, 0.25, 1, and 4 mg/ml[21]. A positive MCCT result was defined as a 20% or greater decrease in FEV₁ after saline diluent challenge in response to 4 mg/mL or less of methacholine.

Children were defined as having asthma if the parent reported asthma symptoms (as previously defined) and the child demonstrated either significant airway reversibility (>12% increase in FEV₁) or a positive MCCT result.

**Environmental exposures**

**Indoor exposures**

Parents were administered a questionnaire gathering information on
parental and child health in the previous year and environmental exposures. Environmental tobacco smoke (ETS) was categorically defined as parental report of at least one current smoker residing in the household. House dust samples were collected from a 2 m² area of floor surface from the infant’s primary living area [22]. Endotoxin concentrations were determined by the limulus amebocyte lysate test (Associates of Cape Cod Inc, Falmouth, MA) in all house dust samples according to methods described by Milton and colleagues[23].

Daycare exposure

History of locations where the child spent 8 or more hours per week (e.g., home, day care, relative’s home) from birth through age 7 was collected. Information on hours/week that the children that attended a daycare was obtained at each clinical visit by asking parents “Please list the places where your baby spends his or her time. You should include all babysitters, daycare providers or relatives if your baby spends more than 8 hours per week at an address different from his/her home”. Thus, daycare was defined as a location outside the infant’s primary residence.

Outdoor exposure

Detail of elemental carbon attributable to traffic (ECAT) measurement and home dust mite sample collection has been described previously[24, 25]. Briefly, particulate matter less than 2.5 mm in diameter (PM2.5) was collected at ambient monitoring stations. Elemental carbon concentrations and absorption coefficients were determined[26]. Multivariable UNMIX and chemical mass balance models were then used to determine ECAT at monitoring stations[26]. A land-use
regression model was applied to estimate ECAT for locations where a child spent greater than 8 hours per week between ages 6 and 12 months. ECAT exposure was treated as a continuous variable.

**Statistical Analysis**

Univariate analyses were conducted to assess the association between asthma at age 7 and daycare attendance, URI, LRI and potential covariates at age 12 months included the following: sex; race (African American and non-African American ethnicity); education status (≤high school vs college); parental history of asthma; duration of breast feeding (<4 and ≥ 4 months); number of other children living in the home (<2 and ≥ 2 siblings); presence of 1 or more dogs in the home (yes/no); presence of 1 or more cats in the home (yes/no); ETS exposure (yes/no), ECAT exposure (≤75% and > 75%) with asthma at age 7. These predictor variables were analyzed as categorical variables and evaluated for association with asthma at age 7 by using the Pearson χ² test. We also analyzed the association between the total number of hours of daycare attendance and the total number of respiratory infections by using spearman’s correlation coefficient. Linear splines of daycare attendance were modeled on separate intervals to allow slopes to change, as determined by statistical and visual assessment. All potential covariates listed in Table 1 were included in an initial multivariate logistic regression model. Variables maintained in the final multiple regression model were chosen by backward stepwise regression, and removed if the P value was greater than 0.05. Odds ratio (OR) and 95% confidence interval (CI) were computed for the final model. Statistical analyses
were performed using SAS version 9.3 (SAS Institute, Inc., Cary, NC).

RESULTS

Demographics and exposure characters

A total of 762 children at age 12 months were enrolled in this cohort. Of these, 589 children completed both a medical examination and a questionnaire at the age of 7. Asthma was identified in 95 (16%) children according to the aforementioned asthma case definitions. Of these 589 children, 323 were male (55%) and 266 female (45%). Among the 589 subjects, 125 (21%) were African American, and 464 (79%) were non–African American.

