

Food allergy, breastfeeding, and introduction of complementary foods in the New York Old Order Mennonite Community



The prevalence of allergic diseases and asthma has been increasing in developed countries for the past 50 years, likely associated with changes in living conditions that have inhibited certain early-life microbial exposures normally instrumental in the development of the infant immune system. Consistent with this, a large body of data to date suggest that living on farms is associated with a major reduction in the risk of asthma and atopic diseases, such as allergic rhinitis, including studies from Europe^{1,2} and North America among the Indiana Amish.^{3,4} Similarly, our recent study found that an Old Order Mennonite (OOM) Anabaptist community of Swiss German ancestry in Penn Yan, New York, practicing traditional, single-family farming with a lifestyle that included large families, home births, horse-and-buggy transportation, infrequent use of antibiotics, and exposure to unpasteurized farm milk had a significantly lower rate of physician-diagnosed asthma, atopic dermatitis, and allergic rhinitis than the general US population.⁵ However, data on food allergies (FAs) are limited. Self-reported and physician-diagnosed FA is lower in the Amish than in the Wisconsin OOM community but overall lower in both communities than reported in the general population.⁶ However, self-report can significantly overestimate FAs, and additional assessments of dietary intakes have been used to resolve some of the discrepancy,⁷ whereas physician diagnosis of FA likely underestimates FA in these communities. Furthermore, because infant feeding practices may affect the prevalence of FA, we sought to assess the prevalence of FA in the OOM community.⁵

Surveys were distributed to 500 families in the OOM community in fall 2015. The surveys queried self-reported FA of parents and children, time of introduction of solid foods, and length of exclusive and total breastfeeding. Survey questions were adapted from the National Health and Nutrition Examination Survey (NHANES) for comparison between the OOM and general US populations and included the question, “Are you/Is your child allergic or had an allergic reaction to any food? If yes, to which food?” FA was explained to be a reaction that caused rash, hives, difficulty breathing, wheezing, or itching of the eyes, mouth, throat, or skin. Surveys that omitted answers to the questions and those from families with no children were excluded. Data from NHANES 2007–2010 were used to assess population prevalence, using the same Stata statistical script as used by McGowan and Keet⁷ (eMethods).

The response rate was 30.8%, which is low compared with 70% in NHANES face-to-face surveys (<https://aspe.hhs.gov/system/files/pdf/255531/Decliningresponse rates.pdf>). We did not

recontact families who did not return the survey. Data were available for 306 parents and 524 children (1–17 years of age). Demographics of all children are given in eTable 1. Solid food introduction data were reported at the family level as the mean for all children in the family. Breastfeeding rates were compared with the Centers for Disease Control and Prevention’s *Breastfeeding Report Card 2014*.⁸

Among parents, analysis revealed the overall prevalence of self-reported FA to be 3.7% (95% CI, 2.1%–6.5%) in the OOM community compared with 9.8% (95% CI, 8.4%–11.2%) in NHANES 2007–2010 for white adults aged 31 to 64 years ($P < .001$). The NHANES subset was similar to the OOM parents in race and age. Further analyses focused on children alone. In children, self-reported FA prevalence was 4.9% (95% CI, 3.4%–7.1%) in the OOM community and 6.5% (95% CI, 5.7%–7.3%) in NHANES ($P = .22$). Regarding specific FA, significantly lower rates of shellfish, tree nuts, egg, fish, and soy allergy were reported in the OOM community vs NHANES (Fig 1A and eTable 2). All families that indicated having a child with FA were contacted for a telephone interview by the study allergist. A dietary history was taken, and if the child was also avoiding the food in question, the child was classified as likely/possibly having a FA, similar to the report by McGowan and Keet.⁷ We noted a significantly lower prevalence of likely/possible FA in the OOM community of 2.7% (95% CI, 1.6%–4.4%) than in the NHANES of 5.5% (95% CI, 4.7%–6.3%) ($P = .008$). Regarding specific foods, likely/possible FA to shellfish, peanut, wheat, and fish allergy was significantly less in the OOM community (Fig 1B and eTable 2). In a comparison of the OOM community with white-only NHANES participants, the differences remained significant to self-reported FA to tree nuts, egg, and soy and likely/possible FA to any food, egg, and combination of tree nut, peanut, fish, and shellfish (data not shown). The low response rate may reflect enrichment for atopic families; the true prevalence in OOM may be lower than perceived in this study.

