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Urban versus Rural Residency and Allergy Prevalence among Adult Women: Iowa Women's Health Study

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Abstract

Background—The association between residence and allergy has been well studied in children living on a farm; however, studies of this association in late adulthood are lacking.

Objective—This study examined the association between residence and allergy in 25,393 women aged 55–69 years in the large prospective Iowa Women's Health Study (IWHS).

Methods—IWHS questionnaires collected information on socio-demographic and anthropometric characteristics, medical history, lifestyle behaviors, dietary intake, residence and allergy. Residence reported at baseline (1986) was categorized into 5 groups based on living on a farm, rural, or urban areas and population size. Allergy was determined from four self-reported

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A. E. had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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questions about physician-diagnosed asthma, hay fever, skin allergy, and other allergy. Logistic regression was used to determine significant risk factors for allergy and prevalence odds ratios (OR) and 95% confidence intervals (CI) for allergy associated with residence.

Results—Compared to large city of >10,000 residents, those living on farm, rural and smaller urban areas had decreased odds ratios of overall, skin, and other allergy in age and multivariable-adjusted models. The multivariable ORs (95% CI) for farm versus large city were decreased for overall allergy: 0.72 (0.66, 0.78) and all allergy types including asthma: 0.87 (0.75, 1.00), hay fever: 0.77 (0.69, 0.88), skin: 0.76 (0.68, 0.86), and other allergy: 0.76 (0.68, 0.86).

Conclusion—This study supports a hypothesis that farm living is inversely associated with allergy, suggesting that environmental exposures may protect against allergy not only in childhood, but also in late adulthood.

Introduction

Allergy symptoms occur when the immune system overreacts to allergens, such as pollen or dust, which are typically harmless to most individuals but induce a potentially severe reaction to those who are sensitive to them. Some allergy symptoms can cause much discomfort, making daily activities difficult, or in rare cases even be life-threatening, making the cause and prevention of allergic conditions a public health concern that should be investigated further.

In 1989, after observing the strongly reduced prevalence of asthma in children living on a livestock farm, David Strachan introduced the hygiene hypothesis, which states that reduced exposure to pathogens during childhood results in deviated immune responses to innocuous antigens later in life.^{1–4} Based on this theory, it has been hypothesized that living in urbanized areas could lead to reduced pathogen exposure and increased risk of allergy, while living in rural areas, particularly on livestock farms, during early childhood may protect against allergic conditions. Studies spanning the last two decades have confirmed that asthma,^{1,4–9} allergic sensitization,^{7,10} wheezing,^{4,11} atopy,^{11,12} and hay fever,^{4,10,13–14} are less commonly reported among farm-reared children than urban counterparts. While the association between residence and allergy has been well studied in children, information is limited on whether this association also exists among adults.

With the lack of information available on allergy in late adulthood, this study aimed to examine the individual characteristics associated with allergy in women of 55 and older living in Iowa who participated in the Iowa Women's Health Study (IWHs). Since intake of food (e.g. nuts, dairy, eggs, shellfish, or meat) have been associated with allergy¹⁵, including asthma^{16–17} and hay fever¹⁷, and diet is highly variable across residence groups, this study also examined these food intakes as risk factors for allergy and as potential confounders of the allergy-residence associations. In addition, number of live births was examined as a potential confounder because a large family size has been associated with higher exposure to infection during early childhood and lower prevalence of allergy.¹ The main hypothesis of this study is that compared to residents living in large urban areas, adult women living on a farm have the lowest prevalence odds of allergy overall and specific subtypes of allergy such

as asthma, hay fever, skin allergy, and other allergic conditions after controlling for allergy risk factors.