Univariate analysis of year one predictors of asthma at age 7

Univariate analyses of independent variables are presented in Table 1. Children who started attending daycare before 12 months had a significant increased risk for asthma at age 7 compared with children who did not attend daycare. Infants experienced any upper or lower respiratory tract infections during the first year had a significantly greater likelihood of asthma. Race (African American), parental history of asthma (Yes) and lower level of education (i.e., high school graduate or less) was also significantly associated with asthma. Breast-feeding duration greater than 4 months was significantly associated with a reduced likelihood of asthma, suggesting a protective effect. Potential covariates that were not predictive of asthma in the univariate analyses included gender, the presence of siblings, cat or dog in the home, indoor exposure to environmental tobacco, high endotoxin level and high ECAT exposure.

Reported respiratory infections and asthma at age 7
Table 2 shows analyses evaluating respiratory infections at different ages and likelihood of asthma at age 7. In this study, the number of children who experienced a URI was 333 (60%) at 12 months, 288 (54%) at 24 months, 261 (50%) at 36 months and 216 (39%) 48 months. In the first two years of life, the frequency of children with any report of a URI was positively and significantly associated with asthma at age 7. The latter association was not significant after 24 months. The highest frequency of any reported LRI was in the first 12 months (34%) compared with 24, 36 and 48 months (22-24%). At age 12 and 36 month, LRI was significantly associated with asthma at age 7. No significant associations were detected between total daycare hours and number of respiratory infections at any age (data not shown).

**Daycare attendance**

The association between asthma and daycare attendance at different ages are presented in Table 3. Of the 589 children, daycare attendance was reported in 52 (9%) at 6 months, 102 (17%) subjects at 12 months, 128 (22%) subjects at 24 months, 143 (24%) at 36 months and 138(23%) at 48 months. Analysis of the ages of daycare attendance revealed that children entering daycare before 6 or 12 month had a significantly greater likelihood of developing asthma at the age of seven (OR [95% CI], 3.1[1.7-5.8], 1.8 [1.1-3.0]; respectively). Although, this trend continued with increasing age, there was no significant association between daycare attendance at 24, 36 and 48 months and asthma at age 7.

A linear spline model was used to visualize the relationship between...
daycare hours and asthma at age seven. Daycare hour attendance ranged from 192 hours to 2640 hours at age 12 months. As shown in Figure 1, during the first 12 months of life, total duration of daycare attendance increased the probability of asthma at age 7 if total cumulative daycare hours were below 1800 hours (Panel A). Interestingly, the likelihood of asthma decreased when daycare attendance exceeded 1800 total hours (Panel B). Of 102 children attending daycare, cumulative duration less than 1800 hours was found in 68 (67%) children. Based on this observation, two daycare continuous variables (i.e. <1800 and ≥ 1800 hours) were included in the final multivariate model.

**Multivariate model of predictors of asthma at age 7**

The final multivariate logistic regression analysis (Table 4) included the following predictor variables: parental asthma, lower maternal education, total number of LRI s at 12 months, and total number of daycare hours at 12 months. After adjusting for the aforementioned environmental exposures and host characteristics, significant predictors of asthma at age 7 years in the final model included parental asthma, low maternal education, number of lower respiratory infections and total hours of daycare attendance by age 12 months. Consistent with the spline curve, cumulative duration of daycare attendance of less than 1800 hours was associated with asthma at age 7 (OR, 1.2 [1.1-1.5], P<0.01), whereas daycare duration exceeding 1800 hours was associated with a reduced likelihood of asthma at age 7 (OR, 0.6[0.4-0.9], p<0.05). The number of LRI s (but not URIs) remained significantly associated with asthma in the multivariate model.

**DISCUSSION**
This study demonstrated significant associations between early daycare attendance during infancy and development of childhood asthma confirmed at age 7. Both age of daycare attendance and cumulative duration of daycare exposure were significant determinants of asthma risk at age 7. Interestingly, we found a bi-directional relationship between early daycare attendance during infancy and likelihood of asthma. In other words, daycare attendance during the first year was significantly associated with an increased likelihood of asthma at age 7 if cumulative day care attendance was less than 1800 hours reported in 67% of infants attending daycare and, conversely, duration of daycare attendance exceeding 1800 hours was associated with reduced risk of asthma. To our knowledge, this is the first study to show that daycare attendance can increase or decrease the likelihood of childhood asthma depending on the total duration of attendance during the first year of life.

