

Original article

Lifelong farm exposure may strongly reduce the risk of asthma in adults

Background: Farm exposures may protect against childhood asthma, hay fever and eczema. Whether farm exposures also confer protection in adult farmers remains unclear. Moreover, little is known about the role of timing of exposure. We assessed the effects of current and childhood farm exposures on asthma, hay fever and eczema in farmers and a rural nonfarming control population.

Methods: We conducted a cross-sectional questionnaire survey in 2509 farming families (response rate 78%) and 1001 nonfarming families (response rate 67%), which included 4288 farmers and 1328 nonfarmers.

Results: Farmers were less likely to have asthma symptoms, hay fever and eczema; no significant differences were observed among dairy, sheep and beef, and horticulture farmers. A combination of current and childhood exposure was more strongly associated with shortness of breath (OR 0.50, CL 0.39–0.66), wheeze (OR 0.60, CL 0.49–0.73), asthma medication (OR 0.48, CL 0.37–0.63); and asthma ever (OR 0.56, CL 0.46–0.68) than current exposure alone (OR 0.63, CL 0.47–0.84; OR 0.80, CL 0.65–0.99; OR 0.68, CL 0.51–0.9; OR 0.69, CL 0.56–0.85 respectively) or childhood exposure alone (OR 0.97, CL 0.65–1.44; OR 1.01, CL 0.75–1.34; OR 0.78, CL 0.51–1.19; OR 0.87, CL 0.63–1.19 respectively). Moreover, the combined number of years of farm exposure in childhood and adulthood showed a dose-dependent inverse association with symptom prevalence.

Conclusions: Although both current and childhood farm exposures may play a role in the observed low prevalence of asthma symptoms in adult farmers, continued long-term exposure may be required to maintain optimal protection.

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An increasing number of studies have reported a reduced risk of atopy, hay fever, asthma and eczema in farmer's children and adolescents (1–4). It is not clear which farming-related factors confer protection, but several studies have suggested that contact with livestock may play an important role (3, 4). Livestock farming is known to be associated with increased exposures to bacterial endotoxin and/or other microbial agents (5) which may inhibit Th₂ cell immune responses and the subsequent development of Th₂-dependent diseases, including allergic asthma, hay fever and eczema (6). It is commonly assumed that these effects only occur in *early life* (7, 8). However, recent studies suggest that 'immune deviation' may take place throughout life (9, 10).

Recent studies among adult farmers have suggested that protection against atopy and atopic asthma may continue into adulthood (11–14), but it is not clear whether the lower prevalence of asthma in farmers is due to early childhood exposure, current exposure, or a

combination of both. Furthermore, not all studies have shown protective effects of farming in adults. For example, in the European Community Respiratory Health Survey (ECRHS) the highest risk of asthma was shown for farmers (OR 2.6; CI 1.3–5.4) and agricultural workers (OR 1.8; CI 1.0–3.2) (15). An increased risk of asthma morbidity and mortality for farmers has also been reported in several other studies (reviewed in Ref. 16).

Previously we have shown that *in utero* exposure may contribute to the low prevalence of allergic diseases in farmers' children, but we also showed that continued exposure may be required to maintain optimal protection (17). In this study we will present the findings in adults from the same cross-sectional study, in which we assessed the effects of current and childhood farm exposure on asthma, hay fever and eczema in farmers and their spouses from dairy, sheep and beef, and horticulture farms, and a rural nonfarming control population.

Materials and methods

Study design and population

The methods for the study were based on those of the European study on atopy and asthma in farmers' children, known as the PARSIFAL study (18), but in addition to children we also included the parents. The study involved a survey of 2509 farming families and 1001 nonfarming families of working age.

Farming families living in the lower half of the North Island were randomly selected from a national database of farms in New Zealand. We aimed for equal numbers of dairy, sheep and beef, and horticulture farms, but there were relatively fewer horticultural farms (crop farms and orchards), resulting in lower numbers for this group. A rural control group of nonfarmers from the same region (adults aged 25–49) was randomly chosen from the New Zealand Electoral Roll.

Subjects were asked to complete a postal survey for themselves and their children (if they had any). Those who had not responded to the postal survey after three reminders were asked to complete the questionnaire(s) by telephone. An overview of the recruitment, exclusions, and refusals is presented in Fig. 1. All subjects gave written informed consent and the study was approved by the Massey University Human Ethics Committee (WGTN protocol 02/105).

