Can selection explain the protective effects of farming on asthma?

Wijnand Eduard1,2, Vivi Schlünssen3, Torben Sigsgaard1, Øyvind Omland3,4, Neil Pearce2,5, Jeroen Douwes2

1 Department of Chemical and Biological Work Environment, STAMI National Institute of Occupational Health, Oslo, Norway
2 Centre for Public Health Research, Massey University, Wellington, New Zealand
3 Department of Public Health, Section for Environment, Work and Health, Aarhus University, Aarhus, Denmark
4 Department of Occupational Medicine, Aalborg University Hospital, Aalborg, Denmark
5 Department of Medical Statistics, London School of Hygiene and Tropical Medicine, London, United Kingdom

Address for correspondence: Wijnand Eduard, Department of Chemical and Biological Work Environment, STAMI National Institute of Occupational Health, P.O. Box 8149 Dep, NO-0033 Oslo, Norway
E-mail: wijnand.eduard@stami.no

INTRODUCTION

Several studies have reported reduced risks of atopy, hay fever, atopic dermatitis and asthma in farmer’s children [1, 2]. Protective effects of farming have also been shown in adolescents and adult farmers, although the evidence has been mixed, with some studies showing increased risks of asthma and atopy and others showing no association or a reduced risk [3].

It has been hypothesized that microbial exposure, and particularly diversity of microbial exposure, may partially account for the reduction in allergy and asthma risk in farmers and farmers’ children [4]. Consumption of raw milk may also be important [5]. Selection effects involving asthmatics avoiding farm jobs with high exposure and/or leaving high-exposed farm jobs have not previously been studied as an alternative explanation, despite the ‘healthy worker effect’ being particularly strong in the case of asthma [6]. If these effects exist in farming, then they may not only explain the reduced risk in adult farmers, they may also (through generations of selection) in part explain the reduced risks in farmers’ children.

OBJECTIVE

To assess selection effects with regards to asthma in Danish farming students and their siblings. Also assessed were the effects on asthma of early retirement and changes in type of farm production among Norwegian farmers.

MATERIALS AND METHOD

Danish study. All second-year students from farming schools in Denmark were invited (1992–1994) to participate in a cross-sectional study of allergies and asthma (N=1,964; participation rate 79%) [7]. Students were asked the following questions: (1) Do you have asthma? (2) Have you ever had asthma? (3) Do any of your siblings have or have had asthma? (4) How many of your siblings have or have had asthma? The number of siblings was obtained from a postal questionnaire completed by the parents. Most farming students were males (89%), 42% had been raised on a farm, 25% were active smokers and mean age was 19.0 years (SD=1.83). Of the siblings, 47% were male; no information, on smoking, age and farm childhood was available. Farm childhood status was therefore assumed to be the same in siblings and students from the same family. Since no gender-specific information on asthma among siblings was available, only students with either sisters or brothers (i.e. 739 students: and 1,105 siblings) were selected.

Norwegian study. Current asthma was assessed in 8,482 farmers from south-east Norway examined in 1991 (participation rate 79%) by a self-administered questionnaire with the questions: (1) Have you ever had asthma? (2) If yes, do you have asthma now? (3) Was asthma diagnosed by a physician? Ever asthma was defined as a positive response to any of these questions [8]. The population included 349 farmers who had retired from farming before the legal
pension age four years prior to the study being conducted, and 104 farmers who had changed production because of dust-related health symptoms. The mean age was 49 years (SD 11), 66% were male, and 30% were current smokers, 24% former smokers and 46% never smokers.

**Ethics approval.** The Danish study was approved by the Danish Ethics Committee in 1991 and all participants gave written consent. The Norwegian study was approved by the Norwegian Data Inspectorate and the Regional Medical Ethics Committee in 1989. Informed consent was not required in Norway in 1989.

**Data analysis.** Comparisons in asthma prevalence between Danish farming students and siblings and current and retired farmers in Norway were made using logistic regression analyses adjusting for gender, age, and smoking.

For the Norwegian farmers we included those who had retired early during the previous four years, but no data for earlier time periods was available. To adjust for this, estimated proportions of retired farmers in the source population (including those who had left prior to the previous four years) was used. This was carried out separately for male and female farmers. The proportion of farmers in the study population who had retired early during the last 4 years was estimated from logistic regression models of retirement with age. Annual retirement rates in age strata were estimated by the proportion of early retired farmers divided by 4 years. The proportion of early retired farmers in the source population was subsequently estimated as per the formula below:

\[
P_{\text{retired}} = (1 - P_{\text{annual}})^{Year_{\text{farming}}}\]

where

\[
Year_{\text{farming}} = \text{arithmetic mean years in farming in age-group}_i\]

Asthma prevalences in age-groups (categorised in quartiles) of active and early retired farmers were estimated in the study population using logistic regression. The asthma prevalence estimate was then adjusted using the proportions of early retired farmers from the estimated source population in each age group.

**RESULTS**

**Danish study.** No difference in asthma prevalence was found between students (5.4%) and siblings (5.2%; OR 1.1; 95% CI 0.7–1.7) (Tab. 1). In a separate logistic regression of students only, age was not associated with asthma (OR 1.00; 95% CI 0.9–1.1). Current smoking was positively associated with asthma, but this was only of borderline statistical significance (OR 1.5; 95% CI 1.0–2.4).

**Norwegian study.** The prevalence of current asthma in farmers who retired early was 6.3%, compared to 3.0% in active farmers (OR 1.8; 95% CI 1.1–2.9), and 22% in farmers who had changed production (OR 9.8; 95% CI 6.0–16). Early retirement was also associated with an increased prevalence of ever asthma (9.2% compared to 6.1% in active farmers (OR 1.6; 95% CI 1.1–2.3). No significant association was found with physician-diagnosed asthma (5.7% compared to 4.0%. OR 1.4; 95% CI 0.9–2.3).

