Food Diversity in the First Year of Life and the Development of Allergic Disease in High-Risk Children

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A Capstone Project Submitted to the Faculty of Graduate Studies

in partial fulfillment of the requirements

for the degree of

MASTER OF PHYSICIAN ASSISTANT STUDIES

Physician Assistant Studies

University of Manitoba

Winnipeg, Manitoba

May 2015

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Abstract

Introduction: Mounting evidence suggests that delaying the introduction of solid food may promote allergic disease, leading to recent changes in infant feeding guidelines. We investigated the association of food diversity during the first year of life and the subsequent risk of asthma, atopy and atopic dermatitis.

Methods: We accessed data from the 1995 Canadian Asthma Primary Prevention Study (CAPPS), a multi-faceted intervention study in high-risk children. 545 families were recruited from Winnipeg and Vancouver and reported on the introduction of 11 foods (rice, soy, wheat, other grains, eggs, dairy, seafood/fish, peanuts, vegetables, fruits, and meat) during the first year of life. Clinical assessments were performed at 1, 2 and 7 years of age to determine physician-diagnosed asthma, atopic dermatitis, and atopy (by skin prick testing). We defined food diversity as the total number of foods introduced by 6, 9 and 12 months and determined associations with using chi-squared tests and multiple regression.

Results: The average food diversity at 6 months was 3.43 $\pm$ 2.01 foods and at 12 months was 8.28 $\pm$ 1.47 foods. More foods were introduced earlier in the control group compared to the intervention group ($p<0.001$) and in Vancouver compared to Winnipeg ($p<0.001$). Maternal food allergy ($p=0.03$) and exclusive breastfeeding for >4 months ($p=0.02$) were associated with lower food diversity. After controlling for these factors, high food diversity (5-11 foods) at 6 months was associated with higher risk of asthma at age 7 (adjusted OR (aOR) 2.52, 95% confidence interval (CI) 1.01–5.74), and atopic dermatitis at age 7 (aOR 8.58 95%CI 2.96-24.86) compared to low food diversity (0-2 foods introduced). Higher food diversity at 12 months tended to be protective against future allergic disease, although fewer associations were detected at this age.

Conclusion: In high-risk children, higher food diversity in the first 6 to 9 months of life may increase the risk of developing certain allergic diseases by age 7, while higher food diversity at 12 months may be protective. Further studies are necessary to clarify the impact of early food diversity on the development of allergic disease, particularly in genetically predisposed children.

Background

Prevalence of Food Allergy in Children

Food allergies in children are a major health concern worldwide. The incidence of food allergy in Canadian children, based on self-reported data, is approximately 7%[1] while an Australian study that found that over 10% of 1 year old infants had an IgE-mediated food allergy proven by oral challenge.[2] The prevalence of food allergy in children ages 0-17 has increased from 3.4% in 1997-1999 to 5.1% in 2009-2011 in the United States[3], and a recent meta-analysis concluded that the prevalence of food allergy may also be increasing in Europe.[4] Peanut allergies have more than tripled in American children from 1997 (0.6%) to 2008 (2.1%).[5]

Introduction of Food and Allergy

It was once thought that if a food allergen could be avoided during fetal development and early childhood, an allergic response to that allergen would be unlikely.[6] Thus, in 2000, the American Academy of Pediatrics recommended delaying the introduction of allergenic foods (eg. cow's milk until 1 year of age, egg until 2 years of age and peanuts or seafood until 3 years of age) in infants at high risk for developing allergy.[6] However, in 2008 and 2013 respectively, the American Academy of Pediatrics and Canadian Pediatric Society reversed their positions with regards to dietary exposure, concluding that there was no convincing evidence that delaying the introduction of foods including egg, peanut and fish beyond 4-6 months of age actually prevents the development of allergic disease, including asthma, eczema, allergic rhinitis and sensitization at age 4 years.[7,8] This applied even to children who were considered at high risk of developing an allergy (who have a parent or sibling with an allergic condition).[7,8] In fact, it has been shown that delaying the introduction of solid food may actually *promote* allergic sensitization to food and inhalant allergens.[9] Other studies have shown that the introduction to complementary food in the first year of life may also have a protective effect against other allergic disorders, including atopic dermatitis[10] and asthma[11]. A recent systematic review of 74 studies on allergy prevention concluded that current evidence is not strong enough to recommend changing current diet or supplements of pregnant or breastfeeding women at normal or high risk, finding that delaying the introduction of solids until later was not protective in infants at high or normal risk.[12]