Rates of breastfeeding at 6 and 12 months were 96.3% and 69.4% in the OOM community and 55.8% and 26.7% in New York State, respectively (Breastfeeding Report Card⁸). The rates of exclusive breastfeeding at 3 and 6 months were 94.9% and 62.7% in the OOM community and 37.1% and 16.9% in New York State, respectively. The mean length of exclusive breastfeeding in the OOM community was 7.4 months (95% CI, 7.08–7.72 months), and the mean total length of breastfeeding was 13.4 months (95% CI, 13.0–13.7 months). The OOM community introduced solids to their children at the following increasing mean ages: fruits, 7.0 months (95% CI, 6.6–7.5 months); yogurt, 7.1 months (95% CI, 6.6–7.5 months); vegetables, 7.9 months (95% CI, 7.2–8.5 months); kefir, 8.2 months (95% CI, 7.0–9.5 months); grains, 8.4 months (95% CI, 7.9–9.0 months); egg, 8.8 months (95% CI, 8.4–9.3 months); meats, 10.1 months (95% CI, 9.4–10.7 months); soy products, 10.7 months (95% CI, 9.6–11.7 months); milk, 11.3 months (95% CI, 10.9–11.8 months); fish, 14.7 months (95% CI, 13.0–16.3 months); seeds, 15.5 months (95% CI, 13.5–17.5 months); shellfish, 18.5 months (95% CI, 15.1–22.0 months); peanut, 20.7 months (95% CI, 18.7–22.6 months); and tree nuts, 21.0 months (95% CI, 19.5–22.5 months). Interestingly, pureed fruits were the first complementary food (as opposed to grains), and introduction of peanut does not occur until toward the end of the second year. Homemade yogurt pudding and other dairy products often made from unpasteurized milk were introduced in the first year along with kefir in 25% of the infants.

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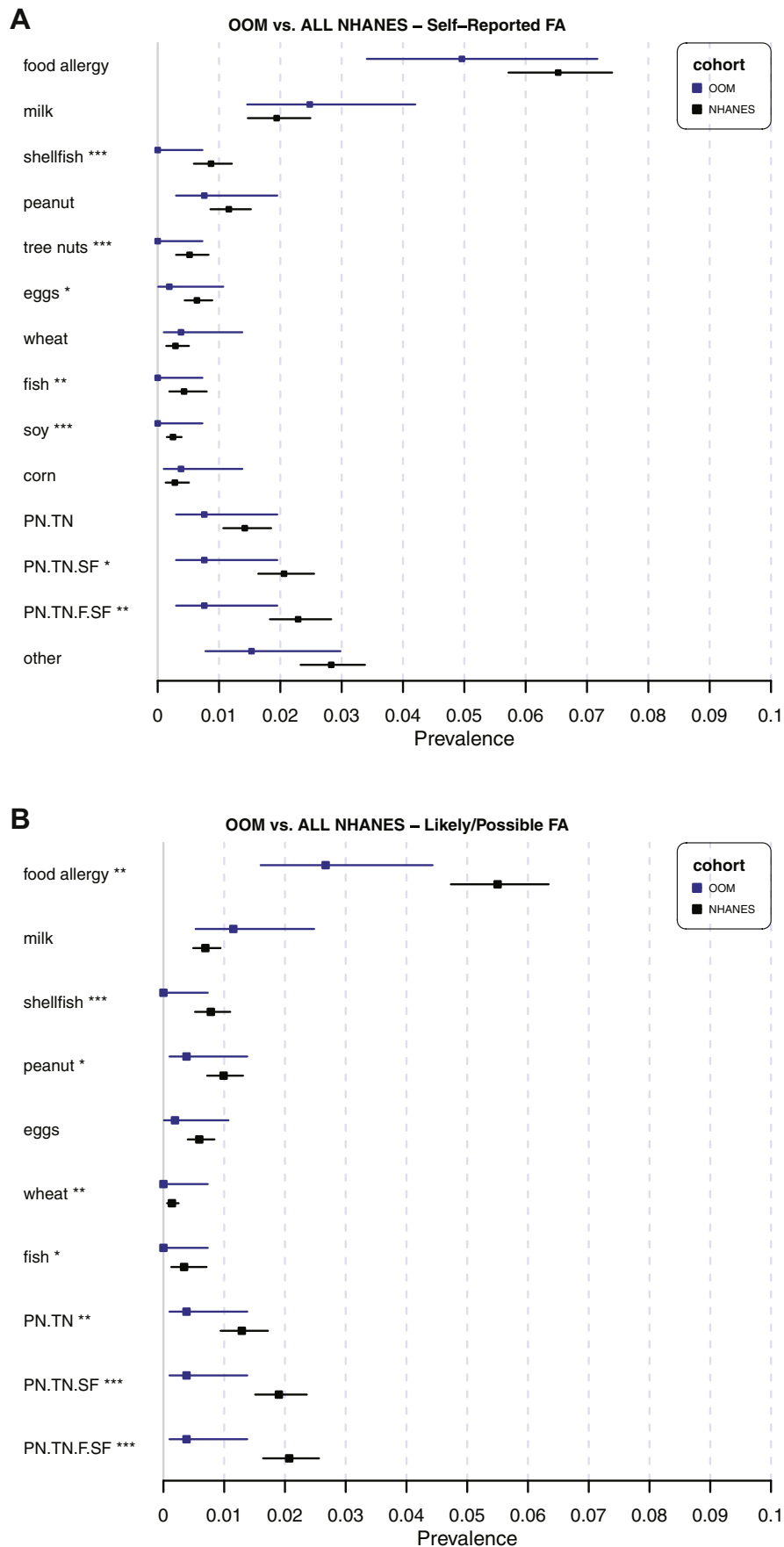