Questionnaire

The symptom prevalence was assessed by using a standardized questionnaire based on the ECRHS postal questionnaire (19). We focussed on the following questions, 'Have you had wheezing or whistling in your chest at any time in the past 12 months?', 'Have you been woken by an attack of shortness of breath at any time in the past 12 months?', 'Have you ever had asthma?', 'Are you currently taking any medicine (including inhalers, aerosols or tablets)

for asthma?', 'Do you have any nasal allergies including hay fever?' and 'Have you ever had eczema?' Those subjects who indicated that they had ever had asthma were asked whether the diagnosis was confirmed by a doctor.

We also assessed whether and how long subjects had lived on a farm during childhood, and how long they worked as a farmer, i.e. 'Did you grow up on a farm?', 'If yes, for how many years (up to 18 years old)', and 'How long have you worked as a farmer?'

Statistical analyses

All statistical analyses were conducted using SAS for Windows version 9.1 (SAS Institute, Cary, NC, USA). We used *t*-tests to test differences in continuous variables between the farmers and reference group and chi-square tests to test differences in percentages. We calculated crude and adjusted prevalence odds ratios (20) using logistic regression. As we included adults from the same household, we applied 'clustered robust standard errors' (21) using the family unit as the cluster variable. We assessed whether there was an additive effect of current and childhood farm exposure by making comparisons between those who were exposed in both periods, those who were only currently exposed, and those who were exposed in childhood but not currently; the reference category comprised subjects who had no exposure in both periods. We also explored the dose–response relationship between the number of years exposed to the farm environment and symptoms. As no prior information was available on whether the association was linear, we used generalized additive modelling (smoothing; SAS 9.1 PROC GAM); these models extend a linear (parametric) model by allowing some or all linear functions to be replaced by arbitrary smoothed functions. The advantage of this approach, compared to conventional linear regression, is that the dose–response relationship can be evaluated in greater detail, without applying *a priori* assumptions about its shape.

Results

The 2509 farming families (response rate, 77.8%) and 1001 reference families (response rate, 67.0%) that participated included 4288 adult farmers and 1328 adult subjects from the reference group (Fig. 1). Compared with the farmers, the reference group was younger, had a lower proportion of males, and a higher proportion of Māori and Pacific people. The reference group also included more smokers (Table 1). When comparing those who responded to the postal survey and those who completed the survey by phone, we found statistically significant differences in prevalence for some symptoms, but with the exception of shortness of breath in the reference population, the differences were very small (Table 2).

Asthma symptoms, hay fever and eczema were significantly less prevalent in farmers, with only minor differences among horticulture, sheep and beef, and dairy farmers (Table 3). The majority (>90%) of subjects who reported that they had ever had asthma had this confirmed by a doctor, and restricting the analyses to those who were diagnosed by a doctor did not change the results (Table 3). This was also the case for all subsequent

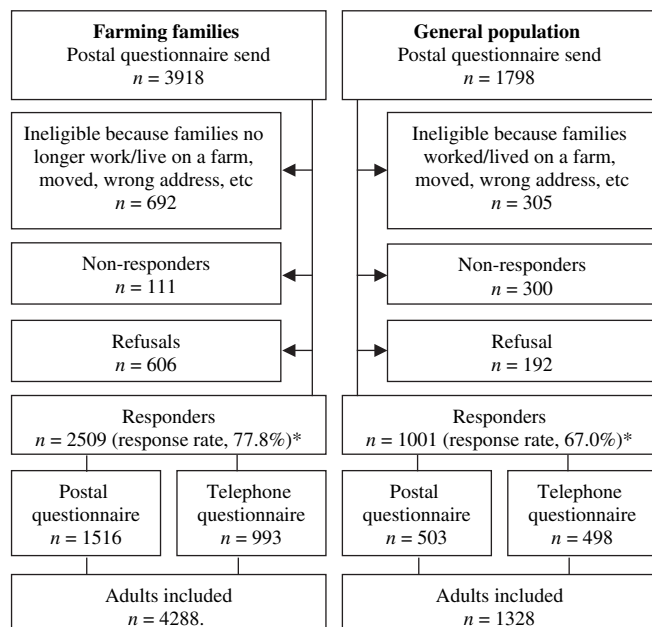


Figure 1. Flow diagram describing subject recruitment, exclusion and refusals. *Response rates were based on the number of responders divided by the total number of eligible families.

