Allergy EUROPEAN JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY

Allergy

ORIGINAL ARTICLE EPIDEMIOLOGY AND GENETICS

Consumption of unpasteurized milk and its effects on atopy and asthma in children and adult inhabitants in rural Poland

B. Sozańska[1], N. Pearce[2,3], K. Dudek[4] & P. Cullinan[5]

[1]1st Department of Pediatrics, Allergology and Cardiology, Wroclaw Medical University, Wroclaw, Poland; [2]London School of Hygiene and Tropical Medicine, London, UK; [3]Centre for Public Health Research, Massey University, Wellington, New Zealand; [4]Institute of Machines Design and Operation, Technical University of Wroclaw, Wroclaw, Poland; [5]Imperial College (NHLI) and Royal Brompton Hospital, London, UK

To cite this article: Sozańska B, Pearce N, Dudek K, Cullinan P. Consumption of unpasteurized milk and its effects on atopy and asthma in children and adult inhabitants in rural Poland. *Allergy* 2013; DOI: 10.1111/all.12147.

Keywords
asthma; atopy; farming; rhinitis; unpasteurized milk.

Correspondence
Barbara Sozańska, MD, 1st Department of Pediatrics, Allergology and Cardiology, Wrocław Medical University, Hoene-Wronskiego 13c, 50-376 Wrocław, Poland.
Tel.: +487703143
Fax: +483281206
E-mail: bsoz@go2.pl

Accepted for publication 11 February 2013

DOI:10.1111/all.12147

Edited by: Bodo Niggemann

Abstract

Background: Consumption of unpasteurized cow's milk has been identified as a possible protective factor for atopy and asthma. Most studies have been conducted among children and in farming populations. We investigated the effects of consumption of unpasteurized milk in early life on atopy, asthma, and rhinitis in village and town inhabitants in a region of Poland and assessed whether any protective effects of milk consumption differed according to place of residence and farming status.

Methods: We surveyed the inhabitants (aged >5 years) of a small town and seven nearby villages in southwest Poland (n = 1700, response rate 88%). Participants (or their parents for those <16 years of age) completed a questionnaire on farm exposures and symptoms of asthma and rhinitis. In particular, information was collected on unpasteurized milk consumption in early life. Atopy was assessed using skin prick tests.

Results: Consumption of unpasteurized milk in the first year of life was inversely associated with atopy and asthma both among town and village inhabitants – town: adjusted odds ratio (aOR) for atopy 0.46 [95% confidence interval (CI) 0.37–0.52] asthma 0.51 (0.32–0.74); villages: atopy 0.59 (0.44–0.70) and asthma 0.59 (0.42–0.74). For atopy, the protective effect was more clearly seen among nonfarmers (0.42; 0.34–0.46) than in farmers (0.82; 0.54–1.11). For doctor-diagnosed hay fever and current rhinitis symptoms, the protective effect was only observed among town inhabitants and/or nonfarmers.

Conclusions: Early-life exposure to unpasteurized milk may protect against atopy, asthma, and related conditions, independently of place of residence and farming status, and in both children and adults.

Many studies have reported protective effects of the farming environment on atopy, asthma, allergic rhinitis, and allergic sensitization (1–4). These appear to be strongest in the early years of life, probably through effects on the developing immune system, although they may persist into adulthood (5, 6). It is unclear which aspects of farming are responsible, but consumption of unpasteurized milk is one possible explanation. Several studies have reported protective effects of drinking unpasteurized milk on atopic sensitization, hay fever, and asthma (1,7–9), although the evidence is inconsistent (10, 11).

The reasons for these possible protective effects are unclear. Homogenization and pasteurization of milk may affect the allergenic or anti-allergenic effects of milk proteins, fat, and vitamin content, and microbial composition (12–15). On the other hand, unpasteurized milk may enhance innate immunity (16–18). Similarly, raw milk is known to have higher viable bacterial counts, which may provide protection, as postulated by the hygiene hypothesis (19). However, the only study to assess this possibility did not find an association with total bacterial count in unpasteurized milk (9).

Most studies have been confined to farming populations, although there is some preliminary evidence from nonfarming environments (7, 20). Moreover, most studies have been conducted in children, and there is little evidence from adults (21).

Previously we have reported the findings of a cross-sectional study conducted in rural southwest Poland, where striking differences in atopy and atopy-related diseases between inhabitants of villages and a nearby small town were seen (22). In contrast to other studies, the differences were greater between town and village inhabitants than between farming and nonfarming study participants. A relatively high proportion of participants had regularly consumed unpasteurized milk in the first year of life. The aims of these analyses were to evaluate the protective effects of consumption of unpasteurized milk in early life on atopy, asthma, and related conditions in this population and to assess whether any protective effects differed according to place of residence and farming status. We have also assessed whether current unpasteurized milk consumption offers additional protective effects.