Mechanisms of Food Allergy

There are several ways that early introduction of solids and food diversity might protect against food allergy. First, oral exposure to food proteins can induce oral tolerance. Observational studies have found that regular fish consumption before age 1 is associated with a reduced risk of asthma and sensitization at age 4[13] while delaying exposure to cereal grain beyond 6 months is associated with an increased risk of IgE-mediated food allergy.[14] Also, peanut allergy is higher in western societies where peanuts tend to be avoided in pregnancy and infancy[15] compared to regions where peanuts are consumed more frequently such as the Middle East and Africa.[16–18] The theory that early introduction of foods can lead to tolerance and protect against food allergy is being tested in several randomized controlled trials. The Learning Early About Peanut Allergy (LEAP) Study randomized high-risk children to consume or avoid peanut until age 5. Of the children who avoided peanut, 17% developed peanut allergy compared to only 3% of children who consumed peanuts on a regular basis.[19] The Enquiring About Tolerance

(EAT) Study is investigating whether introduction of allergenic foods beginning at 3 months of age, together with continued breastfeeding, can prevent food allergies.[20]

A second theory of food allergy development involves the dual-allergen exposure hypothesis: exposure to food allergies through the skin can lead to allergy, while the consumption of these foods at an early age may result in tolerance.[21] Children with atopic dermatitis have a disrupted skin barrier that would allow exposure to food proteins in the environment (i.e. on tabletops, hands and dust), thus, despite avoiding consumption of peanuts orally, these children are more likely to develop a peanut allergy.[21]

Finally, a third mechanism encompasses the association between gut microbiota and development of allergic disease. Consistent with previous studies on asthma and allergic disease,[22,23] recent evidence from Azad et al has shown that infants with fewer varieties of gut microbiota are more likely to develop food sensitization.[24] A recent review by Canani et al[25] suggest that the timing and introduction of solid food and the type of food consumed may change the composition of gut microbiota, in turn affecting the development of food allergy. Stefka et al have selectively colonized gnotobiotic mice and have identified Clostridia containing microbiota that protect against sensitization.[26] The decrease in gut microbiota and subsequent increase in allergies has been associated with the hygiene hypothesis, that limiting childhood exposure to infectious agents results in the development of a weakened immune system and predisposition to allergic disease.[27,28]

Limitations of Current Food Allergy Studies

Existing studies on food introduction and allergic disease have several limitations. Most studies have evaluated individual foods in relation to allergic disease,[13,29,30] while only a few have incorporated the concept of **food diversity** to provide a more realistic view of diet as a whole.[9–11,31] Most studies did not conduct follow-ups beyond age 6, which is a limitation because many infants and young children grow out of their early food allergies by school age.[12] Several food allergy studies have relied on self-report without objective testing or physician diagnosis[32,33] or were retrospective in design and subject to recall bias.[34] To address these limitations, our study uses a prospective design, objective measures of allergic disease, follow-up to age 7, and the concept of food diversity.

Objective

To determine if there is an association between food diversity in the first year of life and the development of allergic disease (atopy, food sensitization, asthma and atopic dermatitis) in high-risk children.

Methods

Study design and population

We accessed data collected in the Canadian Asthma Primary Prevention Study (CAPPS).[35] This prospective, prenatally randomized study was designed to investigate the primary prevention of asthma in high-risk children (those with 1 parent with asthma or 2 first-degree relatives with allergies or atopic disorders) using a multifaceted intervention: avoidance of house dust mite and pet allergens and environmental tobacco smoke, encouragement of breastfeeding, and supplementation with a partially hydrolyzed formula. During the last trimester of pregnancy, mothers were instructed to avoid peanuts, other nuts, fish and other seafood. Parents were advised to delay introduction of solid food until 6 months of age and instructed to exclude cow's milk, seafood and peanuts from the child's diet during the first year of life.[35] These recommendations were consistent with practice guidelines at the time.[6] 545 families were recruited in Winnipeg and Vancouver. Mothers were recruited prenatally and randomly allocated to the multifaceted intervention group or to the control group. Infants were born between October 1994 and August 1996 and assessed at 1, 2 and 7 years of age.[35]

Exposure (early life food diversity)

Families reported the timing of introduction of 11 foods (rice, soy, wheat, other cereal grains, eggs, dairy, seafood/fish, peanuts, vegetables, fruits, and meat) via standardized questionnaires completed at ages 4, 8, 12, 18 and 24 months. These data were used to create a "food diversity score", reflecting the number of different foods introduced before 6, 9 and 12 months, as described below.

Outcomes (allergic disease)

Each infant was assessed by a pediatrician and a pediatric allergist at 1, 2 and 7 years as follows:

- **Atopy:** Defined from skin prick allergy tests conducted by a research nurse using the following allergens: house dust mite, cat, dog, cockroach, alternaria, cladosporium, cow's milk, egg white, wheat, soy and peanut. Atopy was defined as a positive skin prick (mean wheal diameter >= 3mm) to any allergen. Atopy to food and non-food allergens was also classified.

