Raw milk consumption and other early-life farm exposures and adult pulmonary function in the Agricultural Lung Health Study

ABSTRACT

Literature suggests that early exposure to the farming environment protects against atopy and asthma; few studies have examined pulmonary function. We evaluated associations between early-life farming exposures and pulmonary function in 3061 adults (mean age=63) from a US farming population using linear regression. Childhood raw milk consumption was associated with higher FEV_1 (β=49.5 mL, 95% CI 2.8 to 96.1 mL, p=0.04) and FVC (β=66.2 mL, 95% CI 13.2 to 119.1 mL, p=0.01). We did not find appreciable associations with other early-life farming exposures. We report a novel association between raw milk consumption and higher pulmonary function that lasts into older adulthood.

INTRODUCTION

Previous literature suggests that the farming environment protects against childhood asthma and allergy.[1] Along with farm animal contact, raw milk consumption has been an exposure of particular interest.[2] In adults, atopy and, to a lesser degree, asthma have been associated with the early-life farm environment.[3] Studies of early-life farming exposure and adult pulmonary function are few and none have investigated raw milk.[4–6] The two largest studies reported higher FEV_1 or FVC among adults raised on farms.[4 5] Here we investigate associations between early-life farm exposures, including raw milk consumption, and pulmonary function in an adult US farming population.

METHODS

As described previously,[3 7] the Agricultural Lung Health Study (ALHS) is a case–control study of current asthma among farmers and their spouses nested within the prospective Agricultural Health Study (AHS data releases P3REL201209.00, PIREL201209.00 and AHSREL201304.00). Pulmonary function (FEV_1, FVC and FEV_1/FVC) was measured by trained staff during in-home visits with an EasyOne Spirometer (NDD Medical Technologies, Chelmsford, Massachusetts, USA) based on the American Thoracic Society guidelines. Information on early-life exposures was obtained by questionnaire. Raw milk consumption was determined from the following prompt and question: 'We are also interested in whether you ever drank raw or unpasteurized milk, also referred to as 'farm milk'. Have you ever drank raw milk?' Wording of questions for other early-life exposures, including timing of raw milk consumption, is available in online supplementary table 1. This analysis includes 3061 individuals (from 3301 enrolled in ALHS during 2009–2013) with complete data on early-life exposures and covariates, and whose FVC values had a quality attribute of 'C' or better.[8]

Using linear regression we estimated betas and 95% CI for associations between early-life exposures and FEV_1 (in mL), FVC (in mL) and FEV_1/FVC (as a percent) adjusting for age, age^2, height, height^2, sex, race (white, non-white), state (Iowa, North Carolina), smoking status (current, former, never), pack-years of cigarette smoking and current asthma status (case, non-case). FVC models also included weight. Covariates were selected based on previous research on modelling pulmonary function[9] and ALHS analyses.[3 7] Since we analysed actual values for FEV_1 and FVC, we included all variables from standard prediction equations,[9] including race despite the small number of non-white individuals in ALHS.

RESULTS

Approximately half of participants were male farmers and half were female spouses (see online supplementary table 2). Most (98.4%) were white and 71.0% were from Iowa. The mean age was 63 years. Few currently smoked; 66.5% never smoked. Three-fourths (73.8%) reported their family lived on a farm when they were born, 60.9% that their mother worked with farm animals while pregnant with them (in utero exposure) and 75.6% reported contact with farm animals before age 6 years (table 1).

Raw milk consumption was common (73.4%), and most who drank it (84.1%) started before age 6 (tables 1 and 2). Raw milk consumption was associated with higher FEV_1 (β=49.5 mL, 95% CI 2.8 to 96.1 mL, p=0.04) and FVC (β=66.2 mL, 95% CI 13.2 to 119.1 mL, p=0.01; table 1) but not FEV_1/FVC (β=0.4%, 95% CI −0.4 to 1.1%, p=0.33). Associations were most notable for raw milk consumption beginning before age 6 years (FEV_1: β=51.3 mL, 95% CI 2.8 to 99.8 mL, p=0.04; FVC: β=76.7 mL, 95% CI 21.7 to 131.7 mL, p=0.006; table 2) but were also in the positive direction for the smaller group who started after. Estimates for raw milk consumption beginning before and after age 3 years were similar to age 6 estimates (table 2). Although ability to recall timing of events before age 3 years may be limited, when we examined starting raw milk consumption before age 2 years (1458 individuals), the results were slightly stronger (FEV_1: β=61.3 mL, 95% CI 10.9 to 111.8 mL, p=0.02; FVC: β=83.3 mL, 95% CI 26.1 to 140.5 mL, p=0.004). Consuming raw milk as the main milk source in childhood (79.3% of consumers) was most notably associated with higher FVC (β=53.8 mL, 95% CI 7.2 to 100.5 mL), although the association was also in the positive direction for FEV_1 (β=28.3 mL, 95% CI −12.7 to 69.3 mL).