Materials and methods

Study design and population

The study design has been presented elsewhere (22). The survey was conducted in the small town of Sobotka and in the surrounding villages in southwest Poland. This is a nonindustrialized area, and town inhabitants worked mainly in small family-run businesses. The surrounding villages were small (<300 inhabitants) with most people owning and running small (<10 hectares) farms. All inhabitants aged over 5 years of two randomly selected areas of Sobotka and seven randomly chosen villages (less than 10 km away) were invited to take part; participants were visited in their homes by trained study nurses. All participants over 16 years of age gave written informed consent; for those younger than 16, this was signed by a parent. The study was approved by the Ethics Committees at Wroclaw Medical University and at Imperial College London.

Questionnaire

The questionnaire included the questions on symptoms and diagnoses based on the ISAAC protocol (23). We defined a household as 'farming' if at least one of the family members was a farmer. We also enquired into farm-related exposures in the first year of life and, currently, including the frequency of consumption of unpasteurized milk, level of education, smoking, and number of siblings.

Skin prick tests

Atopy was defined by skin prick tests (SPTs) for four aeroallergens: house dust mite (*Dermatophagoides pteronyssinus*), mixed grass pollens, mixed tree pollens, and cat fur (ALK-Abelló, Hungerford, Berkshire, UK). A positive result was where the mean wheal diameter was ≥ 3 mm to at least one of the test allergens.

Statistical analyses

Logistic regression was used to estimate prevalence odds ratios that were adjusted for age, sex, first-born status, maternal age, and current smoking. In addition, the analyses for the village and town subgroups were adjusted for farming; similarly, the analyses for the farm and nonfarm subgroups were adjusted for living in a town or village. All analyses were performed with STATISTICA 9.0 (StatSoft Inc., Tulsa, OK, USA).

Results

Of 1928 eligible inhabitants, 1700 (88%) participated in the study, and 1664 (97.9%) of those were tested with skin prick tests; 55% (547) of those currently living in the village but fewer than 1% (7) of Sobotka inhabitants reported that they currently lived on a farm. The proportion of village residents currently living on a farm did not vary by age group or sex.

Most participants from the villages (74%; 735) had lived on a farm in their first year of life; this increased with age (66% in the youngest age group compared with 84% in the oldest). Few of the younger town residents had lived on farms in the first year of life (4% of 6- to 20-year-olds), but this increased with age (70% of those aged ≥ 60 years); 91% of people currently living in a village reported they had lived in a village in their first year of life, a proportion similar in all age groups. Among town inhabitants, few in the younger age groups had lived in a village in their first year of life (7% of 6- to 20-year-olds), but this increased with age (80% of those aged ≥ 60 years).

About 73.5% (730) of village and 58.0% (410) of town inhabitants reported drinking unpasteurized milk in the first year of life ('sometimes or regularly'); most had consumed it regularly (62.8% and 47.5%, respectively). Consumption in early life was more common in older than younger participants (85% of those aged ≥ 60 years and 45% among 6- to 20-year-olds) (Fig. 1). In those aged 40 years or less,

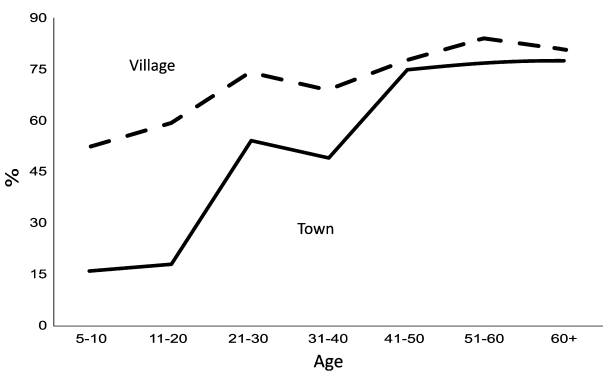

Figure 1 Distribution of unpasteurized milk consumption at age 1 by age in village and town population.

consumption in the first year of life was about twice as high in the villages as in Sobotka (66% and 39%, respectively); 560 (32%) participants had never consumed unpasteurized milk, 806 (46%) had consumed it sometimes or regularly in the first year of life but not currently, 51 (2.9%) consumed it currently but not in the first year of life, and 333 (19%) had consumed it in both periods.

The prevalence of atopy, hay fever diagnosed by a doctor, and rhinoconjunctivitis symptoms not connected with a cold was significantly lower in village than town inhabitants and in farmers compared with nonfarmers (22). For example, the prevalence of atopy was 7.3% in the villages compared with 20.0% in Sobotka and 6.8% in farmers compared with 15.3% in nonfarmers. The prevalence of current rhinitis not connected with cold was much higher than a diagnosis of hay fever both in town and in village; this may be due to underdiagnosis and/or reporting of symptoms that were similar to, but not the same as, hay fever (Table 1).