Table 1. Demographic and other general characteristics of the study participants by type of farming

	Reference (n = 1328)	Farm (all) (n = 4288)	Horticulture (n = 772)	Sheep and beef (n = 1893)	Dairy (n = 1623)
Age (years, SD)	42.6 (7.3)	48.9 (10.5)**	50.5 (10.4)**	49.6 (10.4)**	47.2 (10.5)**
Sex (% males)	46.0	51.9**	51.6*	52.4**	51.6**
Ethnicity (%)					
New Zealand European	76.8	97.4**	97.3**	96.9**	98.2**
Māori	21.2	2.5	2.5	3.0	1.8
Pacific Islander	2.0	0.2	0.3	0.1	0.1
Current smoker (%)	23.2**	11.6**	9.8**	13.4**	11.6**
Ex smoker (%)	30.7	25.9	35.4	31.9	25.9
Grew up on a farm (%)	22.6	65.2**	49.0**	67.9**	69.8**
Siblings (n)	3.3 (2.6)	3.0 (1.9)**	2.8 (1.7)**	2.9 (1.8)**	3.3 (2.1)
Reported asthma in parents (%)	21.2	14.4**	14.9**	14.7**	13.9**
Reported hay fever in parents (%)	21.8	19.1*	21.0	20.6	16.4**
Reported eczema in parents (%)	13.0	12.6	13.0	12.2	12.8

* $P < 0.05$; ** $P < 0.01$ compared to the reference group.

Table 2. Symptom prevalence stratified by postal questionnaire and telephone interview

	Reference population		Farming population	
	Postal (n = 760)	Telephone (n = 568)	Postal (n = 2870)	Telephone (n = 1418)
Woken by SOB in past 12 months	10.9	15.7*	6.2	7.3
Wheeze in past 12 months	23.6	27.8	15.0	18.3*
Asthma medication in past 12 months	11.0	11.1	6.7	6.7
Asthma ever	22.7	24.1	14.7	15.9
Doctor diagnosed asthma ever	21.7	22.9	13.6	14.8
Nasal allergies including hay fever ever	35.8	36.6	33.5	29.0
Eczema ever	24.3	28.7	20.7	20.7

Values are expressed in percentage. SOB, shortness of breath.

* $P < 0.05$ compared to the postal questionnaire.

analyses and we therefore only report the results for ‘ever asthma’.

After adjustment for potential confounders, current farming remained inversely associated with asthma symptoms, but the associations with hay fever and eczema became weaker. Having grown up on a farm

was also associated with a lower prevalence of asthma symptoms. The protective effect of farming on asthma symptoms was somewhat stronger in women than in men (Table 4). Further adjustments for number of siblings, family history of asthma, hay fever and eczema did not significantly alter the results (data not shown).

For all asthma symptoms, the strongest reduced risks were in those subjects with both current and childhood farm exposure (shortness of breath OR 0.50, CL 0.39–0.66; wheeze OR 0.60, CL 0.49–0.73; asthma medication OR 0.48, CL 0.37–0.63; asthma ever OR 0.56, CL 0.46–0.68; Fig. 2). Subjects with current exposure only had an intermediate risk (OR 0.63, CL 0.47–0.84; OR 0.80, CL 0.65–0.99; OR 0.68, CL 0.51–0.9; OR 0.69, CL 0.56–0.85 respectively), whereas those with only childhood exposure had no or only a slightly reduced risk (OR 0.97, CL 0.65–1.44; OR 1.01, CL 0.75–1.34; OR 0.78, CL 0.51–1.19; OR 0.87, CL 0.63–1.19 respectively). A significantly reduced risk for those with both current and childhood exposure was also observed for hay fever, but not for eczema (Fig. 2). The results were similar when we stratified the analyses for men and women (data not shown).

Table 3. Symptom prevalence and odds ratios (OR) and 95% confidence intervals (CI) by type of farming.