- **Asthma:** At ages 1 and 2, children were diagnosed with possible, probable or no asthma. *Possible asthma* was defined as having at least 2 distinct episodes of cough lasting 2 or more weeks; at least 2 distinct episodes of wheeze lasting 1 or more weeks; **or**, in the absence of a cold, at least 1 of the following: nocturnal cough (at least once a week), hyperpnea-induced cough or wheeze. *Probable asthma* was defined as having at least 2 distinct episodes of cough lasting 2 or more weeks; or at least 2 distinct episodes of wheeze, each lasting 1 or more weeks; **plus** at least 1 of the following: nocturnal cough (at least once a week) in the absence of a cold, hyperpnea-induced cough or wheeze at any time, or response to treatment with beta agonist and/or anti-inflammatory drugs.[35] For the current analysis, possible and probable asthma were combined to create a binary variable (possible/probable asthma or no asthma at ages 1 and 2). At age 7, asthma was diagnosed by a pediatric allergist using spirometry (FEV1 decrease of 20%) and methacholine challenge tests (post saline value of less than 7.8mg/mL methacholine).[36]
- **Atopic dermatitis**: presence of a pruritic rash on the face or extensor surface of the arms or legs and flexural lichenification at the time of examination.[37]

Covariates

The following potential confounders (documented in the CAPPS cohort) were considered: environmental tobacco smoke exposure, breastfeeding duration and exclusivity, family history of atopy, gender, socioeconomic status (maternal education), study site (Vancouver vs. Winnipeg), and study group (intervention vs. control).

Analysis

Food diversity scores were developed following methods similar to Roduit et al.[10,11] Total food diversity was defined as the total number of foods introduced before a given point in time. Allergenic food diversity was calculated using "allergenic foods" only: soy, wheat, egg, dairy, seafood and peanuts, which collectively account for 90% of food allergic reactions.[38] The number of total (maximum 11) and allergenic (maximum 6) foods introduced was calculated at 6, 9 and 12 months of age. Food diversity was categorized as low, medium or high. Categories were created to include roughly 1/3 of the infants in each age group (Table 1). Univariate associations between food diversity and covariates were determined by chi-squared test to identify potential confounders. The association of food diversity and physician diagnosed asthma, atopic dermatitis and atopy was determined using multiple regression analyses with adjustment for confounders and reported as odds ratios (OR) with 95% confidence intervals (CI). Analyses were repeated to evaluate food diversity as a categorical variable (with "low" food diversity as the reference group) or as a continuous variable (per food introduced) at 6, 9 and 12 months and to determine associations with outcomes at 1, 2 and 7 years.

Results

Early food diversity and introduction of foods

The average food diversity score was 3.43 $\pm$ 2.01 at 6 months and 8.28 $\pm$ 1.47 at 12 months. Food diversity was greater in the control group compared to the intervention group at all ages throughout the first 2 years of life (Fig. 1). Foods that were commonly introduced before 6 months included rice (94%), other cereals (53%), fruits (56%) and vegetables (54%) (Fig.2). In contrast, meat (14%), dairy (16%), soy (12%), egg (5%), seafood (3%) and peanut (0.6%) were rarely introduced before 6 months. By 12 months, meat, vegetables, fruit, dairy, rice, wheat and other cereals had been introduced in over 90% of infants; however, egg (49%), soy (45%) seafood (33%) and peanut (26%) were avoided by the majority of infants (Fig.2).

More foods were introduced earlier in the control group compared to the intervention group ($p<0.001$) and in Vancouver compared to Winnipeg ($p<0.0001$) (Table 2a). Maternal food allergy ($p=0.03$) and exclusively breastfeeding for >4 months ($p=0.02$) were associated with lower food diversity. No association between food diversity and sex, maternal education, paternal food allergy, parental history of asthma or smoking in the home was found.

Prevalence of allergic disease and associations with food diversity

The prevalence of allergic disease in the CAPPS cohort is shown in Table 3A. 18% of children had possible or probable asthma at age 1 while 19% of children were diagnosed with asthma at age 7. 22% of children were atopic by age 1, increasing to 50% by age 7. Atopy to non-food allergens was found in 4.5% of children at age 1 and by age 7, increased to 50% of children. In contrast, 19% of children were sensitized to food allergens at age 1, decreasing to 14% by age 7. Additionally, 12% of children were diagnosed with atopic dermatitis by age 7.