A diagnosis of asthma was rare, and there was little difference between the villages and Sobotka or between farmers and nonfarmers; however, current and lifetime wheeze was significantly less frequent among farmers (5.1% and 9.0%, respectively) than nonfarmers (7.9% and 14.4%) (Table 1).

Those who regularly drank unpasteurized milk in the first year of life had significantly lower odds ratios (Ors) for atopy (Table 2). This was stronger for town inhabitants (for consumption 'regularly', OR = 0.46, 95% CI 0.37–0.52), but was also evident in village inhabitants (0.59; 0.44–0.70). There was a weaker protective effect in farmers (0.82; 0.54–1.11) than in all nonfarmers (0.42; 0.34–0.46) and those who lived in the village but not on farm (0.44;0.29–0.94). There was an interaction between farming and the frequency of consumption of unpasteurized milk in terms of their effects on atopy ($P = 0.03$). Moreover, the protective effect was only in those who did not live on a farm in the first year of life (OR = 0.50; 0.30–0.84) and not in those who did (OR = 1.19; 0.60–3.19).

Lifetime wheeze was reduced among farmers regularly drinking raw milk (0.75; 0.53–0.95) (Table 3); there was a similar (nonsignificant) effect for current wheeze (0.73; 0.45–1.08). There was little or no evidence for protective effects in other study participants.

Doctor-diagnosed asthma was lower for those drinking raw milk regularly in infancy both among village (0.59; 0.42–0.74) and town (0.51; 0.32–0.74) inhabitants; the protective effect was more pronounced for farmers (0.30; 0.19–0.44) than nonfarmers (0.72; 0.53–0.87) (Table 4).

For doctor-diagnosed hay fever, and to a lesser extent for current rhinitis symptoms, there were also protective effects of unpasteurized milk consumption in the first year of life; however, these were only seen among Sobotka inhabitants and nonfarmers (Table 4).

The protective effect for atopy was stronger in children than in adults (Table 5), both in villages (aOR = 0.59; 0.44–0.70 in children and aOR = 0.69; 0.24–3.70 in adults) and town (0.46; 0.17–0.92 and 0.53; 0.30–0.89, respectively) and in farmers (0.56; 0.04–10.9 in children and 0.82; 0.24–2.71 in adults) and nonfarmers (0.22; 0.07–0.65 and 0.52; 0.30–0.81, respectively).

For those who had never consumed unpasteurized milk, the prevalence of atopy was 20.4% (OR = 1.0; reference category); for consumption in the first year of life, but not currently, the prevalence of atopy was 10.4% (aOR = 0.47; 0.34–0.60); for consumption currently, but not in the first year of life, the prevalence of atopy was 6.1% (aOR = 0.27; 0.10–0.81); for consumption both in the first year of life and currently, the prevalence of atopy was 6.7% (aOR = 0.30; 0.19–0.42). The corresponding odds ratio estimates for current wheeze were 1.29 (0.87–1.88), 0.89 (0.30–2.82), and 0.53 (0.31–0.97), for doctor-diagnosed asthma were 0.85 (0.50–1.46), 1.43 (0.47–4.30), and 0.40 (0.17–0.96), respectively, and for doctor-diagnosed hay fever were 0.60 (0.26–1.39) for early consumption only and 0.51 (0.18–1.43) for early and current consumption. Thus, there was some evidence that continued consumption of unpasteurized milk in adult life offered protective effects in addition to those from early life consumption and that current unpasteurized milk consumption (in the absence of consumption in early life) exerted an independent protective effect.

Discussion

There are four main findings from this study. First, it has confirmed protective effects of unpasteurized milk

Table 1 Prevalence of health outcomes by place of residence and farming status

	Place of residence				Farming status			
Prevalence N (%)	Village ($n = 993$)	Town ($n = 707$)	*P*-value	OR (95% CI)	Farmers ($n = 554$)	Nonfarmers ($n = 1146$)	*P*-value	OR (95% CI)
Atopy	71 (7.3%)	138 (20.0%)	<0.0001	0.32 (0.23–0.43)	37 (6.8%)	172 (15.3%)	<0.0001	0.41 (0.28–0.59)
Current wheeze	64 (6.4%)	54 (7.6%)	0.392	0.83 (0.57–1.21)	28 (5.1%)	90 (7.9%)	0.043	0.62 (0.40–0.97)
Wheeze ever	113 (11.4%)	102 (14.4%)	0.074	0.76 (0.57–1.01)	50 (9.0%)	165 (14.4%)	0.002	0.59 (0.42–0.82)
Asthma*	43 (4.5%)	35 (5.0%)	0.628	0.87 (0.55–1.37)	20 (3.6%)	58 (5.1%)	0.224	0.70 (0.42–1.18)
Hay fever†	30 (3.0%)	50 (7.6%)	<0.0002	0.41 (0.26–0.65)	15 (2.7%)	65 (5.7%)	0.010	0.46 (0.26–0.82)
Current rhinitis‡	257 (25.9%)	329 (46.5%)	<0.0001	0.40 (0.33–0.49)	135 (24.4%)	451 (39.4%)	<0.0001	0.50 (0.40–0.62)

*Asthma diagnosed by a doctor.