**DISCUSSION**

The prevalence of ever asthma in Danish farming students and their siblings was almost identical, i.e. 5.4% and 5.2%, respectively. In Norwegian farmers, current asthma was significantly more prevalent in early retired farmers than in active farmers i.e. 6.3% and 3.0%, respectively. However, due to the relatively small number of early retirees, current asthma in the total population of farmers was underestimated by only 0.6%. The underestimation of doctor-diagnosed asthma and ever asthma was even lower, i.e. 0.3% and 0.5%, respectively. The prevalence of current asthma was considerably higher in farmers who had changed production, i.e. 3% vs. 22%, but this has no effect on asthma prevalence of the total farmers population.

The comparison of Danish students and siblings could not be adjusted for smoking and age as no information was available for siblings. However, age was not significantly associated with asthma in students, and is therefore unlikely to be a major confounder. Smoking may have been a confounder, but the effects would most likely have been small as ‘only’ 25% of the students smoked, and smoking habits between siblings are likely to be similar. Likewise, the genetic background and early life exposures of students and siblings are likely to be reasonably similar and these factors

**Table 1. Prevalence of ever asthma in Danish farming students and their siblings by gender and childhood on a farm**

<table>
<thead>
<tr>
<th>Factor</th>
<th>Students</th>
<th>Siblings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma</td>
<td>N</td>
<td>N %</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>5410</td>
<td>31.6</td>
</tr>
<tr>
<td>Male</td>
<td>5410</td>
<td>31.6</td>
</tr>
<tr>
<td>Farm childhood</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>5410</td>
<td>31.6</td>
</tr>
<tr>
<td>No</td>
<td>5410</td>
<td>31.6</td>
</tr>
</tbody>
</table>

Adjustments for early retirement using estimated proportions of retired farmers in the source population increased the estimates of current asthma from 3.1% to 3.7%, ever asthma from 6.3% to 6.8% and physician-diagnosed asthma from 4.1% to 4.4%. (Tab. 2).

**Table 2. Asthma in Norwegian farmers by gender. Observed prevalences in active farmers, early retired and all farmers and adjusted prevalences using early retirement rates from the estimated source population**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Gender</th>
<th>N</th>
<th>N %</th>
<th>N</th>
<th>N %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current asthma</td>
<td>Male</td>
<td>5410</td>
<td>3.1</td>
<td>158.7</td>
<td>5568</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>2723</td>
<td>2.7</td>
<td>191.5</td>
<td>2914</td>
</tr>
<tr>
<td></td>
<td>All</td>
<td>8133</td>
<td>3.0</td>
<td>349.6</td>
<td>8482</td>
</tr>
<tr>
<td>Doctor-diagnosed asthma</td>
<td>Male</td>
<td>5410</td>
<td>4.2</td>
<td>158.7</td>
<td>5568</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>2723</td>
<td>3.7</td>
<td>191.5</td>
<td>2914</td>
</tr>
<tr>
<td></td>
<td>All</td>
<td>8133</td>
<td>4.0</td>
<td>349.7</td>
<td>8482</td>
</tr>
<tr>
<td>Ever asthma</td>
<td>Male</td>
<td>5410</td>
<td>6.5</td>
<td>158.7</td>
<td>5568</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>2723</td>
<td>5.4</td>
<td>191.5</td>
<td>2914</td>
</tr>
<tr>
<td></td>
<td>All</td>
<td>8133</td>
<td>6.1</td>
<td>349.9</td>
<td>8482</td>
</tr>
</tbody>
</table>
A healthy survivor selection was observed in Norwegian farming among Danish farming students born in 1974. There was no evidence for healthy worker selection into between farmers with different production types is small. The number of all farmers who had left the study population due to early retirement was estimated, based on early retirement data for the four year period prior to commencing the study. These calculations were based on the assumption that the early retirement rate was constant during all years in farming within all age groups. However, these trends may have been lower earlier in life especially in the older age groups. The adjusted prevalences are therefore probably overestimated.

When the presented data is compared with a study of the general population in south-west Norway conducted a few years before the current study, it was found that ever physician-diagnosed asthma in rural and urban populations was 5.7% and 7.6%, respectively, which was significantly higher by 1.7% and 3.6% than in our farming population [11]. In fact, the difference was considerably greater than the underestimation of 0.3% found for physician-diagnosed asthma in the presented analysis. Thus, it seems unlikely that the small selection effects from early retirement of asthmatic farmers observed in this study can fully explain the lower asthma prevalence in Norwegian farmers.

Farmers who had changed the type of production had an increased risk of current asthma (OR 9.8), compared with those who had not changed production, indicating a strong selection effect. Such selection may distort the asthma prevalence among farmers with a specific type of production, but not in the whole farming population. However, only 1.3% of the Norwegian farmers had changed production during the last 10 years, therefore the resulting bias in comparisons between farmers with different production types is small.

CONCLUSIONS

There was no evidence for healthy worker selection into farming among Danish farming students born in 1974. A healthy survivor selection was observed in Norwegian farmers, but it was too small to fully explain the reduced risk of asthma observed in this population. A strong selection effect was observed among farmers who had changed production type, which may bias comparisons between different type of farmers, but not the asthma risk in the whole farming population. Thus, the postulated protective effects of farming on asthma appear unlikely to be attributable to selection effects alone.

Acknowledgements

The study was supported by Norwegian Research Council Grant No. 103544/110 and Danish Medical Research Council Grant No. 09-060086, sponsored by the Health Research Council (HRC) of New Zealand.

REFERENCES