Univariate analysis demonstrated that food diversity at 6 months was associated with all measured outcomes at age 7 (Table 3A, Fig 3C). Atopic dermatitis was most common among children with high food diversity (21% vs. 13% and 5% for children with medium and low food diversity, respectively; $p=0.0004$). Asthma was diagnosed in 24% of children with medium or high food diversity, compared to 10% of children with low food diversity (p=0.005). Atopy, including sensitization to food and non-food allergens, was most common among children with medium food diversity. Fewer associations were observed for outcomes at 1 and 2 years, and for food diversity at 9 and 12 months (Table 3A, Fig 3).

Results from multivariate analyses are shown in Table 4A. After controlling for study group, study site, maternal food allergy and exclusive breastfeeding for 4 months, both medium and high food diversity at 6 months were associated with higher risk of asthma at age 7 (aOR 2.44, 95% CI 1.18 – 5.05 and aOR 2.52 95%CI 1.01–5.74, respectively), and atopic dermatitis at age 7 (aOR 3.20 95%CI 1.20-8.48, aOR 8.58 95%CI 2.96-24.86, respectively) compared to low food diversity. In models evaluating food diversity as a continuous variable, each additional food introduced before 6 months increased the risk of atopic dermatitis at age 7 by 44% (aOR 1.44 95%CI 1.18-1.76).

Fewer associations were observed for food diversity at 9 and 12 months of age. For each additional food introduced by 9 months, the risk of non-food atopy at age 1 increased by 59% (aOR 1.59 95%CI 1.15-2.20) and the risk of atopic dermatitis at age 7 increased by 34% (aOR1.34 95%CI 1.05-1.70) (Table 4A). Results for food diversity at 12 months of age indicated a null or protective effect: each additional food tended to decrease the risk of atopy to non-food allergens at age 7 (aOR 0.85 95%CI 0.71-1.03), while there was no association for asthma or atopic dermatitis (Table 4A).

Associations between food diversity in the first year of life and allergic outcomes are summarized and illustrated in Figure 5. High food diversity at 6 months shows a general trend towards an increased risk for allergic outcomes. At 9 months, this trend shifts to no association with allergic outcomes while at 12 months the trend shifts towards a protective association (Fig. 5).

Allergenic food diversity

Sensitivity analyses addressing the introduction and diversity of allergenic foods only (soy, wheat, egg, dairy, seafood and peanuts) yielded similar results, although there were fewer significant associations for "allergenic" compared to "total" food diversity. More allergenic foods were introduced earlier in the control group compared to the intervention group ($p<0.0001$) and exclusive breastfeeding for >4 months ($p=0.04$) was also associated with lower allergenic food diversity (Table 2B). In contrast to findings for total food diversity, allergenic food diversity was not associated with maternal food allergy.

High allergenic food diversity at 6 months (2-6 foods) was strongly associated with increased risk for sensitization to non-food allergens at age 1 (aOR 4.48 95%CI 1.29-15.59) and atopic dermatitis at age 7 (aOR 8.35 95%CI 3.20-21.76). Associations for allergenic food diversity at 9 and 12 months were generally null or protective; for example, each additional allergenic food introduced at 12 months predicted a 26% decreased risk of atopic dermatitis at age 1 (aOR 0.74 95%CI 0.56-0.99) (Table 4B, Fig. 6).

Discussion

Main findings

Our results from a population of genetically predisposed children suggest that higher food diversity in the first 6 to 9 months of life may increase the risk of developing asthma, atopy or atopic dermatitis by age 7, while higher food diversity at 12 months may be protective. Only a few previous studies have investigated the effect of early life food diversity on allergic disease outcomes, and ours is the first to explore this association in a high risk population.

Comparison with other food diversity studies

Table 5 presents a comparison of the four existing food diversity studies including our own CAPPS investigation. Similar to our results for food diversity at 12 months, the PASTURE/EFRAIM study by Roduit et al. observed a protective effect on asthma, food allergy, and food sensitization with an increased food diversity in the first year of life; however, in contrast to our results they also reported protective associations for food diversity at 6 months.[11] There may be several reasons for this disagreement, including differences in the study populations and time periods. The PASTURE/EFRAIM study involved children born in 2002-2005 from rural areas in 5 European countries whereas CAPPS children were born in 1994-96 from 2 urban centers in Canada. In addition, CAPPS was an intervention study of high-risk children, whereas the PASTURE/EFRAIM study was observational and did not specifically enroll children at high risk of allergic disease. Finally, the specific foods reported also differed between the studies. Both studies evaluated vegetables, fruit, meat, cereals, nuts, fish, eggs and soy, but CAPPS additionally asked parents about wheat, other grains, and dairy, while the

PASTURE/EFRAIM study asked specifically about cake, yogurt, margarine, butter, chocolate, cow's milk and other milk products and.[11,35]