	Reference, (n = 1328) %	Farm (all) (n = 4288)		Horticulture (n = 772)		Sheep and beef (n = 1893)		Dairy (n = 1623)	
		%	OR [95% CI]	%	OR [95% CI]	%	OR [95% CI]	%	OR [95% CI]
Woken by SOB in past 12 months	12.9	6.6	0.47 [0.39–0.58]*	4.7	0.33 [0.23–0.48]*	7.2	0.52 [0.41–0.66]*	6.7	0.49 [0.38–0.63]*
Wheeze in past 12 months	25.4	16.1	0.56 [0.48–0.66]*	14.9	0.51 [0.41–0.65]*	16.4	0.57 [0.48–0.69]*	16.4	0.58 [0.48–0.69]*
Asthma medication in past 12 months	11.0	6.7	0.58 [0.47–0.71]*	7.3	0.63 [0.46–0.87]*	6.7	0.58 [0.45–0.75]*	6.4	0.55 [0.42–0.71]*
Asthma ever	23.3	15.1	0.58 [0.50–0.68]*	14.3	0.55 [0.43–0.69]*	15.6	0.61 [0.51–0.73]*	14.8	0.57 [0.47–0.69]*
Doctor diagnosed asthma ever	22.2	14.0	0.57 [0.49–0.67]*	13.5	0.55 [0.43–0.70]*	14.4	0.59 [0.49–0.71]*	13.8	0.56 [0.46–0.68]*
Nasal allergies including hay fever ever	36.2	32.0	0.83 [0.73–0.95]*	33.2	0.88 [0.73–1.06]	32.9	0.87 [0.75–1.01]	30.4	0.77 [0.66–0.90]*
Eczema ever	26.2	20.7	0.73 [0.64–0.85]*	19.0	0.66 [0.53–0.83]*	20.7	0.74 [0.62–0.87]*	21.4	0.77 [0.65–0.91]*

SOB, shortness of breath.

* $P < 0.01$ compared to the reference group.

Table 4. Adjusted odds ratio (OR) and 95% confidence interval (CI) for the associations between farm exposures and asthma symptoms, hay fever and eczema

	Woken by SOB in past 12 months†	Wheeze in past 12 months†	Asthma medication in past 12 months†	Asthma ever†	Nasal allergies including hay fever ever†	Eczema ever†
Women						
Current farming	0.58 [0.43–0.79]**	0.67 [0.53–0.84]**	0.59 [0.44–0.79]**	0.62 [0.50–0.78]**	0.97 [0.80–1.17]	0.87 [0.71–1.06]
Grew up on farm	0.77 [0.57–1.03]	0.71 [0.58–0.88]**	0.69 [0.52–0.92]*	0.79 [0.64–0.97]*	0.72 [0.61–0.85]**	0.97 [0.82–1.16]
Men						
Current farming	0.61 [0.42–0.89]**	0.83 [0.64–1.08]	0.79 [0.53–1.19]	0.76 [0.58–0.99]*	0.94 [0.75–1.18]	0.86 [0.65–1.12]
Grew up on farm	0.94 [0.67–1.32]	0.91 [0.72–1.14]	0.75 [0.52–1.07]	0.83 [0.65–1.06]	0.86 [0.71–1.05]	1.00 [0.78–1.28]
Women and men						
Current farming	0.60 [0.47–0.77]**	0.75 [0.63–0.90]**	0.66 [0.52–0.85]**	0.68 [0.56–0.81]**	0.97 [0.84–1.13]	0.86 [0.73–1.02]
Grew up on farm	0.85 [0.68–1.06]	0.80 [0.69–0.94]**	0.73 [0.59–0.91]**	0.82 [0.70–0.96]*	0.78 [0.69–0.89]**	0.98 [0.85–1.13]

Values are expressed as OR [95% CI].

* $P < 0.05$; ** $P < 0.01$; †Mutually adjusted with further adjustments for age, sex (where appropriate), ethnicity and smoking.