Previous studies examining possible associations between daycare attendance and asthma are conflicting. There are four published cross-sectional studies that reporting that daycare attendance increase the risk of asthma at ages ranging from 6-14 years[11, 12, 14, 27]. Conversely, two population based birth cohort studies suggested that daycare attendance in the first year of life was associated with reduced likelihood of development of asthma at ages ranging from 5-11 years[7, 28]. Two other population based cohort studies showed no association between daycare attendance before 12 months and asthma at age 8 or 11 [29, 30]. It is noteworthy that another birth cohort study of children selected on the basis of parental atopy (comparable to this study) found that daycare
attendance in early life was associated with a decreased risk of asthma at the age 6 [31], but only among children without a maternal history of asthma. No association between daycare attendance and the development of asthma at age 6 was reported in another high-risk asthma cohort[32]. These aforementioned studies, however, are difficult to compare with our study because daycare attendance was not quantified and asthma outcomes were not objectively defined.

In this study, our asthma definition required objective confirmation with demonstration of ≥ 12% bronchodilator reversibility in FEV1 or a positive methacholine challenge test (PC20≤ 4 mg/ml) as defined by ATS guidelines[21] whereas the aforementioned studies defined asthma exclusively based on parental reporting. Moreover, we ascertained the duration of daycare attendance, which has not been performed in previous studies. Our finding of a relationship between cumulative duration of daycare attendance and development of asthma is novel. If confirmed, this finding could guide future recommendations to parents regarding the risks and/or benefits of daycare attendance in the first year of life.

The mechanisms to explain why duration of daycare attendance less than 1800 hours increased the risk for asthma and why daycare attendance greater than 1800 hours could reduce the likelihood of asthma are not clear. It is noteworthy that the association between daycare attendance and asthma persisted in the multivariate model along with other significant covariates including parental asthma, maternal education and LRI s. We found no associations between multiple siblings, pet ownership, endotoxin level at home
and the development of asthma at age 7. Thus, the exposure-dependent effect of
daycare attendance cannot otherwise be explained by other early environmental
exposures, which have been previously associated with decreased risk of
childhood asthma[7, 33, 34]. Lu et al reported that daycare attendance is
associated with increased incidence of gastrointestinal infections[35]. However,
in the largest birth cohort study to date investigating the gut microbiome during
infancy, Bisgaard et al found that reduced microbiota diversity was not
associated with asthma at age 6; the effect of daycare attendance was not
examined [36]. Therefore, future large prospective studies investigating the
impact of the daycare attendance on the gut and respiratory microbiome and
subsequent risk of childhood asthma are warranted.

Our results also indicated that the number of LRIs at 12 months were
positively associated with the development of asthma at age 7. This is in line with
several studies that reported lower respiratory infections increase the risk of
asthma at ages ranging from 6-10 years[30, 31, 37]. Although our study did not
collect airway specimens, we suspect that most episodes of LRIs during infancy
were likely associated with respiratory syncytial viral or rhinovirus [38]. Lower
respiratory infections caused by human rhinovirus during infancy have been
recognized to be a strong predictor of school-age asthma[32, 39].

Our findings in the multivariate model demonstrate strong and significant
relationships between childhood asthma, parental history of asthma, lower
maternal education and are similar to previous studies indicating that infants of
parents with asthma or lower education were more likely to develop asthma later in life[40, 41].

Several limitations of this study need to be considered in this study. First, the data regarding daycare attendance was obtained retrospectively, but at each annual clinical exam. Secondly, we assessed the presence of respiratory infections in early life based on parental reporting, which is subject to recall bias. In some cases this may have led to some misclassification, but this type of misclassification is most likely non-differential, which can make associations weaker but not change their direction[42]. Finally, the children enrolled in the CCAAPS cohort are high-risk children (i.e. born to at least one atopic parent), and these results may not be generalizable to children born to non-atopic parents.