Two other studies have reported on early food diversity and allergic outcomes. In the prospective population-based German birth cohort study LISA (Influences of Lifestyle-Related Factors on the Immune System and the Development of Allergies in Childhood), Zutavern et al showed that while food diversity at 4 months was not associated with the risk of asthma, allergic rhinitis, or sensitization to inhalant allergens at age 6, there was a decreased risk of food sensitization and an increased risk of eczema (atopic dermatitis) with higher food diversity.[31] Consistent with these results, we observed an increased risk of atopic dermatitis at age 7 with high food diversity at 6 months, although we found no evidence for protection against food sensitization. In the Finnish Type 1 Diabetes Prediction and Prevention (DIPP) Study, a prospective cohort of children at high genetic risk for Type 1 diabetes, Nwaru et al investigated the timing and diversity of complementary foods during infancy and atopic sensitization at age 5. They found that early introduction of cereals, fish and egg may confer some protection against atopic sensitization and that less food diversity at 3 months was associated with an increased risk for atopic sensitization to wheat, timothy grass and birch allergens.[39] They also showed that low food diversity at 6 months was associated with an increased risk for sensitization to any food allergen, which is contradictory to our findings that medium or high food diversity at 6 months tended to be associated with increased risk for atopic sensitization. Contrary to CAPPS but similar to the PASUTRE/EFRAIM study, children in the DIPP and LISA cohorts were not selected for predisposition to allergic disease. In addition, the DIPP and LISA studies evaluated food diversity at earlier ages (3 and 4 months, respectively) compared to our study. These differences in timing and genetic risk could explain why we observed different associations of food diversity and allergic disease in the CAPPS cohort. It is possible that early food diversity may differentially affect allergic disease development in high versus low risk children, perhaps due to inherent differences in immune physiology, capacity for oral tolerance, or gut microbiota. Further research is required to confirm our findings and explore these possibilities.

Strengths and Limitations

The major strengths of our study were the prospective design and frequent and detailed collection of data with regards to food introduction: questionnaires were administered at 2 weeks and 4, 8, 12, 18 and 24 months to avoid recall bias. In addition, allergic disease outcomes were determined by standardized diagnosis. To our knowledge, this is the first study to specifically investigate allergenic food diversity. Finally, only 14% of children were lost to follow-up at 7 years of age,[36] which is relatively low compared to other studies such as PASTURE/EFRAIM (24%)[11], DIPP (52%)[9] and LISA (33%).[31] Limitations of our study included the relatively small sample size (N=502) compared to other studies [9,11,31,39] and the selected high-risk population in Winnipeg and Vancouver, which may not be applicable to the general population.

Future Directions

An important future direction for this study will involve assessment of food diversity at earlier ages, and sensitivity analyses to address potential confounding by reverse causality. This is a potential bias in that children with early symptoms of atopic disease, and those with allergic parents may have delayed introduction to complementary foods, especially allergenic foods [11].

Conclusion

In high-risk children, higher food diversity in the first 6 to 9 months of life may increase the risk of developing certain allergic diseases by age 7, while higher food diversity at 12 months may be protective. Further studies are necessary to clarify the impact of early food diversity on the development of allergic disease, particularly in genetically predisposed children.