Among the 2246 individuals who ever drank raw milk, the majority (n=2044; 91.0%) no longer drank it (stopped on average 45.0 years prior), while 168 (7.5%) drank it within the last 10 years (stopped on average 3.3 years prior). Raw milk associations did not change when we accounted for consumption within the last 10 years or excluded 197 ever raw milk drinkers for whom we could not be certain that consumption started in childhood (ie, before age 18 years) (see online supplementary table 3). Among those starting before age 6 we could examine lifetime duration and found no association (see online supplementary table 3). Results for raw milk consumption were also virtually unchanged when we excluded 360 individuals with an FVC quality attribute of 'C' (see online supplementary table 3).

Raw milk associations were more apparent in the much larger group of non-asthmatics (n=1936; FEV_1: β=61.0 mL, 95% CI 4.9 to 117.1 mL; FVC: β=66.2 mL, 95% CI 0.9 to 131.5 mL) than in asthmatics (n=1125; FEV_1: β=23.1 mL, 95% CI −59.3 to 105.5 mL; FVC: β=53.2 mL, 95% CI −36.7 to 143.0 mL), but these differences were not statistically significant (FEV_1: $p_{interaction}$=0.07; FVC: $p_{interaction}$=0.30; see online supplementary table 4). In addition, raw milk associations among non-asthmatics were not materially altered by excluding individuals with childhood asthma (n=25), childhood pneumonia (n=166) or either (n=184), suggesting that the associations were not driven by susceptibility to childhood respiratory illnesses. For example, the estimate for raw milk consumption and FEV_1 among non-asthmatics was 61.1 mL after excluding individuals with either condition. Raw milk associations for FEV_1 were more apparent in women (β=58.0 mL, 95% CI 9.9 to 106.0 mL) than men (β=36.5 mL, 95% CI −48.4 to 121.3 mL), but this difference was of borderline statistical significance ($p_{interaction}$=0.05; see online supplementary

Table 1 Associations between early-life farm exposures and pulmonary function in the Agricultural Lung Health Study, 2009–2013

		FEV_1 (mL)		FVC (mL)		FEV_1/FVC (%)	
Early-life exposures	**N**	**β (95% CI)***	**p Value**	**β (95% CI)***	**p Value**	**β (95% CI)***	**p Value**
Total	3061						
Mother lived on farm while pregnant							
No	771	Referent		Referent		Referent	
Yes	2250	−16.6 (−59.1 to 26.0)	0.45	−11.7 (−60.1 to 36.6)	0.63	−0.6 (−1.2 to 0.1)	0.11
Missing	40						
Mother performed farm activities while pregnant							
No	940	Referent		Referent		Referent	
Yes	1962	6.0 (−33.8 to 45.8)	0.77	−6.6 (−51.9 to 38.8)	0.78	0.3 (−0.3 to 1.0)	0.32
Missing	159						
Mother worked with farm animals while pregnant							
No	957	Referent		Referent		Referent	
Yes	1863	−4.4 (−44.4 to 35.7)	0.83	−9.5 (−55.2 to 36.2)	0.68	0.2 (−0.5 to 0.8)	0.61
Missing	241						
Family lived on farm when born							
No	767	Referent		Referent		Referent	
Yes	2259	−19.7 (−62.3 to 23.0)	0.37	−11.8 (−60.2 to 36.7)	0.63	−0.6 (−1.3 to 0.05)	0.07
Missing	35						
Farm animal exposure before age 3							
No	822	Referent		Referent		Referent	
Yes	1958	−1.8 (−43.4 to 39.8)	0.93	−9.1 (−56.6 to 38.3)	0.71	0.3 (−0.4 to 0.9)	0.46
Missing	281						
Farm animal exposure before age 6							
No	625	Referent		Referent		Referent	
Yes	2314	3.5 (-42.2 to 49.2)	0.88	9.2 (-42.8 to 61.3)	0.73	0.01 (−0.7 to 0.7)	0.99
Missing	122						
Breast fed							
No	1057	Referent		Referent		Referent	
Yes	1439	20.3 (−21.8 to 62.3)	0.35	20.1 (−27.7 to 67.9)	0.41	−0.2 (−0.8 to 0.5)	0.66
Missing	565						
Indoor furry pets before age 6							
No	2204	Referent		Referent		Referent	
Yes	800	−7.3 (−47.6 to 33.1)	0.72	−34.7 (−80.6 to 11.2)	0.14	0.9 (0.2 to 1.5)	0.01
Missing	57						
Mother smoked cigarettes when pregnant							
No	2637	Referent		Referent		Referent	
Yes	275	−25.1 (−87.5 to 37.3)	0.43	−11.6 (−82.8 to 59.7)	0.75	0.1 (−0.9 to 1.2)	0.77
Missing	149						
Parents smoked cigarettes in house before age 6							
No	1362	Referent		Referent		Referent	
Yes	1611	−12.4 (−48.9 to 24.0)	0.50	−21.0 (−62.4 to 20.4)	0.32	0.4 (−0.2 to 1.0)	0.16
Missing	88						
Raw milk							
No	643	Referent		Referent		Referent	
Yes	2246	49.5 (2.8 to 96.1)	0.04	66.2 (13.2 to 119.1)	0.01	0.4 (−0.4 to 1.1)	0.33
Missing	172						