†Hay fever diagnosed by a doctor.

‡Current rhinitis not connected with cold.

Table 2 Prevalence, crude and adjusted odds ratio (aOR), and 95% confidence intervals (CI) for the associations between raw milk consumption in first year of life and atopy (a positive, mean wheal diameter $\geq$3 mm, result of skin prick test to at least one of the tested allergens)

	Atopy *n* (%)	Crude OR (95% CI)	Adjusted* OR (95% CI)	Adjusted†,‡ OR (95% CI)
Villages *N* = 973	71 (7.3)			
Raw milk consumed in the first year of life				
Never *n* = 254 (26.1%)	24 (9.4)	1.00 (ref)	1.00 (ref.)	1.00 (ref.)
Sometimes *n* = 105 (10.8%)	12 (11.4)	1.34 (0.65–2.74)	1.37 (0.94–1.81)	1.37 (0.97–1.76)
Regularly *n* = 614 (63.1%)	35 (5.7)	0.56 (0.33–0.97)	0.59 (0.44–0.72)	0.59 (0.44–0.70)
Town *N* = 691	138 (20.0)			
Raw milk consumed in the first year of life				
Never *n* = 291 (42.0%)	80 (27.5)	1.00 (ref)	1.00 (ref.)	1.00 (ref.)
Sometimes *n* = 72 (10.5%)	13 (18.1)	0.58 (0.30–1.11)	0.59 (0.42–0.76)	0.59 (0.43–0.74)
Regularly *n* = 328 (47.5%)	45 (13.7)	0.42 (0.28–0.63)	0.46 (0.37–0.53)	0.46 (0.37–0.52)
Farmers *N* = 541	37 (6.8)			
Raw milk consumed in the first year of life				
Never *n* = 116 (21.4%)	8 (6.9)	1.00 (ref)	1.00 (ref.)	1.00 (ref.)
Sometimes *n* = 57 (10.5%)	8 (14.0)	2.16 (0.77–6.09)	2.11 (1.22–3.29)	2.12 (1.29–3.15)
Regularly *n* = 368 (68.0%)	21 (5.7)	0.82 (0.35–1.90)	0.82 (0.52–1.15)	0.82 (0.54–1.11)
Nonfarmers *N* = 1123	172 (15.3)			
Raw milk consumed in the first year of life				
Never *n* = 429 (38.2%)	96 (22.4)	1.00 (ref)	1.00 (ref.)	1.00 (ref.)
Sometimes *n* = 120 (10.7%)	18 (15.0)	0.61 (0.36–1.06)	0.63 (0.46–0.77)	0.63 (0.48–0.75)
Regularly *n* = 574 (51.1%)	58 (10.1)	0.39 (0.27–0.55)	0.42 (0.34–0.47)	0.42 (0.34–0.46)

*Adjusted odds ratio for age, sex, first-born status, maternal age, and current smoking.
†Adjusted odds ratio for age, sex, first-born status, maternal age, current smoking, and farming (for villages and town).
‡Adjusted odds ratio for age, sex, first-born status, maternal age, current smoking, and town/villages (for farmers and nonfarmers).

Table 3 Prevalence, adjusted odds ratio (aOR), and 95% confidence intervals (CI) for the associations between raw milk consumption in first year of life and wheeze in last 12 months and lifetime wheeze