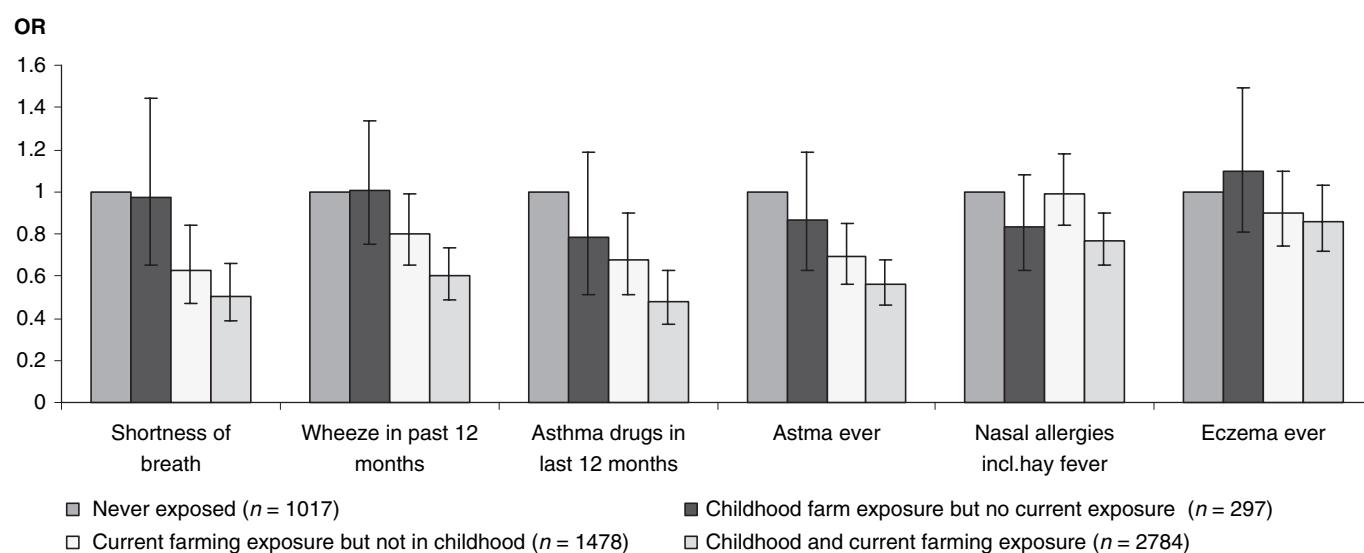


Figure 2. Adjusted odds ratios for the independent and joint effects of current and childhood farm exposure. The analyses were adjusted for age, sex, ethnicity and smoking.

Using nonparametric smoothing techniques, we assessed the association between the total number of years exposed to the farm environment and symptoms. Exposure was defined as the sum of the number of years living on a farm as a child and those worked on a farm as an adult. Years of exposure were inversely associated in a dose-dependent fashion with all asthma symptoms and asthma medication for the first 40–50 years (Fig. 3A–D). After the initial decrease in the first 40–50 years, the prevalence remained constant for current wheeze and asthma medication, as well as asthma ever. In contrast, the prevalence of current shortness of breath increased after the initial decline (Fig. 3A). The dose response for hay fever was very similar to that of wheeze, asthma and asthma medication. The prevalence of eczema was also inversely associated, but rather than levelling of or increasing after 40–50 years, there was a further linear decline in prevalence; the overall decline was, however, very small (Fig. 3F).

We also assessed whether similar dose–response relationships could be found for farm exposure in childhood and adulthood separately. For this purpose we repeated the analyses in two separate groups: (i) all subjects who were never exposed and all subjects who lived on a farm as a child but never worked on a farm in adulthood; and (ii) all subjects who were never exposed and all subjects who had worked on a farm but did not live on a farm as a child. These analyses showed inverse associations between numbers of years of exposure during childhood and asthma ever and hay fever ever, but not current shortness of breath, current wheeze, current asthma medication or eczema ever (data shown only for current wheeze; Fig. 4A). Adult years of exposure were inversely associated with current shortness of breath, current wheeze and hay fever ever, but not current asthma medication and eczema ever. Adult years of exposure also showed an inverse dose response with asthma ever, but only for the first