In conclusion, our study is the first to report that both the timing and duration of daycare attendance in a high-risk cohort might influence the risk of asthma. Cumulative hours of daycare attendance in the first year of life less than 1800 hours was found to increase the risk of asthma in the majority of children. In contrast, cumulative hours of daycare attendance in the first year of life exceeding 1800 hours reduced the likelihood of asthma at age 7. Lower respiratory infections in the first year of life, parental history of asthma and lower maternal education were also identified as risk factors for the development of childhood asthma.


27. Salam MT, Li YF, Langholz B, Gilliland FD, Children's Health S, Early-life environmental risk factors for asthma: findings from the Children's Health Study. Environmental health perspectives 2004;112: 760-5.


36. Bisgaard H, Li N, Bonnellykke K, Chawes BL, Skov T, Paludan-Muller G, Stokholm J, Smith B, Krogfelt KA, Reduced diversity of the intestinal microbiota during infancy is associated with increased risk of allergic


Table 1. Asthma odds ratio and 95% confidence limits of primary independent variables at age 12 months and other covariates. Cell entries are number, % of column total.

<table>
<thead>
<tr>
<th>Primary Independent variables</th>
<th>Total N=589</th>
<th>Asthma at age 7</th>
<th>OR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=95</td>
<td>N=494</td>
<td></td>
</tr>
<tr>
<td>Daycare attendance (Yes)</td>
<td>102(17)</td>
<td>24(25)</td>
<td>78(16)</td>
</tr>
<tr>
<td>URI (Yes)</td>
<td>333(60)</td>
<td>66(76)</td>
<td>265(57)</td>
</tr>
<tr>
<td>LRI (Yes)</td>
<td>186(34)</td>
<td>45(51)</td>
<td>141(31)</td>
</tr>
</tbody>
</table>

Other covariates

<table>
<thead>
<tr>
<th></th>
<th>N=95</th>
<th>N=494</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>266(45)</td>
<td>37(39)</td>
<td>229(46)</td>
</tr>
<tr>
<td>Race (African American)</td>
<td>131(22)</td>
<td>35(37)</td>
<td>96(19)</td>
</tr>
<tr>
<td>Parental Asthma (Yes)</td>
<td>240(41)</td>
<td>54(57)</td>
<td>186(38)</td>
</tr>
<tr>
<td>Breastfeeding ≥ 4mos</td>
<td>312(53)</td>
<td>37(39)</td>
<td>275(56)</td>
</tr>
<tr>
<td>Mother Education ≤ High School</td>
<td>147(25)</td>
<td>41(43)</td>
<td>106(21)</td>
</tr>
<tr>
<td>At least one sibling</td>
<td>381(66)</td>
<td>57(61)</td>
<td>324(67)</td>
</tr>
<tr>
<td>Dog in home</td>
<td>208(35)</td>
<td>25(26)</td>
<td>183(37)</td>
</tr>
<tr>
<td>Cat in home</td>
<td>132(22)</td>
<td>14(15)</td>
<td>118(24)</td>
</tr>
<tr>
<td>ECAT&gt;75th %tile</td>
<td>166(28)</td>
<td>33(35)</td>
<td>133(27)</td>
</tr>
<tr>
<td>Endotoxin&gt;75th %tile</td>
<td>134(23)</td>
<td>26(27)</td>
<td>108(22)</td>
</tr>
<tr>
<td>ETS</td>
<td>112(21)</td>
<td>24(25)</td>
<td>88(18)</td>
</tr>
</tbody>
</table>
Table 2. Unadjusted OR and 95% CI measuring associations between asthma at age 7 and infections (Yes/No) for 589 subjects