	Current wheeze *n* (%)	Adjusted*,† OR (95% CI)	Wheeze ever *n* (%)	Adjusted*,† OR (95% CI)
Villages *N* = 993	64 (6.4)		113 (11.4)	
Raw milk consumed in the first year of life				
Never *n* = 263 (26.5%)	17 (6.5)	1.00 (ref)	31 (11.8)	1.00 (ref.)
Sometimes *n* = 106 (10.7%)	6 (5.7)	0.87 (0.33–2.27)	9 (8.5)	0.70 (0.48–0.92)
Regularly *n* = 624 (62.8%)	41 (6.6)	0.99 (0.57–1.83)	73 (11.7)	0.98 (0.77–1.13)
Town *N* = 707	54 (7.6)		102 (14.4)	
Raw milk consumed in the first year of life				
Never *n* = 297 (42.0%)	21 (7.1)	1.00 (ref)	42 (14.1)	1.00 (ref.)
Sometimes *n* = 74 (10.5%)	5 (6.7)	0.95 (0.35–2.62)	11 (14.9)	1.07 (0.75–1.38)
Regularly *n* = 336 (47.5%)	28 (8.3)	1.15 (0.66–2.15)	49 (14.6)	1.01 (0.79–1.17)
Farmers *N* = 554	28 (5.1)		50 (9.0)	
Raw milk consumed in the first year of life				
Never *n* = 123 (22.2%)	7 (5.7)	1.00 (ref)	13 (10.6)	1.00 (ref.)
Sometimes *n* = 58 (10.5%)	4 (6.9)	1.22 (0.67–1.98)	6 (10.3)	0.98 (0.60–1.46)
Regularly *n* = 373 (67.3%)	17 (4.6)	0.73 (0.45–1.08)	31 (8.3)	0.75 (0.53–0.95)
Nonfarmers *N* = 1146	90 (7.9)		165 (14.4)	
Raw milk consumed in the first year of life				
Never *n* = 437 (38.1%)	31 (7.1)	1.00 (ref)	60 (13.7)	1.00 (ref.)
Sometimes *n* = 122 (10.6%)	7 (5.7)	0.79 (0.51–1.12)	14 (11.5)	0.82 (0.60–1.01)
Regularly *n* = 587 (51.2%)	52 (8.8)	1.23 (0.96–1.42)	91 (15.5)	1.12 (0.91–1.24)

*Adjusted odds ratio for age, sex, first-born status, maternal age, current smoking, and farming (for villages and town).
†Adjusted odds ratio for age, sex, first-born status, maternal age, current smoking, and town/villages (for farmers and non-farmers).

Table 4 Prevalence, adjusted odds ratio (aOR), and 95% confidence intervals (CI) for the associations between raw milk consumption in first year of life and asthma ever diagnosed by the doctor, rhinoconjunctivitis not connected with cold in the last 12 months, and doctor diagnosis of hay fever ever

	Doctor-diagnosed asthma *n* (%)	Adjusted*·† OR (95% CI)	Current rhinitis symptoms *n* (%)	Adjusted*·† OR (95% CI)	Doctor-diagnosed hay fever *n* (%)	Adjusted*·† OR (95% CI)
Villages *N* = 993	43 (4.5)		257 (25.9)		30 (3.0)	
Raw milk consumed						
Never *n* = 263 (26.5%)	16 (6.5)	1.00 (ref)	64 (24.3)	1.00 (ref.)	6 (2.3)	1.00 (ref)
Sometimes *n* = 106 (10.7%)	4 (3.9)	0.59 (0.35–0.89)	29 (27.4)	1.19 (0.91–1.40)	6 (5.7)	2.58 (1.47–4.11)
Regularly *n* = 624 (62.8%)	23 (3.8)	0.59 (0.42–0.74)	164 (26.3)	1.11 (0.92–1.21)	18 (2.9)	1.29 (0.83–1.81)
Town *N* = 707	35 (5.0)		329 (46.5)		50 (7.6)	
Raw milk consumed						
Never *n* = 297 (42.0%)	18 (6.1)	1.00 (ref)	146 (49.2)	1.00 (ref.)	33 (11.1)	1.00 (ref)
Sometimes *n* = 74 (10.5%)	6 (8.1)	1.37 (0.86–1.97)	40 (54.1)	1.22 (0.94–1.43)	4 (5.4)	0.44 (0.27–0.65)
Regularly *n* = 336 (47.5%)	11 (3.3)	0.51 (0.32–0.74)	143 (42.5)	0.78 (0.65–0.84)	13 (3.9)	0.34 (0.24–0.43)
Farmers *N* = 554	20 (3.6)		135 (24.4)		15 (2.7)	
Raw milk consumed						
Never *n* = 123 (22.2%)	8 (6.5)	1.00 (ref)	28 (22.8)	1.00 (ref.)	3 (2.4)	1.00 (ref)
Sometimes *n* = 58 (10.5%)	4 (6.9)	1.06 (0.61–1.65)	14 (24.2)	1.07 (0.75–1.38)	3 (5.2)	2.14 (1.05–3.93)
Regularly *n* = 373 (67.3%)	8 (2.1)	0.30 (0.19–0.44)	93 (24.9)	1.12 (0.87–1.30)	9 (2.9)	0.96 (0.52–1.60)
Nonfarmers *N* = 1146	58 (5.1)		451 (39.4)		65 (5.7)	
Raw milk consumed						
Never *n* = 437 (38.1%)	26 (5.9)	1.00 (ref)	182 (41.6)	1.00 (ref.)	36 (8.2)	1.00 (ref)
Sometimes *n* = 122 (10.6%)	6 (4.9)	0.81 (0.51–1.15)	55 (45.1)	1.18 (0.95–1.33)	7 (5.7)	0.68 (0.44–0.94)
Regularly *n* = 587 (51.2%)	26 (4.4)	0.72 (0.53–0.87)	214 (36.5)	0.82 (0.70–0.86)	22 (3.7)	0.45 (0.34–0.54)