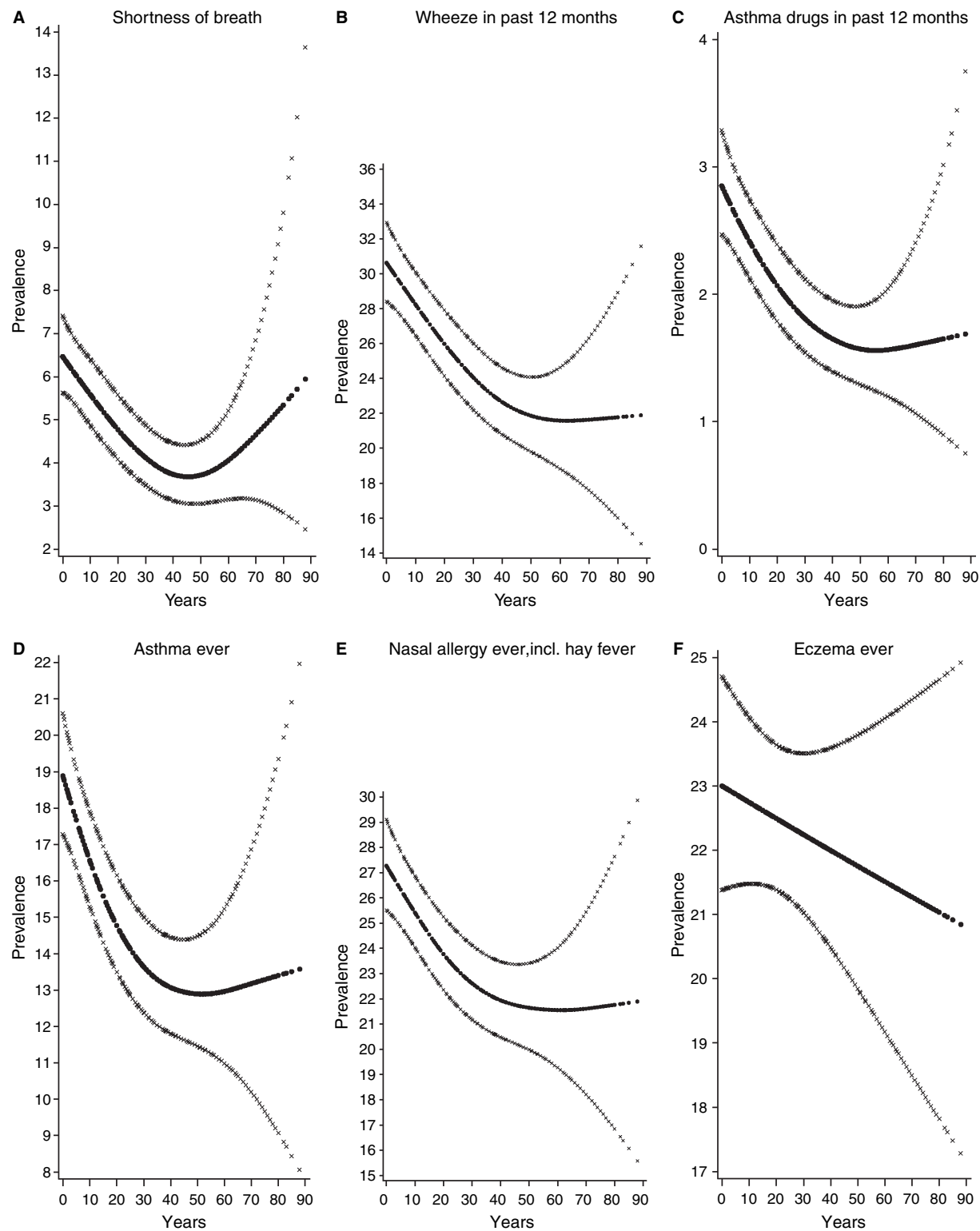


Figure 3. Smoothed associations between combined number of years of exposure to a farming environment in childhood and adulthood and shortness of breath in the past 12 months (A), wheeze in the past 12 months (B), asthma medication in the past 12 months (C), asthma ever (D), nasal allergy including hay fever ever (E) and eczema ever (F). •: nonparametric adjusted model (smooth); + + +: 95% confidence limit. The analyses were adjusted for age, sex, ethnicity and smoking ($n = 5578$).