Methods

Study Design and Population

This was a cross-sectional analysis utilizing data from the IWHs cohort to investigate the relationship between residence and allergy in women of 55 and older women. The detailed methods for the IWHs are described elsewhere.¹⁸ Briefly, 41,836 Iowan women aged 55 to 69 years were mailed a baseline (1986) and five additional follow-up questionnaires in 1987, 1989, 1992, 1997, and 2004 (response rates were 91%, 90%, 83%, 79%, and 69%, respectively).¹⁹ Questionnaires collected information about socio-demographic and anthropometric characteristics, pertinent medical history, diet and lifestyle behaviors. At baseline, participants reported their demographic information (e.g. marital status and education level), anthropometrics (weight and height), and lifestyle behaviors (e.g. smoking history, alcohol consumption, and physical activity). Diet was assessed using a standard 127-item semi-quantitative Willett food frequency questionnaire, for which the validity and reliability in the study population was previously reported.²⁰ Body mass index (BMI, kg/m²) was calculated as weight (kg) divided by height in meters, squared. The University of Minnesota Institutional Review Board (IRB) approved the IWHs study, and consent was inferred if questionnaires were returned. The University of Minnesota IRB also approved this study prior to any data analysis (performed in 2016–2018).

Ascertainment of Residence

On the baseline questionnaire, participants were also asked to indicate the residence area in which they currently resided: 1) on a farm; 2) rural area but not a farm; 3) a city or town population under 1,000 residents; 4) a city or town population 1,000–2,499; 5) a city or town population 2,500–10,000; or 6) a city or town population over 10,000. Those who did not answer this question were excluded from this study. Since two residence categories (i.e. a city or town population under 1,000 residents and a city or town population 1,000–2,499 residents) were similar in regard to demographic and exposure characteristics, they were combined for data analysis.

The questions about residence were not asked during follow-up; neither was direct information about residence history collected. However, the duration of residence in adulthood was estimated by a surrogate measure – duration of using the residential water source that was queried at the 1989 questionnaire.²¹ About 90% of the women reported using their drinking water source for at least 6 years, and 69%, for at least 20 years, suggesting the residential stability of this cohort in the adulthood.

Ascertainment of Allergy

On the 1997 follow-up questionnaire, participants answered four questions about having a physician diagnosis of any of the following allergic conditions: (1) asthma, (2) hay fever, (3) eczema or allergy of the skin (hereafter called skin allergy), or (4) other allergic conditions (i.e. diagnosis with allergic condition not listed explicitly on the questionnaire) by answering

‘yes’, ‘no’, or ‘not sure’ to each question. In this study, participants (aged 66+ years in 1997) were defined as having an allergy if they answered ‘yes’ to at least one of these questions, and not having an allergy if they answered ‘no’ to all of these questions. If participants did not answer or chose ‘not sure’ for any of the allergy questions, and did not answer ‘yes’ to at least one question, they were considered as having missing information and were excluded from the main analysis.

Of the 41,836 participants included in the IWHs, 16,443 participants (39.3%) were excluded for the following reasons: 1) those who had 30 missing values on the food questionnaire or had a total energy intake of <600 kcal/d or >5,000 kcal/d (N=3,096); 2) did not answer the residence question (N=250); 3) died or did not respond to 1997 questionnaire (N=11,127); or 4) did not answer all allergy questions or answered ‘not sure’ to one or more allergy questions without answering ‘yes’ to at least one (N=1,970). In total, 25,393 participants (60.7%) were included in this study.

Statistical Analysis

Chi-square tests were performed to study the distribution of participants’ baseline characteristics across residence groups. Logistic regression models were used to calculate odds ratios (ORs) with 95% confidence intervals (CIs) for allergy status in relation to each potential risk factor. Also, age- and multivariate-adjusted logistic models were utilized to examine an association of residence groups with allergy status overall and each allergy type. The potential confounders included risk factors associated with residence and allergy in previous studies in the IWHs²² and were included in a multivariate model if a characteristic was associated with both residence and allergy in this study (Table 1 and Figure 1). The following risk factors were included: age (continuous), smoking status (never, former, or current), pack-years of smoking (>1, 1.0–19.9, 20.0–39.9, or ≥40.0 years), education level (some high school, completed high school, or more than high school), BMI (less than 25.0, 25–29.9, or ≥30 kg/m²), use of hormone replacement therapy (HRT) (yes/no), number of live births (0, 1–2, 3–4, ≥4), total calories (<1497, 1497–1986, or ≥1986 kcal/day), total meat (<10.5, 10.5–15, or ≥15 servings/week), total fruits and vegetables (<33.5, 33.5–48.5, or ≥48.6 servings/week), total fish/seafood (<1, 1–1.4, 1.5 servings/week), alcohol consumption (0, 1–4, or ≥4 g of alcohol per day), and marital status (married/not married). The same multivariate-adjusted model was used to examine interaction between residence and three risk factors for allergy: education, smoking status, and the number of live births. To increase power for the analysis of interaction, three residence groups were combined: 1) A rural area but not a farm, 2) A city or town population under 2,499 residents, and 3) A city or town population 2,500–10,000 residents.