Figure 1. A, Self-reported food allergy (FA) prevalence and 95% CIs for children (aged ≥ 1 and < 18 years) in the Old Order Mennonite (OOM) community vs all National Health and Nutrition Examination Survey (NHANES) 2007–2010 data. B, Likely/possible FA prevalence and 95% CIs after changing allergy status to no allergy for children who reported eating the food to which they reported an allergy in the OOM community vs all NHANES 2007–2010 data. * $P < .05$; ** $P < .01$; *** $P < .001$.

Table 1

National Health and Nutrition Examination Survey Data Files

Short file description	Data file name (prefix)	Notes
Demographics	DEMO	Patient identification number (SEQN), age, sex, etc. Also includes weights and other complex survey variables.
Dietary behavior	DBQ	Food allergy data; milk consumption (30-day food frequency questions). Milk only counted if regular, 2%, 1%, or fat free/skim (not goat's milk, soy milk, etc).
Total nutrient intake file, day 1	DR1TOT	Fish and shellfish consumption (30-day food frequency).
Individual food files (day 1 and day 2)	DR1IFF, DR2IFF	Contains all foods eaten (remembered) from midnight to midnight the day before the questionnaire. Each row is a patient's food item, so each patient has multiple rows in the table.
Food codes	DRXFCD	Translates food codes used in DRxIFF files.

K.M.J. examined the DRXFCD food codes file in Excel and marked the codes considered evidence of consuming peanuts, milk, wheat, and eggs. However, McGowan and Keet¹ only did this for peanuts.

DEMO and DBQ were merged into one file. FA and milk consumption variables were created (0/1). DR1TOT and DRxIFF files were not merged into the main file. Instead the patient's identification numbers (SEQN) were found in which the various foods were eaten. This list of patient identification numbers were then used to create 0/1 flags on the main NHANES data file, including combination allergy variables, such as PN.TN (peanut OR tree nut allergy).

Although many highly allergenic foods, such as peanut, are not introduced to OOM children until the second year of life, these children have lower rates of peanut and many other FAs than the general US population. Protective factors may include vaginal home births and longer duration of breastfeeding or consumption of unpasteurized farm milk^{1,2} exposure to farm animals and stables.¹ Our study provides rationale for engaging the OOM community as a model population for low rates of FA. It remains to be seen whether the same farm-life mechanisms as seen with asthma (ie, increased regulatory T cells,⁹ innate immune system,^{2,4} or greater microbial diversity and endotoxin in house dust¹⁰) can provide protection against the early manifestations of atopic diseases, such as FA.

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Supplementary Data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.jana.2019.12.019>.