Figures

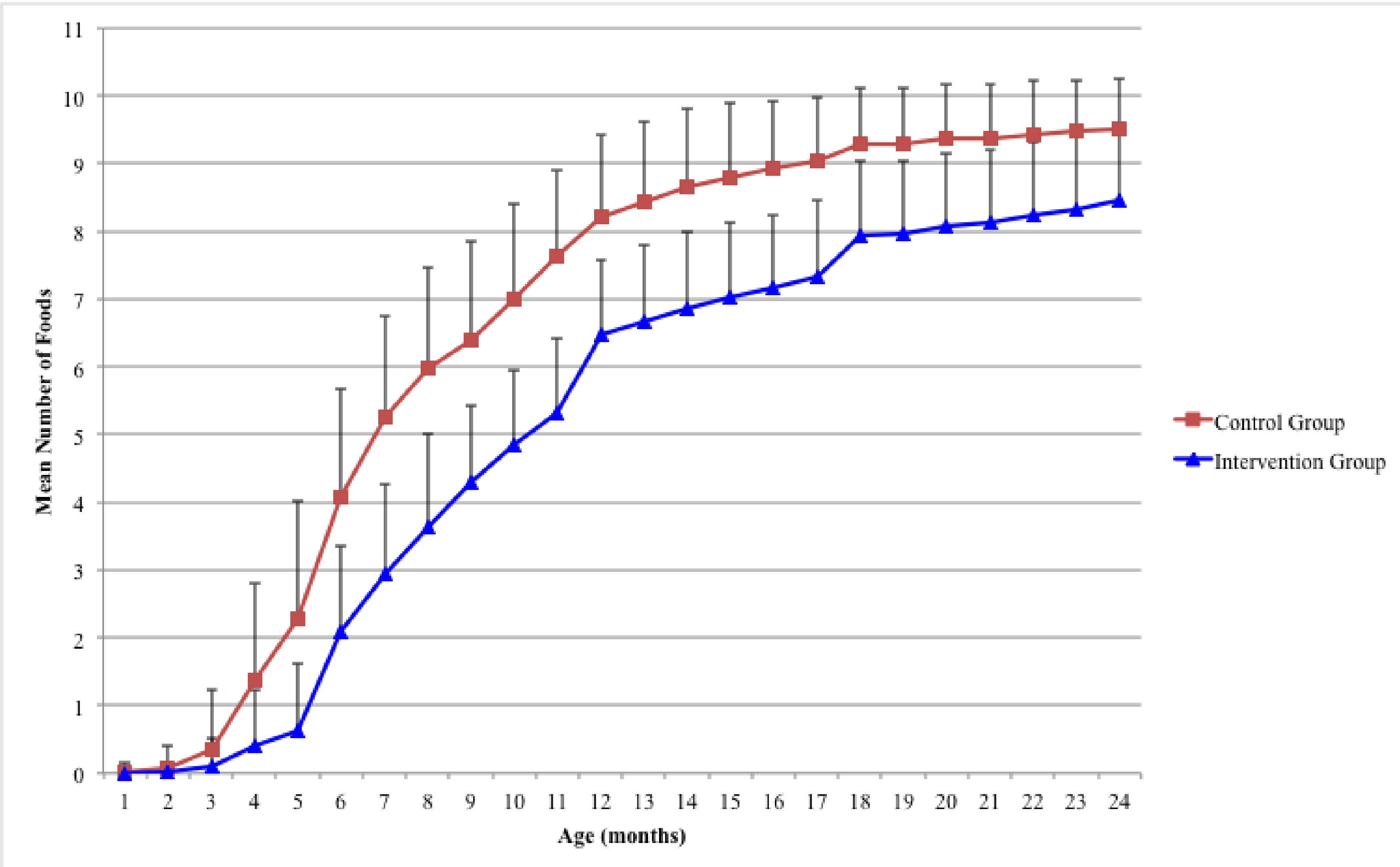


Figure 1. Mean number of foods introduced by age in the Canadian Asthma Primary Prevention Study (CAPPS) cohort, according to study group (control group: n=257; intervention group: n=267). Error bars indicate standard deviation.