*Estimates represent the difference in mean response (FEV_1 and FVC in millilitres and FEV_1/FVC as a percent) between a subject who experienced the exposure and one who did not, holding all covariates constant. Covariates were selected based on previous research on modelling pulmonary function and Agricultural Lung Health Study analyses and included age, age^2, gender, race, state (Iowa or North Carolina), height, height^2, smoking status, pack-years, asthma status, and for FVC, weight. CIs were calculated as the beta coefficient plus or minus 1.96 times the standard error (β ±1.96×SE).

Table 2 Associations between raw milk exposure and pulmonary function in the Agricultural Lung Health Study, 2009–2013

		FEV_1 (mL)		FVC (mL)		FEV_1/FVC (%)	
Raw milk exposure	**N**	**β (95% CI)***	**p Value**	**β (95% CI)***	**p Value**	**β (95% CI)***	**p Value**
Total	3061						
Raw milk started before or after age 6							
Never drank raw milk	643	Referent		Referent		Referent	
Start before age 6	1888	51.3 (2.8 to 99.8)	0.04	76.7 (21.7 to 131.7)	0.006	0.3 (–0.5 to 1.1)	0.51
Start age 6 or after	336	42.7 (–22.3 to 107.8)	0.20	35.3 (–38.5 to 109.0)	0.35	0.7 (–0.4 to 1.7)	0.23
Missing	194						
Raw milk started before or after age 3							
Never drank raw milk	643	Referent		Referent		Referent	
Start before age 3	1688	51.1 (1.6 to 100.6)	0.04	74.3 (18.2 to 130.4)	0.01	0.3 (–0.5 to 1.1)	0.48
Start age 3 or after	536	46.0 (–11.0 to 103.0)	0.11	53.9 (–10.8 to 118.5)	0.10	0.5 (–0.4 to 1.7)	0.31
Missing	194						
Was raw milk the main milk in childhood							
No	1173	Referent		Referent		Referent	
Yes	1781	28.3 (–12.7 to 69.3)	0.18	53.8 (7.2 to 100.5)	0.02	–0.1 (–0.8 to 0.5)	0.68
Missing	107						
Ever raw milk/main milk in childhood							
Never drank raw milk	643	Referent		Referent		Referent	
Drank raw but not main milk	415	56.9 (–3.8 to 117.6)	0.07	60.6 (–8.2 to 129.5)	0.08	0.7 (–0.3 to 1.7)	0.19
Main milk was raw	1781	45.2 (–4.4 to 94.8)	0.07	66.4 (10.1 to 122.7)	0.02	0.2 (–0.6 to 1.0)	0.56
Missing	222						

*Estimates represent the difference in mean response (FEV_1 and FVC in millilitres and FEV_1/FVC as a percent) between a subject who experienced the exposure and one who did not, holding all covariates constant. Covariates were selected based on previous research on modelling pulmonary function and Agricultural Lung Health Study analyses and included age, age^2, gender, race, state (Iowa or North Carolina), height, height^2, smoking status, pack-years, asthma status, and for FVC, weight. CIs were calculated as the beta coefficient plus or minus 1.96 times the standard error (β ±1.96×SE).

table 4). For FVC, the results differed little by gender (female: β=68.1 mL, 95% CI 14.4 to 121.8 mL; male: β=56.4 mL, 95% CI −40.4 to 153.3 mL; $p_{interaction}$=0.19). No material differences by atopy status (defined as specific Immunoglobulin E (IgE) >0.70 IU/mL to at least one of ten allergens measured in blood[3]) or number of siblings (dichotomised into 0–2 or 3+, used as an indicator of exposure to infections in early-life[10]) were noted (see online supplementary table 4).

