

Letter to the Editor

Farm exposure in early childhood is associated with a lower risk of severe respiratory illnesses

To the Editor:

Environmental exposures in early life play a major role in allergic disease susceptibility. Notably, children raised on farms are at a lower risk for these diseases compared with children raised in either rural or urban nonfarm settings.¹ Exposure to farm-related microbes during early life may enhance mechanisms of immune tolerance.^{2,3} Early life immune development likely influences respiratory viral infection outcomes. Low interferon responses in cord blood cells are associated with greater severity of viral illnesses and increased risk of wheezing.^{4,5} These results suggest that by altering immune development in early life, farm exposures might reduce the risk of both allergic diseases and respiratory illnesses in childhood.

To test this hypothesis, we used a large epidemiologic study population in rural Wisconsin (the Marshfield Epidemiologic Study Area, or “MESA”).⁶ Within MESA, a cohort of children aged 5 to 17 years born onto dairy farms was compared with children who grew up in similar rural areas but lacked farm exposure. A random sample of 1000 out of 9510 children was selected for the survey on the basis of a weighted sampling strategy to overselect for probable farm residency and asthma (see this article’s Online Repository at www.jacionline.org). Completed surveys and detailed outcomes information were available for 268 children who lived on a farm from birth to 5 years and 247 children who never lived on a farm.

Early life exposures were determined by parental questionnaires. Clinical outcomes included asthma, eczema, hay fever, and respiratory illnesses (see [Table E1](http://www.jacionline.org) in this article’s Online Repository at www.jacionline.org), and were determined by parental questionnaire and extraction of data from electronic medical records.

We first calculated descriptive statistics using chi-square (discrete variables) or *t* test (continuous variables) to compare demographic and early exposure characteristics and clinical features between children with early farm exposure and with no farm exposure. Children with early farm exposure were significantly more likely to be exposed to indoor pets (82.1% vs 62.3%; $P = .003$) and less likely to have attended day care (38.6% vs 63.1%; $P = .002$) compared with nonfarm children. Family history of asthma/atopic disease, breast-feeding

incidence, and exposure to second-hand smoke were not significantly different between the study groups (see [Table E2](http://www.jacionline.org) in this article’s Online Repository at www.jacionline.org).

For the clinical outcomes, the frequency of asthma was similar in both groups (see [Table E3](http://www.jacionline.org) in this article’s Online Repository at www.jacionline.org). Conditions that were significantly less common in farm-exposed children included allergic rhinitis based on medical record (5.2% vs 12.4%; $P = .02$) and chronic skin rash or eczema based on interview (6.8% vs 19.5%; $P < .001$). Most striking was a significantly decreased frequency of early life severe respiratory illnesses based on interview (15.7% vs 31.4%; $P = .006$) and medical record (6.8% vs 17.6%; $P < .001$) in farm children compared with nonfarm children.

We conducted logistic regression analysis to identify relationships between early life exposures and outcomes. In the univariate analysis, farm exposure was significantly associated with a decreased risk for allergic rhinitis based on medical record (odds ratio [OR], 0.39; 95% CI, 0.17-0.86; [Fig 1, A](http://www.jacionline.org)), with a similar trend based on interview (OR, 0.54; 95% CI, 0.28-1.04; $P = .07$; [Fig 2, A](http://www.jacionline.org)). Breast-feeding was significantly positively associated with allergic rhinitis based on medical record (OR, 3.67; 95% CI, 1.62-8.34; [Fig 1, A](http://www.jacionline.org)). A family history of asthma or atopy was significantly associated with increased risk for allergic rhinitis based on interview (OR, 4.05; 95% CI, 1.64-10.04; [Fig 2, A](http://www.jacionline.org)). Day care was significantly associated with a reduced risk of eczema based on medical record (OR, 0.35; 95% CI, 0.15-0.80; [Fig 1, B](http://www.jacionline.org)), while early farm exposure, early household pets, and household smoking were all significantly associated with a reduced eczema risk based on interview ([Fig 2, B](http://www.jacionline.org)). Early farm exposure was significantly associated with reduced risk of early life severe respiratory illness based on both medical record and interview (OR, 0.45; 95% CI, 0.24-0.85 [medical record]; OR, 0.41; 95% CI, 0.21-0.79 [interview]; [Figs 1, C, and 2, C](http://www.jacionline.org)).

In multivariable analyses controlling for age, sex, family size, household smoking, daycare, breast-feeding, and family history, early farm exposure remained a statistically significant protective factor for respiratory illness (OR, 0.44; 95% CI, 0.21-0.91) and allergic rhinitis based on medical record (OR, 0.33; 95% CI, 0.12-0.89; [Fig 1, D](http://www.jacionline.org)). Using interview data, early farm exposure was a protective factor for eczema (OR, 0.30; 95% CI, 0.14-0.65; [Fig 2, D](http://www.jacionline.org)).