In addition, census data was used to identify residence (farm versus non-farm) of the IWHs participants in 1930, i.e. during their childhood. This was done for two reasons. First, this study aimed to estimate the residence change over participants’ lifetimes among those who had information about residence at both time points: 1930 and 1986 (N=9,577). Second, since the association between childhood residence and allergy has been established,^{1,4–9,10–14} and adult residence-allergy association in adults could be driven by childhood

residence, this study examined the association between childhood residence and allergy prevalence in 1997 (N=4353).

Finally, to address the concern that excluded women could be different from those who answered the allergy questions, a comparison of characteristics was made among those who did and did not respond to the allergy questionnaire (including those who died between 1986 and 1997). All statistical analyses were performed using RStudio (RStudio Version 0.99.484 - © 2009–2015 RStudio, Inc.). All-tests were two-sided and a p-value of 0.05 was considered significant for all analyses performed in this study.

Results

Among IWHS women included in this analysis, 20.3% lived on a farm; 7.4% lived in a rural area but not a farm; 21.1% lived in a city or town population under 2,499 residents; 17.2% lived in a city or town population 2,500–10,000 residents; and 34.0% lived in a city or town population over 10,000 residents (Table 1). Compared to non-farm residents, those who resided on a farm were less likely to be current or former smokers, drink over 4 g of alcohol/day, eat fish/seafood, and use HRT (Table 1). They were also more likely to be married and have higher BMI, have more children, consume more calories and fat, meat and total fruit and vegetables. Those who lived in large cities >10,000 were more educated and more involved in leisure physical activity. Further, respondents to the allergy questions were very similar to those who were alive but did not respond to the questionnaire on allergy except that responders were more educated (Supplementary Table 1). As expected, those who died were more likely to smoke, be older and slightly heavier, and were less likely to live on a farm.

Age, smoking status, education, BMI, history of HRT, number of live births, total calories, total meat, total fruits and vegetables, total fish/seafood, and marital status were significantly associated with allergy (Figure 1). Older age (60–64 years: OR = 0.93 (95% CI: 0.88, 0.99); >64 years: OR = 0.92 (95% CI: 0.86, 0.99) vs. <60 years), being married (OR = 0.88 (95% CI: 0.83, 0.94) vs. unmarried), and having higher number of births (1–2: OR = 0.88 (95% CI: 0.80, 0.98); 3–4: OR = 0.86 (95% CI: 0.78, 0.95); >4: OR = 0.77 (95% CI: 0.69, 0.85) vs. 0 live births) were significantly associated with lower odds ratios of allergy, while former and current smokers (vs. never), higher level of education, being obese, having a history of HRT, or consuming more calories, meat, fish/seafood and fruits and vegetables were associated with higher odds ratios of allergy. Physical activity was not associated with allergy.

Age- and multivariate-adjusted odds ratios of overall allergy and its subtypes (Table 2) were calculated for each residence category using “a city or town population over 10,000 residents” as the reference group. In the age-adjusted model, compared to reference, residents of smaller urban and rural areas had decreased odds of overall, skin, and other allergy. The inverse associations for these residence groups remained in the multivariate-adjusted model. Further, in the multivariate analysis, participants who lived on a farm had the lowest odds ratios of overall allergy (OR = 0.72 (95% CI: 0.66, 0.78)) and all allergy types: asthma (OR = 0.87 (95% CI: 0.75, 1.00)), hay fever (OR = 0.77 (95% CI: 0.69,

0.88)), skin allergy (OR = 0.76 (95% CI: 0.68, 0.86)), and other allergy (OR = 0.76 (95% CI: 0.68, 0.86)). However, the inverse associations between rural (non-farm) residence and hay fever or asthma disappeared after multivariate adjustment.