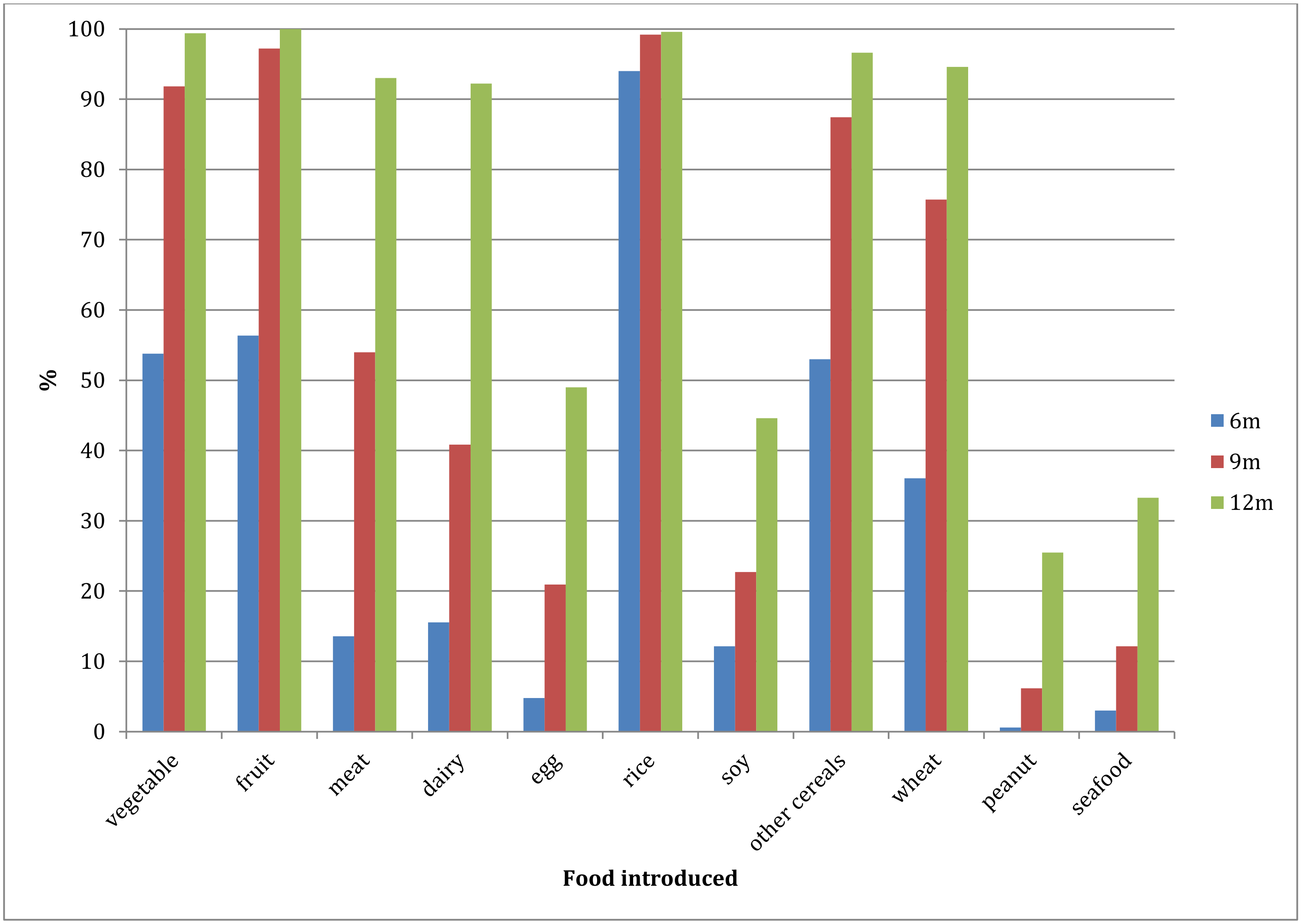


Figure 2. Percent of children consuming specific foods at 6, 9 and 12 months of age in the CAPPS cohort (n=503).