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References

1. Riedler J, Braun-Fahrlander C, Eder W, et al. Exposure to farming in early life and development of asthma and allergy: a cross-sectional survey. *Lancet*. 2001; 358(9288):1129–1133.
2. Loss G, Bitter S, Wohlgensinger J, et al. Prenatal and early-life exposures alter expression of innate immunity genes: the PASTURE cohort study. *J Allergy Clin Immunol*. 2012;130(2):523–530.e529.
3. Holbreich M, Genuneit J, Weber J, Braun-Fahrlander C, Waser M, von Mutius E. Amish children living in northern Indiana have a very low prevalence of allergic sensitization. *J Allergy Clin Immunol*. 2012;129(6):1671–1673.
4. Stein MM, Hrusch CL, Gozdz J, et al. Innate immunity and asthma risk in Amish and Hutterite farm children. *N Engl J Med*. 2016;375(5):411–421.
5. Martina C, Looney RJ, Marcus C, Allen M, Stahlhut R. Prevalence of allergic disease in Old Order Mennonites in New York. *Ann Allergy Asthma Immunol*. 2016;117(5):562–563.e1.
6. Tantoco JC, Elliott Bontrager J, Zhao Q, DeLine J, Seroogy CM. The Amish have decreased asthma and allergic diseases compared with old order Mennonites. *Ann Allergy Asthma Immunol*. 2018;121(2):252–253.e251.
7. McGowan EC, Keet CA. Prevalence of self-reported food allergy in the National Health and Nutrition Examination Survey (NHANES) 2007–2010. *J Allergy Clin Immunol*. 2013;132(5):1216–1219.e1215.
8. Centers for Disease Control and Prevention's *Breastfeeding Report Card 2014*. Atlanta, GA: Division of Nutrition, Physical Activity, and Obesity, National Center for Chronic Disease Prevention and Health Promotion; 2015.
9. Lluís A, Depner M, Gaugler B, et al. Increased regulatory T-cell numbers are associated with farm milk exposure and lower atopic sensitization and asthma in childhood. *J Allergy Clin Immunol*. 2014;133(2):551–559.
10. Schuijs MJ, Willart MA, Vergote K, et al. Farm dust and endotoxin protect against allergy through A20 induction in lung epithelial cells. *Science*. 2015; 349(6252):1106–1110.

Supplementary Data

eMethods

Old Order Mennonite Community

The Old Order Mennonite (OOM) community responded to a food allergy (FA) survey. Data were double entered into an Excel spreadsheet² (Microsoft Corp) by 2 individuals and checked for errors. J.P. compiled the adult data and performed first analyses of those results.

The child data were placed in a spreadsheet in which each row represented 1 child. This spreadsheet included columns titled “Current FA,” which listed the allergies for this child, and “McGowan Definition FA,”¹ which flagged those children who did not eat foods for which they self-reported FAs. Note that the McGowan definition was for a child rather than for each separate food the child was reported allergic to. Children included were 1 through 17 years old.

NHANES

For each National Health and Nutrition Examination Survey (NHANES) 2-year cycle (2007–2008 and 2009–2010), the NHANES data files (Table 1) were used (Centers for Disease Control and Prevention, National Center for Health Statistics, 2016).

Prevalence of FA

The prevalence of each FA was calculated. Because the values for each patient are 0 (no allergy) or 1 (allergy), this is a binomial distribution, and therefore, the CIs are skewed. However, as the sample size becomes large and/or the proportion approaches 0.5, the distribution approximates the normal distribution. Nevertheless, we used routines in R, which give the binomial CIs. The differences are usually quite small.

Statistical Analysis

The R statistical system, version 3.5.3 (R Foundation for Statistical Computing) was used. The prevalences in the OOM community were simple means with binomial CIs. The NHANES means were determined using the complex survey procedures in the SURVEY package written by Thomas Lumley.² Because we were using 2 NHANES cycles (2-year sets of data) and therefore had 4 years of data, the weights were divided by 2 to approximate the US population total. Tables and forest plots were used to display the prevalences and CIs. The forest plot was created using the FORESTPLOT package.³

Subtracting Patients Who Ate the Allergic Food

As was done in the study by McGowan and Keet,¹ prevalence of FAs was determined for the entire group and after recoding as not allergic any patient who claimed to have an FA but then was found to have eaten that food. This approach is based on the concept that FAs are more likely to be real if the allergic symptoms are preventing consumption entirely.

Three sources of food consumption were used. The DBQ file contains milk consumption as frequency of consumption in the last 30 days, with the following answers: often, sometimes, rarely, varied, never, refused, and don't know. REFUSED and DON'T KNOW were set to MISSING, and these patients were not included in the without milk analysis. Any other answer but never was considered evidence of consuming milk.

DR1TOT contained Food Frequency Questionnaire 30-day questions regarding fish and shellfish. Unlike milk, fish and shellfish responses were only yes, no, refused, or don't know. The general shellfish question included noncrustaceans, and so, as was done by McGowan and Keet,¹ we only selected crustacean shellfish eaters (ie, crabs, crayfish, lobsters, and shrimp but not mussels, oysters, scallops, and other shellfish).

The 24-hour dietary history files (DR1IFF, DR2IFF) contain the individual foods reported for these two 24-hour periods. The food code lookup file DRXFCF was marked by K.J.S. to identify milk, egg, peanut, and wheat codes. If patients had 1 of these food codes listed in the DR1IFF files, they were marked as a food eater for that food.