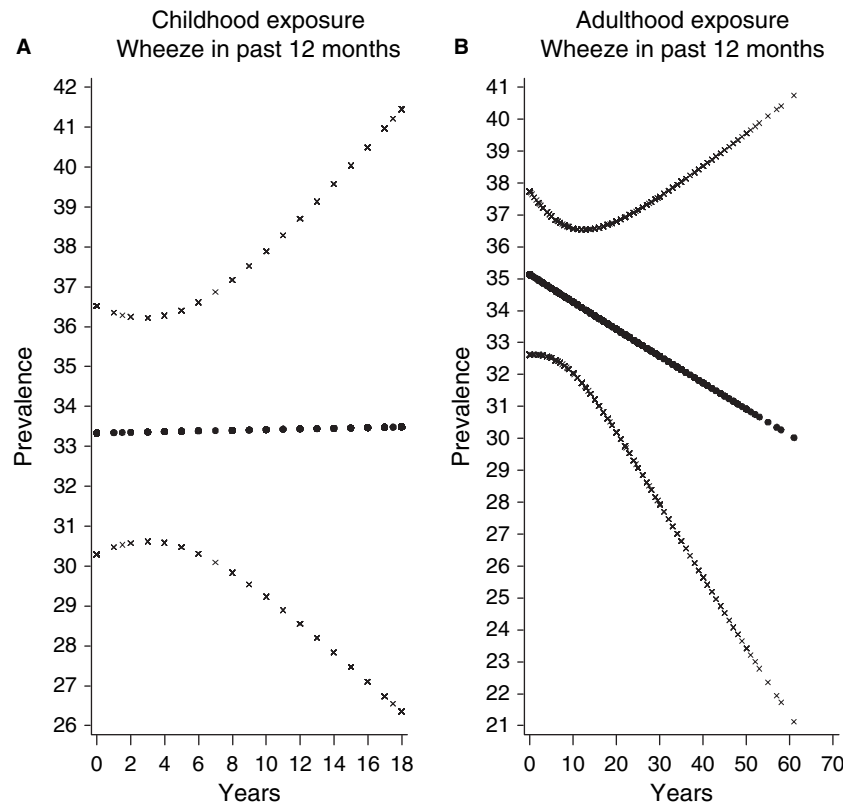


Figure 4. Smoothed associations between number of years of exposure and wheeze in the past 12 months in two separate groups: (i) all subjects who were never exposed and all subjects who lived on a farm as a child but never worked on a farm in adulthood ($n = 1314$) (A); and (ii) all subjects who were never exposed and all subjects who had worked on a farm but did not live on a farm as a child ($n = 2495$) (B).

20 years of exposure (data shown only for current wheeze; Fig. 4B).

Discussion

In this cross-sectional study we found that symptoms of asthma were less common in adult farmers than in a rural reference population. A reduced risk for nasal allergies including hay fever and eczema was also shown, but the association was relatively weak. The strongest protective effects were observed for those farmers who were exposed both currently and during childhood, with this group showing an inverse dose–response trend for cumulative lifetime exposure.

These reduced risks were consistent for all asthma symptoms after adjusting for several confounders including smoking, ethnicity and age. As the differences in ethnicity between the reference and the farmers population were substantial (Table 1), we also repeated the analyses excluding all Māori and Pacific Island people but this did not significantly change the results (data not shown). Parental hay fever and asthma were also significantly more prevalent in the reference population, but further adjustment for this did not change the results. In

addition, excluding the analyses to those whose asthma had been diagnosed by a doctor did not change our results. We also tested for nonresponse bias by comparing symptom prevalence between those who responded to the postal survey and those who only responded after being telephoned. With the exception of shortness of breath in the past 12 months in the reference population we found only marginal differences in symptom prevalence (Table 2) suggesting that nonresponse did not bias our results. In any case, response rates were relatively high (78% for farmers and 67% for the reference population), limiting the potential for significant nonresponse bias.

The finding that adult farmers have a relatively lower prevalence of asthma symptoms is consistent with several other studies (11–14). In our study, current exposures appeared to contribute more than childhood exposures with regard to the observed reduced risk of asthma symptoms (Table 3 and Fig. 2); the lowest risk was for the combination of current and past exposure. Consistent with this finding, other studies have shown that the combination of childhood and current farm exposure was associated with the lowest risk of allergic sensitization (12, 13), and hay fever (22). Similarly, a recent study in Mongolia found that the risks of allergic conjunctivitis and allergic sensitization were the lowest

in subjects living in a village from birth, and were intermediate in subjects who had relocated from a village to a town, compared with those who were living in a town from birth (23). Thus, current exposures may play a role in the continued protection of asthma symptoms later in life. This is plausible as there is substantial evidence that the immune system is not 'fixed' after the first years of life and that 'immune deviation' may take place throughout life (9), although others have argued that immunological reactivity expressed in childhood is fully established in infancy and early childhood (7, 8). Our finding that childhood exposure in the absence of continued exposure provided no or only little protection in adulthood is in agreement with this, and suggests that the immunological processes underlying these protective effects are temporary and reversible.