*Adjusted odds ratio for age, sex, first-born status, maternal age, current smoking, and farming (for villages and town).
†Adjusted odds ratio for age, sex, first-born status, maternal age, current smoking, and town/villages (for farmers and nonfarmers).

consumption in the first year of life on the subsequent development of atopy. These protective effects occurred in all study participants, that is, farmers and nonfarmers, and village and Sobotka participants. Second, it has found similar (weaker) protective effects of current milk consumption. Third, it has also found protective effects for doctor-diagnosed asthma (in all participants) and weaker (and in some cases nonstatistically significant) protective effects for current wheeze and wheeze ever in farmers, but not in other study participants. Fourthly, it has identified protective effects for doctor-diagnosed hay fever and (to a lesser extent) current rhinitis symptoms, in town (but not village) inhabitants and in nonfarmers (but not farmers).

Some of the limitations of this data should be considered. We conducted objective measurements of atopy, but not asthma and hay fever. The questionnaire was identical for participants at all ages, but we cannot exclude the possibility of differences in interpretation of symptoms at different ages. Moreover, we cannot rule out recall bias, particularly for the questions about early-life exposures, although we tried to minimize this by asking mothers about the first year of life of their children. The cross-sectional nature of the study limits the interpretation of our findings; however, it is likely that the early-life exposures preceded the development of symptoms and certainly preceded the diagnosis of asthma. On the other hand, a strength of this study is its relatively high response rates.

Bearing these strengths and limitations in mind, the findings of this study are of considerable interest. This is one of the first studies of unpasteurized milk consumption in which the majority of participants were not farmers and in which the majority were adults. Most previous studies have involved farming populations, although some have indicated that these effects are independent of other farm/rural exposures (1, 7, 20). In our population, almost three-quarters of villagers and more than half of the town inhabitants had consumed unpasteurized milk in the first year of life. The distinction between villagers and townspeople diminished with age, and the higher rates of unpasteurized milk consumption at age 1 in older town residents probably reflects their higher frequency of sometime rural living, a 'cohort effect'. However, we were unable to assess this hypothesis directly, as this was a cross-sectional study.

As noted above, in previous studies, the findings have been inconsistent. In our study, the protective effects of unpasteurized milk consumption were observed for atopy and doctor-diagnosed asthma in all study groups. For current or lifetime wheeze, the protection was only present among farmers; for doctor-diagnosed hay fever and current rhinitis symptoms, it was only present among town inhabitants and nonfarmers.

Table 5 Adjusted odds ratio (aOR) and 95% confidence intervals (CI) for the associations between regular raw milk consumption in the first year of life and atopy, wheeze in the last 12 months, lifetime wheeze, asthma ever diagnosed by the doctor, rhinoconjunctivitis not connected with cold in the last 12 months, and doctor diagnosis of hay fever ever in children and adults

	Children Adjusted OR (95% CI)	Adults Adjusted OR (95% CI)
Atopy		
Villages	0.59 (0.44–0.70)	0.69 (0.24–3.70)
Town	0.46 (0.17–0.92)	0.53 (0.30–0.89)
Farmers	0.56 (0.04–10.9)	0.82 (0.24–2.71)
Nonfarmers	0.22 (0.07–0.65)	0.52 (0.30–0.81)
Current wheeze		
Villages	0.46 (0.04–5.07)	0.90 (0.41–1.97)
Town	0.42 (0.02–7.62)	1.49 (0.25–8.87)
Farmers	0.16 (0.02–1.46)	1.08 (0.18–6.69)
Nonfarmers	0.84 (0.19–3.64)	1.27 (0.69–2.32)
Wheeze ever		
Villages	0.89 (0.36–2.18)	0.89 (0.49–1.57)
Town	0.18 (0.01–3.18)	1.34 (0.72–2.48)
Farmers	0.60 (0.16–2.19	0.97 (0.37–2.53)
Nonfarmers	0.55 (0.21–1.45)	1.25 (0.76–2.21)
Doctor-diagnosed asthma		
Villages	0.62 (0.19–1.99)	0.57 (0.25–1.31)
Town	0.47 (0.03–8.50)	0.69 (0.27–1.75)
Farmers	0.06 (0.00–1.17)	0.62 (0.16–2.40)
Nonfarmers	1.17 (0.40–3.46)	0.68 (0.34–1.37)
Current rhinitis symptoms		
Villages	0.85 (0.46–1.59)	1.07 (0.70–1.62)
Town	0.17 (0.04–0.80)	0.86 (0.59–1.26)
Farmers	0.96 (0.39–2.35)	1.05 (0.58–1.91)
Nonfarmers	0.31 (0.16–0.60)	0.90 (0.66–1.23)
Doctor-diagnosed hay fever		
Villages	0.70 (0.18–2.65)	4.21 (0.55–32.3)
Town	0.17 (0.01–3.85)	0.34 (0.16–0.72)
Farmers	0.68 (0.09–4.98)	1.67 (0.20–13.8)
Nonfarmers	0.29 (0.07–1.28)	0.50 (0.26–0.95)

Adjusted odds ratio for age, sex, first-born status, maternal age, current smoking, town/villages (for farmers and nonfarmers), and farming (for villages and town).