Childhood indoor furry pet exposure was associated with modestly higher FEV_1/FVC (β=0.9%, 95% CI 0.2 to 1.5%, p=0.01; table 1). Aside from this, no other early-life farming exposures were associated with adult pulmonary function (table 1). Given the childhood furry pet association, we examined raw milk models additionally adjusted for that exposure, but found no evidence of confounding (FEV_1: β=49.7 mL, p=0.04; FVC: β=67.9 mL, p=0.01).

DISCUSSION

Childhood raw milk consumption was related to higher FEV_1 and FVC in this older adult US farming population. Few previous studies have addressed the relationship between early-life farm exposure and FEV_1 or FVC in adults,[4–6] and none examined early-life raw milk consumption. The two largest studies—the European Community Respiratory Health Survey II (ECRHS II, n=10 201) and a Finnish study (n=5666)—both found that being born or raised on a farm was associated with higher FEV_1 and/or FVC.[4 5] The ECRHS study specifically noted a stronger positive association between living on a farm in childhood and FEV_1 in women than in men,[4] similar to our finding of a slightly stronger raw milk–FEV_1 association in women.

Although we found positive associations of raw milk consumption with both FEV_1 and FVC, we did not see an association with FEV_1/FVC, suggesting that the beneficial effect of raw milk is predominantly on lung growth rather than airway calibre. In support of this hypothesis, we did not see an effect of raw milk consumption on either adult non-atopic asthma or atopic asthma (both compared with individuals with neither asthma nor atopy) in a previous publication.[3] We also observed a slight increase in FEV_1/FVC for indoor furry pets before age 6 years. However, in a previous publication we did not find a protective association between indoor furry pets before age 6 years and either asthma, atopy or their combination.[3]

Mechanisms of our observed association are speculative. Differences in the nutrient composition of raw and commercial milk, including total fat content and specific fatty acid composition,[2] could theoretically influence rates of growth, including the lungs, in childhood. Raw milk contains micro-organisms absent from pasteurised commercial milk; some may influence the developing immune system in ways that could account for the reported protective effect of early raw milk consumption on allergic disease.[2] Several studies have reported that raw milk consumption in pregnancy or childhood leads to greater production of interferon γ (IFNγ) in children.[2 11] In a US birth cohort, higher IFNγ production by stimulated peripheral blood mononuclear cells at age 1 year was related to higher FEV_1 and FVC, but not FEV_1/FVC, at age 8.[12] Elevated IFNγ may protect young children against airway infections, contributing to better pulmonary function in adulthood.

As described in detail in a previous ALHS paper,[3] we sought to enhance the quality of information about early-life exposures

by sending participants questionnaires in advance of home visits, encouraging participants to speak with family members (eg, siblings) and asking about exposures by 6 years of age when memories are more reliably formed. Although we could not directly assess selective entry into our study based on raw milk consumption and pulmonary function, we performed a quantitative selection bias analysis[13] based on childhood farm animal exposure and asthma in a previous publication[3]; we did not find evidence for selection bias from AHS into ALHS. Nevertheless, a biased association could still result if choosing to remain in farming before the initial AHS enrolment period (1993–1997) was jointly related to early-life raw milk consumption and better pulmonary function. Finally, we had limited ability to assess duration of raw milk consumption in the minority who started after age 6 and lacked data on the quantity consumed.

Previous literature examining the hygiene hypothesis in farm environments has identified protective associations with in utero and childhood exposures using several metrics, including farm animal contact and farm work performed by mothers while pregnant, residing on a farm at birth or in childhood, and farm animal contact and farm work performed by individuals during childhood.[1 2] Our study examined similar metrics which, not surprisingly, were highly correlated. The first six variables in table 1 had tetrachoric correlations ranging from 0.84 to 0.99 in ALHS.[3] However, raw milk consumption—the only farming variable that we found to be related to pulmonary function—was less strongly correlated with the other farm variables, with correlations ranging from 0.47 to 0.55.[3] In addition, pulmonary function parameters were correlated with each other to varying degrees; partial correlations, adjusted for age, height, gender and race, were 0.84 for FEV_1 with FVC, 0.60 for FEV_1 with the FEV_1/FVC, and 0.15 for FVC with FEV_1/FVC. Given the hypothesis-driven nature of our research[14 15] and the correlations of several early-life farming exposures as well as pulmonary function measures, we did not correct for multiple comparisons, thereby increasing the possibility of false-positives but reducing the risk of false-negatives.

A strength of our study is the large farming population of older adults, allowing us to assess possible persistence of associations across the life course in the USA. Our data suggest that raw milk consumption, particularly early in life, is associated with better pulmonary function in adulthood.

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