The interaction between residence and education level was marginally statistically significant ($P_{\text{for interaction}} = 0.06$) (Supplementary Table 2). The odds ratios of allergy among those who live on a farm versus large city (>10,000) were lower among all education levels but were lowest among those who had completed more than high school (OR = 0.63 (95% CI: 0.55, 0.71)). The association between residence and overall allergy stratified by smoking status and the number of live births was also examined, but the interactions were not statistically significant ($P_{\text{for interaction}} = 0.26$ and $P_{\text{for interaction}} = 0.81$, respectively).

Lastly, in the analysis of 9,577 IWHs participants with information about their residence in 1930 and 1986, more than half of the participants lived on a farm in 1930, but only 22% lived on a farm in 1986, i.e. 72% of farmers in 1930 became non-farmers in 1986, whereas only 11% of non-farmers (N=454; 5% of the analytical cohort) became farmers in 1986 (Supplementary Table 3). Compared to those who did not live on a farm during childhood, those who had a childhood farm residence had decreased unadjusted odds of overall allergy (OR = 0.61 (95% CI: 0.54, 0.69)).

Discussion

This study utilized data from a large cohort of 25,393 women of 55 and older who participated in the IWHs. In this study, the following risk factors were positively associated with allergy: older age, smoking, higher education, higher BMI, history of using HRT, and intake of several dietary factors such as fruits and vegetables, fish/seafood, and meat, while being married and having higher number of live births appeared to reduce the risk of allergy. Compared to those living in a city or town of >10,000 residents, farm residents were 22–38% less likely to have allergy overall, asthma, hay fever, skin allergy, and other allergies. These statistically significant trends for farm residence remained in multivariate-adjusted models. Compared to large cities of >10,000 residents, the odds ratios of overall, skin, and other allergies were also significantly decreased for smaller urban and rural areas, while asthma and hay fever were not associated with living in a rural (non-farm) area after multivariate adjustment.

Residents of farms and smaller rural areas or towns may have lower odds ratio of overall, skin, and other allergies versus residents of large cities (over 10,000), because they reside in areas where pollution is lower than in larger urban regions. It has been shown that traffic-related air pollution leads to higher prevalence of allergy disease in urban cities, and diesel exhaust particles increase airway inflammation.¹³

The results of this study also suggest that certain environmental exposures specifically attributed to living on a farm (e.g. gram-negative bacteria endotoxins, fungi, animal feed exposure, pesticide use) may protect against respiratory allergies like asthma and hay fever even in adulthood. This study's findings are in agreement with the hygiene hypothesis stating that reduced exposure to innocuous environmental agents early in life may lead to

deviated immune responses (i.e. allergy), while increased exposure early in life may suppress these responses.

The inverse association observed between residence and allergy may be partially attributed to a “healthy farmer effect”, which could occur if participants who lived on a farm during childhood developed allergic disease, and then left the farming environment where exposure to environmental hazards (e.g. pesticides, molds, ammonia, pollen, grain dust) may be higher, leaving “healthy” farmers to remain.^{13,23}

This study’s findings of a reduced risk of allergy with farm residence may reflect a true association between residence and allergy, or may be partially attributed to detection bias as urban residents may have better access to health care. However, this study found no associations between a non-farm rural area with asthma or hay fever in a multivariate model, implying a likely association with farm residence. The existence of a similar inverse association between farm residence in childhood and allergy (OR = 0.61 (95% CI: 0.54, 0.69)) also corroborates a likely association with allergy in adulthood, since (1) the protective role of childhood farm residence in allergy development has been established and (2) the association between residence and allergy in adults, most likely, originated in childhood. Further, indirect evidence also suggests allergy ascertainment is not strongly related to health care access: in a previous IWHS study²², investigators found an inverse association between allergy and colorectal cancer risk. If those with allergy visited physicians more often, they would have more frequent colonoscopy screening and higher risk of colorectal cancer, especially among those diagnosed at an early stage of colorectal cancer. However, this study observed an inverse association at all stages.