Furthermore, drinking unpasteurized milk early in life did not explain the protective effect of farming on atopy; both factors (farming and unpasteurized milk) were independently protective.

We can only speculate about the possible etiological mechanisms for the observed associations. It is possible that the processing of milk differs between farmers and urban/nonfarmers and that this may influence its protective properties on different outcomes and in different environments. In a recently published study, Loss et al. reported that consumption of unpasteurized farm milk was inversely associated with atopy and asthma, but that heated farm milk was not associated with these outcomes (9). In the PASTURE study, differences in the storage conditions and temperature during transportation of raw milk, influencing endotoxin levels in samples, were reported between farming and nonfarming families (24).

Previous studies of associations between exposure to farm environments in early life and atopic sensitization and asthma in adulthood have yielded inconsistent results. There are studies indicating that rural/farming childhood may decrease the risks of atopy and asthma (5, 25), although long-term continual exposure may be required to maintain optimal protection (6, 26). In our study, there was also evidence that continued consumption of unpasteurized milk in adulthood offered additional protective effects; this is consistent with other evidence indicating that farming in adult life may additionally offer protective effects (6). However, some studies have suggested that farming may in fact be a risk factor for asthma in adults (27). Even less is known about the possible protective role of unpasteurized milk consumption in infancy in adult populations. In the study of young adults by Radon et al., no independent protection of unpasteurized milk on atopy was seen (21).

While the possibility of using the protective components of farm milk in primary prevention of allergic diseases and asthma has great potential, it is currently a distant prospect. The mechanism of protection is unclear, but may be related to bacterial composition (12), protective protein (9) or fat components (14), and the methods of processing milk (9, 14). With the accumulating body of evidence, the nature of the protective effects of farm milk consumption has become more complex, depending on different phenotypes and different populations. However, our study has added to this body of evidence, particularly by demonstrating strong protective effects, of unpasteurized milk consumption, particularly for atopy, in both farming and nonfarming families and in both children and adult participants. These protective effects appear to be strongest for consumption in early life, but continued consumption in adult life may provide additional benefits.

Acknowledgments

This work was partly funded by the Fifth Programme of the European Union (QLK4-CT-2000-00263) and supported by a grant from National Science Centre of Poland (DEC-2011/01/B/NZ7/05464). The Centre for Public Health Research is supported by a Programme Grant from the Health Research Council of New Zealand.

Authors' contributions

BS, NP and PC designed the study. BS and PC conducted the study and managed data collection. KD performed the statistical analyses. BS, NP, and PC wrote the manuscript. All authors contributed to the interpretation of the results, editing of the manuscript, and have approved the final manuscript.

Conflict of interest

BS, NP, KD, and PC have no conflict of interest.