We also found an inverse dose-response relationship between the combined years of farming exposure in childhood and adulthood and asthma, hay fever and eczema symptoms, with the lowest prevalence in those with 40 or more years of farming exposure. These effects were independent of age and other potential confounders (Fig. 3) and provide further evidence that continuous exposure may be required for optimal protection. It is not clear why the prevalence of shortness of breath in the past 12 months increased after the initial decrease in the first 50 years, but it may be related to occupational respiratory symptoms other than asthma, e.g. chronic obstructive pulmonary disease. However, it should be noted that the number of subjects with a combined exposure of > 50 years is relatively low, resulting in large confidence intervals and subsequent limited interpretability. The inverse associations observed for years of exposure in childhood and adulthood separately (Fig. 4, shown only for current wheeze) were smaller than those for the combined child and adult exposure (Fig. 3), implying that continuing exposure throughout life is more effective in reducing the risk of asthma, hay fever and possibly eczema.

An alternative explanation for the lower prevalence of symptoms in farmers could be self-selection – often referred to as the 'healthy worker effect' – i.e. farmers with symptoms may be more likely to giving up farming than those with no symptoms. This has been suggested by Radon et al. (13), who in a cross-sectional study among adult farmers found that the reduced risk of atopic sensitization associated with the combination of current and past exposure was confined only to those subjects with no symptoms. However, for childhood exposures only, the authors found the same pattern, i.e. a significant reduction in risk of sensitization only in those with no symptoms, and no association in those with symptoms. One would not expect to see this pattern if the reduced risk were due to self-selection in adulthood. Thus, the evidence for a healthy worker effect is weak. Furthermore, in our study the effects were relatively large with

OR of 0.5–0.6 which would have required many affected subjects to give up farming. In fact, in our study only 2.6% indicated that any of their biological relatives had stopped farming, or not become a farmer, because of diseases such as asthma, hay fever or eczema. Selection is therefore unlikely to explain these strong effects. Nonetheless, in the absence of prospective data, a healthy worker effect cannot be excluded.

Studies in farmers' children have suggested that one of the contributing factors to the observed lower prevalence of atopy and symptoms is animal contact (3, 4). In fact, when we analysed the data for the children of the adults included in the current study, we also found that prenatal and current exposure to animals was strongly associated with a reduction in asthma symptoms, hay fever and eczema (17). However, in the children's study, animal contact was also strongly associated with other farm exposures such as hay and grain. In the current analysis in adults, we found no differences in risk among livestock and horticulture farmers. This suggests that protective factors contributing to the lower prevalence in adult farmers may be different from those in farmers' children.

Other studies have shown that farming may be a risk factor for asthma rather than being protective (15, 16). The reasons for these contradictory findings are not clear, but may be related to different asthma phenotypes (i.e. atopic vs nonatopic) as suggested previously (24, 25). Another explanation may be the quantitative and qualitative differences in farming exposure. For instance, in New Zealand livestock is kept out in the field year round, whereas in Europe it is kept in stables for at least part of the year. Farmers in New Zealand are therefore likely to be less highly exposed than their counterparts in Europe.

Previous studies in adult farmers have reported a lower prevalence of atopy (12–14) (see above), suggesting that farming may inhibit the atopic immune response, as has been suggested for farmers' children. If so, then a reduction in both allergic asthma and hay fever and eczema would be expected. However, in our study the inverse associations for farming were strongest for asthma symptoms, whereas the effects for hay fever and eczema were weaker. The reasons for this are not clear, but may point to immunological mechanisms independent of atopy. Alternatively, the environmental risk and/or protective factors for asthma, hay fever and eczema may be different. This is not entirely improbable given that the protective effect of the farming environment may be allergy specific (26). To investigate the potential aetiological mechanisms further, we are currently conducting a phase II study, in a sample of the study participants, involving the collection of information on atopy and indoor exposures to endotoxin and allergens.

In conclusion, although both current and childhood farm exposures may play a role in the observed low prevalence of asthma symptoms in adult farmers, continued exposure may be required to maintain optimal protection.

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