The results of this study are in agreement with several studies investigating allergy among adult participants. A study of 1,236 adult male participants aged 30–40 years reported that the prevalence and odds of allergic sensitization overall and certain allergens (measured by IgE), and self-reported rhinitis decreased with decreasing degree of urbanization.²⁴ Another cross-sectional study of participants aged 16–75 found that living on a farm during the first five years of life was associated with a lower prevalence of allergic rhinitis in adult life, even when stratified by age.¹³ However, prevalence of allergic rhinitis increased with increasing degree of urbanization, regardless of childhood farm living.¹³ Furthermore, a study of 10,201 participants aged 26–54 from 14 countries found that as compared with a city upbringing, those with early-life farm exposure has less atopic sensitization, atopic asthma and atopic rhinitis.²⁵ Results of this study are also consistent with studies that reported higher prevalence of allergy in urban versus farm-reared children and adolescents.^{26–28}

However, not all studies in adults reported similar results. A survey of Montana residents older than 18 years found no association between residence in rural versus urban areas and prevalence of self-reported asthma; no other allergy subtypes were investigated.²⁹ Yet, in that study, the residence could be misclassified as rural-urban continuum codes were used to classify residence categories. As such, participants in the same residence category may live in a city or town that has between 2,500 and 20,000 residents. Another study found that compared to non-farmers, adult farmers had a reduced risk of atopic sensitization, but similar prevalence of self-reported hay fever and asthma prevalence.¹² That study was

limited by its sample size (N=2,081) and an examination of farming lifestyle only from the past 5 years; no other previous farming exposures were investigated.

Strengths and Limitations

To the authors' knowledge, this study is the first to investigate the association between multiple allergy subtypes and residence in adult females living in the United States. Other strengths of this study include a large sample size, and detailed information about potential confounders including demographics, anthropometrics and lifestyle behaviors. One of the study limitations is potential inaccurate ascertainment of atopic allergy, for instance, participants could have reported a drug or insect sensitivity as other allergy, or non-allergic urticaria or pruritus as skin allergy. However, they reported allergic conditions diagnosed by physician which has been shown to be more reliable than being asked to recall allergy events.³⁰ Although misclassification of allergy cannot be excluded, the percentages of participants reporting asthma (7.6%) and hay fever (8.3%) in this study are similar to those reported by the National Center for Health Statistics in 2000 of women aged 65+ years in the United States (8.4% for ever asthma; 7.9% for hay fever), suggesting an accurate report of allergy in the IWHS respondents.³¹ Further, some of the participants died or did not answer allergy questions. However, respondents to the allergy question were very similar to those who were alive but did not respond to the allergy questions, and to those who died, with the exception that responders were more educated. Another limitation is that the residence in 1986 may not reflect the residence over participants' lifetimes; however, the earlier IWHS by Jones et al (2014) showed that this cohort is residentially stable in adulthood.²¹ It is also possible that higher education level may play a role in recognizing presence and reporting symptoms of an allergy to a physician. However, controlling for education (Table 2) did not change the results, suggesting the association was not confounded by education status. In addition, the association existed in all three groups: some high school, completed high school, and more than high school (Supplementary Table 2). Finally, a married lifestyle may be more protective against allergy. However, this study found that controlling for marital status along with other variables only slightly attenuated the association, but an inverse association with farm residence remained in multivariate model.

In summary, the study hypothesis has been confirmed: a statistically significant inverse association was observed between living on a farm and prevalence odds ratios of overall allergy and all allergy subtypes in late adulthood. Thus, this study supplements the studies on residence and allergy in children that strongly suggest an inverse association between early childhood exposure to farm and allergy. As allergies can cause a significant daily burden, prospective studies are needed to investigate specific farming-associated environmental exposures that may induce a protective effect against allergy subtypes. This study provides insight into the role that environmental exposures may play on protection against allergy, not only in childhood, but also at older age.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

Unadjusted odds ratios and 95% confidence intervals for allergy by baseline characteristics