**A. Upper Respiratory Infections (URI)**

<table>
<thead>
<tr>
<th>Age (Month)</th>
<th>URI (Yes) N(% of total)</th>
<th>Asthma Number of subjects (% URI)</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>333 (60%)</td>
<td>Yes 68 (76%) 265 (57%)</td>
<td>2.4 (1.4-4.1)</td>
</tr>
<tr>
<td>24</td>
<td>288 (54%)</td>
<td>Yes 56 (66%) 232 (50%)</td>
<td>1.8 (1.1-3.0)</td>
</tr>
<tr>
<td>36</td>
<td>261 (50%)</td>
<td>Yes 50 (59%) 211 (48%)</td>
<td>1.5 (0.9-2.5)</td>
</tr>
<tr>
<td>48</td>
<td>216 (39%)</td>
<td>Yes 37 (42%) 179 (38%)</td>
<td>1.2 (0.7-1.8)</td>
</tr>
</tbody>
</table>

**B. Lower Respiratory Infections (LRI)**

<table>
<thead>
<tr>
<th>Age (Month)</th>
<th>LRI (Yes) N(% of total)</th>
<th>Asthma Number of subjects (% LRI)</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>186 (34%)</td>
<td>Yes 45 (51%) 141 (31%)</td>
<td>2.3 (1.5-3.7)</td>
</tr>
<tr>
<td>24</td>
<td>120 (22%)</td>
<td>Yes 22 (26%) 98 (22%)</td>
<td>1.2 (0.7-2.1)</td>
</tr>
<tr>
<td>36</td>
<td>126 (24%)</td>
<td>Yes 33 (39%) 93 (21%)</td>
<td>2.4 (1.4-3.9)</td>
</tr>
<tr>
<td>48</td>
<td>126 (23%)</td>
<td>Yes 23 (26%) 103 (22%)</td>
<td>1.2 (0.7-2.1)</td>
</tr>
</tbody>
</table>
Table 3. Unadjusted OR and 95% CI measuring associations between asthma at age 7 and daycare attendance (Yes/No)

<table>
<thead>
<tr>
<th>Age (Month)</th>
<th>Daycare Attendance N (% of 589)</th>
<th>Asthma Number of subjects (% Daycare)</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Yes (N=95)</td>
<td>No (N=494)</td>
</tr>
<tr>
<td>6</td>
<td>52 (9%)</td>
<td>18 (19%)</td>
<td>34 (7%)</td>
</tr>
<tr>
<td>12</td>
<td>102 (17%)</td>
<td>24 (25%)</td>
<td>78 (16%)</td>
</tr>
<tr>
<td>24</td>
<td>128 (22%)</td>
<td>24 (25%)</td>
<td>104 (21%)</td>
</tr>
<tr>
<td>36</td>
<td>143 (24%)</td>
<td>27 (28%)</td>
<td>116 (23%)</td>
</tr>
<tr>
<td>48</td>
<td>138 (23%)</td>
<td>23 (24%)</td>
<td>115 (23%)</td>
</tr>
</tbody>
</table>
Table 4. Adjusted OR and 95% CI measuring the effects of daycare attendance and LRI, at 12 months on asthma at age 7

<table>
<thead>
<tr>
<th>Primary variables and covariates</th>
<th>OR [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parental Asthma (Yes)</td>
<td>2.0 (1.1-3.6)</td>
</tr>
<tr>
<td>Mother Education (≤ High School)</td>
<td>3.4 (2.1-6.0)</td>
</tr>
<tr>
<td>LRI (+1)</td>
<td>1.4 (1.2-1.8)</td>
</tr>
<tr>
<td>Daycare hours &lt;1800 hours (+100)</td>
<td>1.2 (1.1-1.5)</td>
</tr>
<tr>
<td>≥1800 hours (+100)</td>
<td>0.6 (0.4-0.9)</td>
</tr>
</tbody>
</table>

OR are expressed as a +1 unit increase in LRI, and +100 hours increase in daycare attendance.
Figure 1. Linear spline models on two interval daycare hours (<1800, ≥1800) of age 12 months and asthma prediction at age 7