Our study confirmed previous findings that living on a farm at an early age may be protective against eczema and allergic

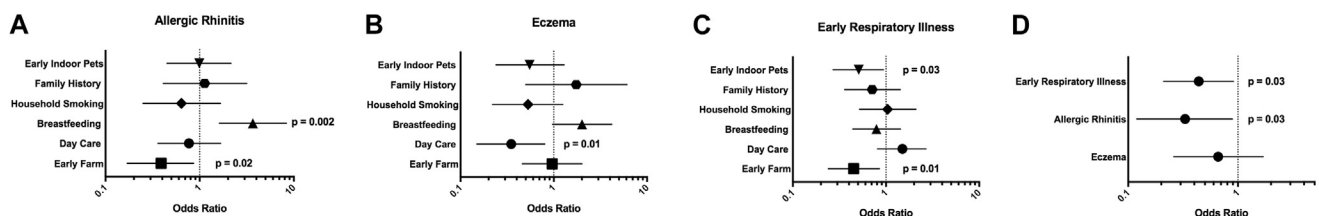


FIG 1. Early farm exposure and risk for early respiratory illness or atopic disease based on medical record. **A-C,** Logistic regression analysis of univariate analysis with measured outcome noted above graph. **D,** Multivariable weighted logistic regression of early farm exposure using full main effects models adjusted for age (continuous), sex, family size (number of siblings), household smoking, daycare, breast-feeding, and family history (atopy or asthma).

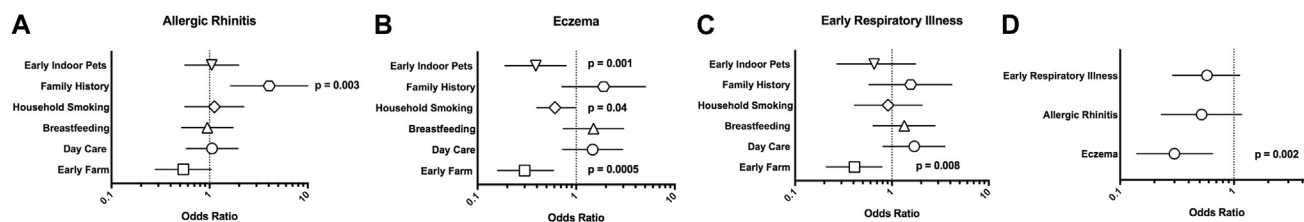


FIG 2. Logistic regression analysis of early farm exposure and risk for early respiratory illness or atopic disease based on interview. **A-C**, Univariate analysis with measured outcome noted above graph. **D**, Multivariable weighted logistic regression of early farm exposure using full main effects models adjusted for age (continuous), sex, family size (number of siblings), household smoking, daycare, breast-feeding, and family history (atopy or asthma).

rhinitis. In addition, Wisconsin farm children had a lower incidence of early life severe respiratory illnesses, as defined by parental recall or by the medical record. Our results are in agreement with recent studies in Western Europe, where farm exposures are inversely related to allergic disease and transient wheezing illnesses, predominantly associated with recurrent infections.⁷⁻⁹ Our results extend these findings to US farming exposures, and also demonstrate inverse relationships between early life farm exposures and severe respiratory illnesses. Our finding that day care attendance was not associated either with early childhood severe respiratory illness or with asthma adds to the conflicting data on this association.

A strength of our study is the near-complete capture of medical events through access to an electronic medical record system that dates back to the early 1960s. One potential limitation of our findings is that our definition of severe respiratory illness was based on a clinical diagnosis and lacks pathogen detection data. Furthermore, there are some differences in findings for outcomes based on interview versus chart abstraction, possibly related to differences in ascertaining outcomes from these 2 sources. A prospective birth cohort study, Wisconsin Infant Study Cohort, is in progress and will help to address these shortcomings and test for additional effects of farm exposures on immune maturation, antiviral responses, and viral illnesses during early childhood. Additional studies to test whether farm exposures are related to beneficial respiratory health outcomes in minority children would also be of interest.

In summary, farming environments in Wisconsin are associated with a reduced risk for developing common childhood allergic and infectious conditions. These studies support and extend studies of traditional farming environments in Europe, and further suggest that exposure to factors related to farming may lessen susceptibility to respiratory illnesses, *perhaps by promoting the development of antiviral defenses*. Given the considerable morbidity caused by childhood respiratory infections and paucity of effective treatments, understanding the mechanisms of these relationships is important to direct new strategies to prevent respiratory illnesses in childhood.

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