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Characteristic	Residence				
	Farm N ^a (%)	A rural area but not a farm N ^a (%)	A city or town population under 2,499, N ^a (%)	A city or town population 2,500–10,000, N ^a (%)	A city or town population over 10,000, N ^a (%)
3–4	2217 (43.1)	772 (41.2)	2169 (40.6)	1720 (39.5)	3356 (39.1)
>4	1233 (24.0)	388 (20.6)	1091 (20.5)	792 (18.2)	1337 (15.6)
History of HRT					
No	3372 (65.6)	1140 (60.7)	3241 (60.6)	2599 (59.6)	4841 (56.2)
Yes (current/past)	1766 (34.4)	738 (39.3)	2104 (39.4)	1762 (40.4)	3766 (43.8)
Total calories (kcal/day)					
Low tertile (<1497)	1320 (25.6)	628 (33.3)	1792 (33.4)	1520 (34.8)	3159 (36.6)
Middle tertile (1497–1968)	1684 (32.7)	652 (34.6)	1822 (34.0)	1460 (33.4)	2971 (34.5)
High tertile (1968)	2151 (41.7)	604 (32.1)	1746 (32.6)	1390 (31.8)	2494 (28.9)
Total meat (servings/week)					
Low tertile (<10.5)	1277 (24.8)	628 (33.3)	1832 (34.2)	1544 (35.3)	3240 (37.6)
Middle tertile (10.5–15)	1553 (30.1)	610 (32.4)	1631 (30.4)	1376 (31.5)	2841 (32.9)
High tertile (15)	2325 (45.1)	646 (34.3)	1897 (35.4)	1450 (33.2)	2543 (29.5)
Total fruits and vegetables (servings/week)					
Low tertile (<33.5)	1472 (28.5)	603 (32.0)	1847 (34.5)	1523 (34.8)	2834 (32.9)
Middle tertile (33.5–48.5)	1793 (34.8)	671 (35.6)	1792 (33.4)	1463 (33.5)	2943 (34.1)
High tertile (48.6)	1890 (36.7)	610 (32.4)	1721 (32.1)	1384 (31.7)	2847 (33.0)
Fish/Seafood (servings/week)					
Low (<1)	1562 (30.3)	549 (29.1)	1600 (29.9)	1230 (28.1)	2296 (26.6)
Medium (1–1.4)	1245 (24.1)	406 (21.6)	1234 (23.0)	1004 (23.0)	1868 (21.7)
High (1.5)	2348 (45.6)	929 (49.3)	2526 (47.1)	2136 (48.9)	4460 (51.7)
Total Milk (servings/week)					
Low (<3)	1257 (24.4)	480 (25.5)	1395 (26.0)	1078 (24.7)	2185 (25.4)
Medium (3–6.9)	1049 (20.3)	397 (21.1)	1230 (23.0)	963 (22.0)	1926 (22.3)
High (7)	2849 (55.3)	1007 (53.4)	2735 (51.0)	2329 (53.3)	4513 (52.3)
Total Eggs (servings/week)					

Characteristic	Residence				
	Farm N ^a (%)	A rural area but not a farm N ^a (%)	A city or town population under 2,499, N ^a (%)	A city or town population 2,500–10,000, N ^a (%)	A city or town population over 10,000, N ^a (%)
Low (<1)	1210 (23.5)	480 (25.5)	1357 (25.3)	1074 (24.6)	2102 (25.8)
Medium (1–1.9)	1255 (24.3)	477 (25.3)	1500 (28.0)	1194 (27.3)	2172 (25.2)
High (2)	2690 (52.2)	927 (49.2)	2503 (46.7)	2102 (48.1)	4222 (49.0)
Total Nuts (servings/week)					
Low (<1)	1747 (33.9)	637 (33.8)	1810 (33.8)	1413 (32.3)	2618 (30.4)
Medium (1–1.9)	1651 (32.0)	580 (30.8)	1656 (30.9)	1333 (30.5)	2600 (30.1)
High (2)	1757 (34.1)	667 (35.4)	1894 (35.3)	1624 (37.2)	3406 (39.5)
Physical Activity					
Low	2325 (46.9)	819 (45.0)	2478 (47.4)	1972 (46.2)	3718 (44.2)
Medium	1445 (29.2)	507 (27.8)	1464 (28.0)	1174 (27.5)	2326 (27.6)
High	1186 (23.9)	495 (27.2)	1284 (24.6)	1120 (26.3)	2374 (28.2)
Alcohol (g/day)					
0	3275 (63.5)	1042 (55.3)	3013 (56.2)	2270 (51.9)	3804 (44.1)
4	1264 (24.5)	449 (23.8)	1348 (25.2)	1074 (24.6)	2324 (27.0)
>4	616 (12.0)	393 (20.9)	999 (18.6)	1026 (23.5)	2496 (28.9)