References

1. Riedler J, Braun-Fahrlander C, Eder W, Schreuer M, Waser M, Maisch S et al. Exposure to farming in early life and development of asthma and allergy: a cross-sectional survey. *Lancet* 2001;**358**:1129–1133.
2. Douwes J, Cheng S, Travier N, Cohet C, Niesink A, McKenzie J et al. Farm exposure in utero may protect against asthma, hay fever and eczema. *Eur Respir J* 2008;**32**: 603–611.
3. Illi S, Depner M, Genuneit J, Horak E, Loss G, Strunz-Lehner C et al. Protection from childhood asthma and allergy in Alpine farm environments - The GABRIEL Advanced Studies. *J Allergy Clin Immunol* 2012;**129**:1470–1477.
4. Brunekreef B, von Mutius E, Wong GK, Odhiambo JA, Clayton TO. ISAAC Phase Three Study Group. Early life exposure to farm animals and symptoms of asthma, rhinoconjunctivitis and eczema: an ISAAC Phase Three Study. *Int J Epidemiol* 2012;**41**:753–761.
5. Lampi J, Canoy D, Jarvis D, Hartikainen AL, Keski-Nisula L, Jarvelin MR et al. Farming environment and prevalence of atopy at age 31: prospective birth cohort study in Finland. *Clin Exp Allergy* 2011;**41**:987–993.
6. Douwes J, Travier N, Huang K, Cheng S, McKenzie J, Le Gros G et al. Lifelong farm exposure may strongly reduce the risk of asthma in adults. *Allergy* 2007;**62**: 1158–1165.
7. Waser M, Michels KB, Bieli C, Floistrup H, Pershagen G, von Mutius E et al. Inverse association of farm milk consumption with asthma and allergy in rural and suburban populations across Europe. *Clin Exp Allergy* 2006;**37**:661–670.
8. Perkin MR, Strachan D. Which aspects of the farming lifestyle explain the inverse association with childhood allergy? *J Allergy Clin Immunol* 2006;**117**:1374–1381.
9. Loss G, Apprich S, Waser M, Kneifel W, von Mutius E, Genuneit J et al. The protective effect of farm milk consumption on childhood asthma and atopy: The GABRIELA study. *J Allergy Clin Immunol* 2011;**128**:766–773.
10. Wickens K, Lane JM, Fitzharris P, Siebers R, Riley G, Douwes J et al. Farm residence and exposures and the risk of allergic diseases in New Zealand children. *Allergy* 2002;**57**:1171–1179.
11. Remes ST, Iivanainen K, Koskela H, Pekkanen J. Which factors explain the lower prevalence of atopy amongst farmers' children? *Clin Exp Allergy* 2003;**33**:427–434.
12. Perkin MR. Unpasteurized milk: health or hazard? *Clin Exp Allergy* 2007;**37**:627–630.
13. Roth-Walter F, Berin MC, Arnaboldi P, Escalante CR, Dahan S, Rauch J et al. Pasteurization of milk proteins promotes allergic sensitization by enhancing uptake through Peyer's patches. *Allergy* 2008;**63**: 882–890.
14. Pfefferle PI, Buchele G, Blumer N, Roponen M, Ege M, Krauss-Etschmann S, et al. Cord blood cytokines are modulated by maternal farming activities and consumption of farm dairy products during pregnancy: the PASTURE Study. *J Allergy Clin Immunol* 2010;**125**:108–115 e1-3.
15. Michalski MC. On the supposed influence of milk homogenization on the risk of CVD, diabetes and allergy. *Br J Nutr* 2007;**97**: 598–610.
16. Puddu P, Valenti P, Gessani S. Immunomodulatory effects of lactoferrin on antigen presenting cells. *Biochimie* 2009;**91**: 11–18.
17. Rusu D, Drouin R, Pouliot Y, Gauthier S, Poubelle PE. A bovine whey protein extract can enhance innate immunity by priming normal human blood neutrophils. *J Nutr* 2009;**139**:386–393.
18. Rusu D, Drouin R, Pouliot Y, Gauthier S, Poubelle PE. A bovine whey protein extract stimulates human neutrophils to generate bioactive IL-1Ra through a NF-kappaB- and MAPK-dependent mechanism. *J Nutr* 2010;**140**:382–391.
19. Braun Fahrlander C, von Mutius E. Can farm milk consumption prevent allergic diseases? *Clin Exp Allergy* 2011;**41**:29–35.
20. Barnes M, Cullinan P, Athanasaki P, MacNeill S, Hole AM, Harris D et al. Crete: does farming explain urban and rural differences in atopy? *Clin Exp Allergy* 2001;**31**:1822–1828.
21. Radon K, Windstetter D, Eckart J, Dressel H, Leitritz L, Reichert J et al. Farming exposure in childhood, exposure to markers of infections and the development of atopy in rural subjects. *Clin Exp Allergy* 2004;**34**:1178–1183.
22. Sozanska B, Macneill SJ, Kajderowicz-Kowalik M, Danielewicz H, Wheatley M, Newman Taylor AJ et al. Atopy and asthma in rural Poland: a paradigm for the emergence of childhood respiratory allergies in Europe. *Allergy* 2007;**62**:394–400.
23. Asher MI, Keil U, Anderson HR, Beasley R, Crane J, Martinez F et al. International Study of Asthma and Allergies in Childhood (ISAAC): rationale and methods. *Eur Respir J* 1995;**8**:483–491.
24. Gehring U, Spithoven J, Schmid S, Bitter S, Braun-Fahrländer C, Dalphin JC et al. Endotoxin levels in milk samples from farming and non-farming families –the Pasture study. *Environ Int* 2008;**34**:1132–1136.
25. Wennergren G, Ekerljung L, Alm B, Eriksson J, Lotvall J, Lundback B. Asthma in late adolescence-farm childhood is protective and the prevalence increase has leveled off. *Pediatr Allergy Immunol* 2010;**21**: 806–813.
26. Douwes J, Brooks C, Pearce N. Protective effects of farming on allergies and asthma: have we learnt anything since 1873? *Expert Rev Clin Immunol* 2009;**5**:213–219.
27. Kogevinas M, Anto JM, Sunyer J, Tobia A, Kromhout H, Burney P. Occupational asthma in Europe and other industrialized areas: a population-based study. European Community Respiratory Health Survey Study Group. *Lancet* 1999;**353**:1750–1754.