Note that DR1TOT contains a field that indicates whether the 24-hour dietary history was considered of acceptable quality. A total of 96 children were flagged as having an unacceptable quality of dietary history. These patients had no records in the DR1IFF files. We excluded these patients from any analyses.

P Values for Differences in Prevalence Between the OOM Community and NHANES

A special method is required to compare the prevalence of FA in the OOM, a small cohort, vs the general population as represented by the NHANES complex survey. We used the method of Lumley and Scott.⁴ The OOM persons are assigned a strata number that was different from the strata used in NHANES. The family identification numbers were used as the OOM sampling units (pseudo-sampling units in NHANES), therefore treating the family as the sampling unit, and so the analyses for individual children are nested within family. Each patient received a weight of 1. *P* values were generated using the survey rank test (svyranktest) function from Lumley's SURVEY package.²

eTable 1

Demographics of OOM and NHANES, 2007–2010 children (1–17 Years Old)

	OOM	NHANES weighted
N	524	70532446
Sex		
Female	50.2%	49.0%
Male	46.0%	51.0%
NA	3.8%	0%
Age		
Mean	7.6	9.1
Median (25th, 75th)	7 (3,11)	9 (5,14)
Race		
Mexican american		14.6%
Other hispanic		6.7%
White	100%	56.9%
Black		14.2%
Other/mixed		7.6%

Abbreviations: NHANES, National Health and Nutrition Examination Survey; OOM, Old Order Mennonite.

References

1. McGowan EC, Keet CA. Prevalence of self-reported food allergy in the National Health and Nutrition Examination Survey (NHANES) 2007–2010. *J Allergy Clin Immunol*. 2013;132(5):1216–1219.e1215.
2. Lumley T. Survey: analysis of complex survey samples. *R package version 3.35-1*. 2019.
3. Lumley T. forestplot: Advanced Forest Plot Using "grid" graphics. 2017
4. Lumley T. Two-sample rank tests under complex sampling. *Biometrika*. 2013;100:831–842.

eTable 2

Prevalence of Self-reported and Likely/Possible FA for OOM vs All NHANES Children

Food	Prevalence (95% CI) for OOM vs all NHANES children		
	OOM	NHANES	P value
Self-reported FA			
Any food allergy	4.96 (3.41–7.17)	6.53 (5.72–7.41)	.22
Milk	2.48 (1.46–4.2)	1.94 (1.47–2.49)	.54
Shellfish	0 (0–0.73)	0.87 (0.59–1.21)	<.001
Peanut	0.76 (0.3–1.95)	1.16 (0.86–1.52)	.43
Other nuts	0 (0–0.73)	0.52 (0.3–0.83)	<.001
Eggs	0.19 (0.01–1.07)	0.64 (0.44–0.89)	.04
Wheat	0.38 (0.1–1.38)	0.29 (0.14–0.51)	.74
Fish	0 (0–0.73)	0.43 (0.19–0.8)	.004
Soy	0 (0–0.73)	0.25 (0.15–0.39)	<.001
Corn	0.38 (0.1–1.38)	0.28 (0.13–0.51)	.72
PN and TN	0.76 (0.3–1.95)	1.42 (1.07–1.85)	.19
PN, TN, and SF	0.76 (0.3–1.95)	2.06 (1.64–2.55)	.01
PN, TN, F, and SF	0.76 (0.3–1.95)	2.29 (1.83–2.83)	.004
Other	1.53 (0.78–2.98)	2.83 (2.33–3.38)	.08
Likely/Possible FA			
Any food allergy	2.67 (1.6–4.43)	5.5 (4.73–6.34)	.008
Milk	1.15 (0.53–2.48)	0.69 (0.49–0.94)	.497
Shellfish	0 (0–0.73)	0.78 (0.52–1.1)	<.001
Peanut	0.38 (0.1–1.38)	0.99 (0.72–1.31)	.049
Eggs	0.19 (0.01–1.07)	0.59 (0.4–0.84)	.06
Wheat	0 (0–0.73)	0.14 (0.06–0.25)	.003
Fish	0 (0–0.73)	0.34 (0.13–0.71)	.02
PN and TN	0.38 (0.1–1.38)	1.29 (0.94–1.72)	.007
PN, TN, and SF	0.38 (0.1–1.38)	1.9 (1.51–2.36)	<.001
PN, TN, F, and SF	0.38 (0.1–1.38)	2.07 (1.64–2.56)	<.001

Abbreviations: F, fish; FA, food allergy; NHANES, National Health and Nutrition Examination Survey; OOM, Old Order Mennonite; PN, peanut; SF, shellfish; TN, tree nut.