Abbreviations: HRT - hormone replacement therapy

^aNot all participants answered all questions

Table 2
Odds ratio and 95% confidence interval for overall allergy and allergy subtypes by residence

Allergy					
Residence	Yes (N=8069), N ^a	No (N=17,324), N ^a	Age-adjusted OR (CI)	Multivariable-adjusted ^b OR (CI)	
A city or town population over 10,000	3040	5584	Reference	Reference	
A city or town population 2,500–10,000	2249	4772	0.87 (0.80, 0.94)	0.90 (0.83, 0.97)	
A city or town population under 2,499	832	1877	0.83 (0.77, 0.90)	0.87 (0.81, 0.94)	
A rural area but not a farm	584	1300	0.81 (0.73, 0.90)	0.85 (0.76, 0.95)	
Farm	1364	3791	0.66 (0.61, 0.71)	0.72 (0.66, 0.78)	
P-trend			<0.001	<0.001	
Asthma					
	Yes (N=1939), N ^a	No (N=17,324), N ^a	Age-adjusted OR (CI)	Multivariable-adjusted ^b OR (CI)	
A city or town population over 10,000	705	5584	Reference	Reference	
A city or town population 2,500–10,000	520	4772	0.86 (0.75, 0.99)	0.93 (0.81, 1.07)	
A city or town population under 2,499	214	1877	0.87 (0.76, 0.99)	0.94 (0.82, 1.08)	
A rural area but not a farm	164	1300	0.99 (0.83, 1.19)	1.10 (0.91, 1.32)	
Farm	336	3791	0.71 (0.61, 0.81)	0.87 (0.75, 1.00)	
P-trend			<0.001	0.20	
Hay Fever					
	Yes (N=2120), N ^a	No (N=17,324), N ^a	Age-adjusted OR (CI)	Multivariable-adjusted ^b OR (CI)	
A city or town population over 10,000	811	5584	Reference	Reference	
A city or town population 2,500–10,000	589	4772	0.86 (0.76, 0.99)	0.94 (0.83, 1.08)	
A city or town population under 2,499	195	1877	0.78 (0.68, 0.88)	0.87 (0.77, 0.99)	
A rural area but not a farm	169	1300	0.86 (0.72, 1.03)	0.98 (0.82, 1.18)	
Farm	356	3791	0.65 (0.57, 0.74)	0.77 (0.69, 0.88)	
P-trend			<0.001	<0.001	
Skin Allergy					

Allergy					
Residence	Yes (N=8069), N ^a		No (N=17,324), N ^a		Multivariable-adjusted ^b OR (CI)
	Age-adjusted OR (CI)		Age-adjusted OR (CI)		
	Yes (N=3098), N ^a		No (N=17,324), N ^a		Multivariable-adjusted ^b OR (CI)
A city or town population over 10,000	1206		5584		Reference
A city or town population 2,500–10,000	821		4772		0.82 (0.73, 0.92)
A city or town population under 2,499	316		1877		0.76 (0.68, 0.85)
A rural area but not a farm	219		1300		0.78 (0.66, 0.91)
Farm	536		3791		0.65 (0.58, 0.72)
P _{trend}					<0.001
Other Allergy					
	Yes (N=4599), N ^a		No (N=17,324), N ^a		Multivariable-adjusted ^b OR (CI)
	Age-adjusted OR (CI)		Age-adjusted OR (CI)		
A city or town population over 10,000	1779		5584		Reference
A city or town population 2,500–10,000	1276		4772		0.85 (0.78, 0.94)
A city or town population under 2,499	473		1877		0.81 (0.74, 0.88)
A rural area but not a farm	324		1300		0.76 (0.67, 0.87)
Farm	747		3791		0.62 (0.56, 0.68)
P _{trend}					<0.001

^aThe participants reporting this allergy subtype may include those who reported other allergy types.

^bAdjusted for age, residence, pack-years of smoking, smoking status, education, BMI, hormone replacement therapy, total calories (kcal/day), total meat (servings/week), total fruits and vegetables (servings/week), total fish/seafood (servings/week), number of live births, alcohol, and marital status.

^cBoldface indicates statistical significance (*P*-value 0.05).