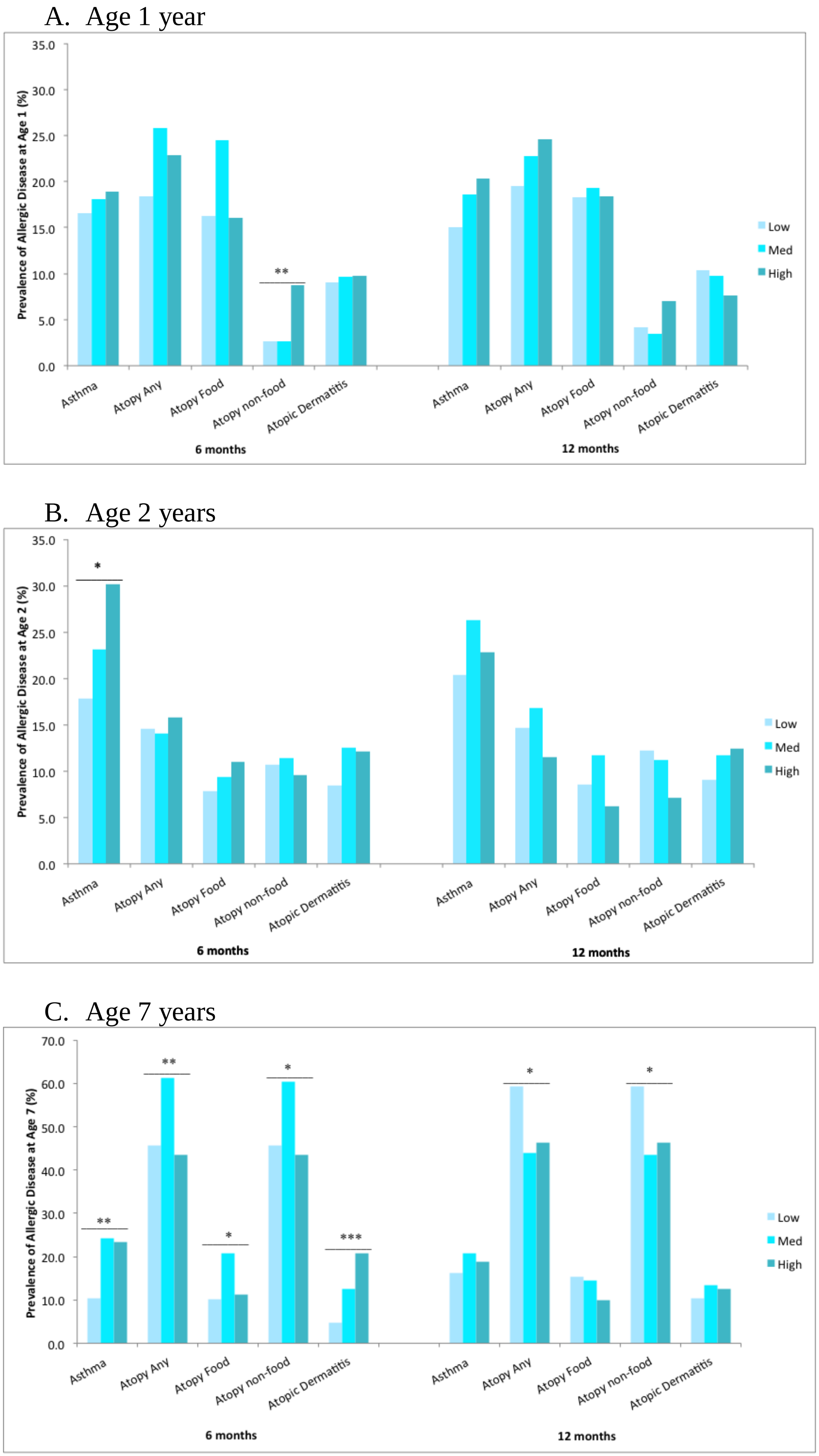
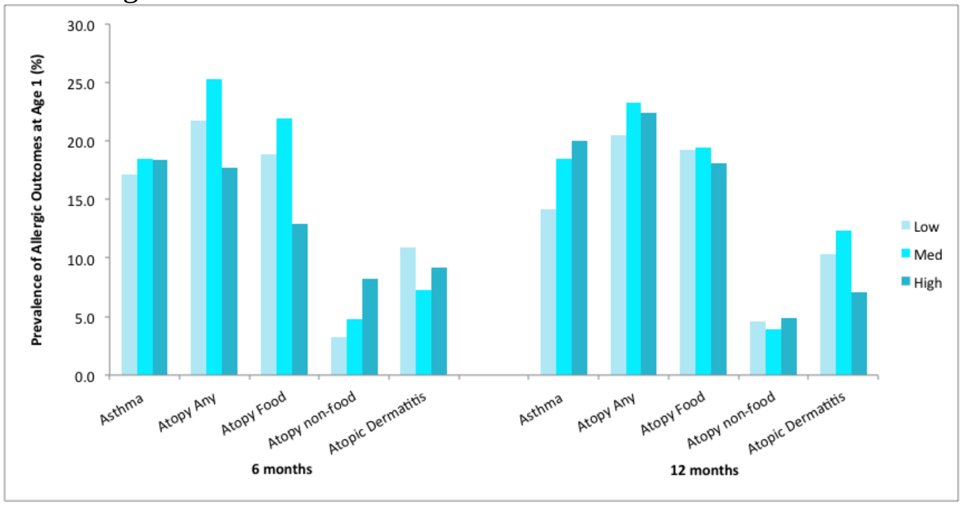
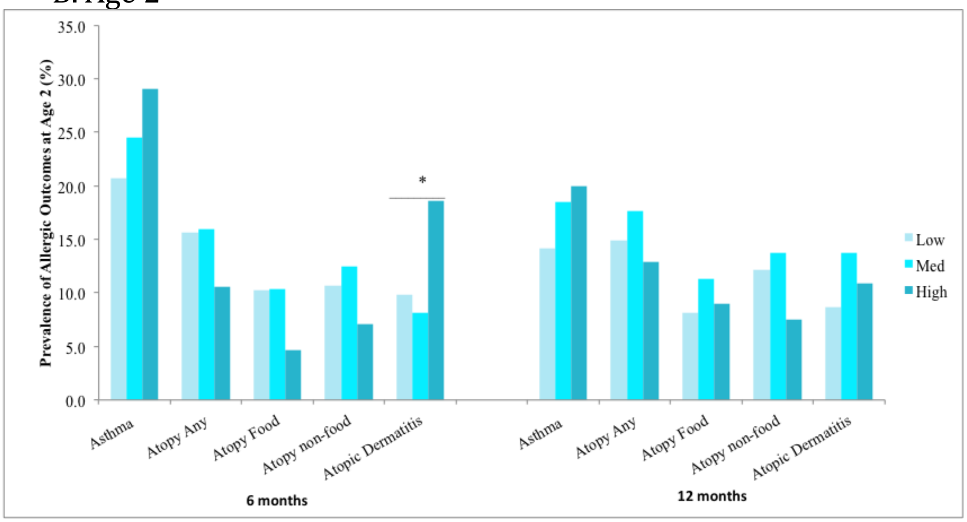


Figure 3. Prevalence of allergic outcomes in the CAPPS cohort at 1, 2 and 7 years of age according to total food diversity at 6 months (low=0-2 foods, medium=3-4 foods, high=5-11foods) and 12 months (low=0-7 foods, medium=8-9 foods, high=10-11foods) Comparisons by chi-squared test for differences across food diversity groups: ***P<0.001, **P<0.01, *P<0.05.

A. Age 1



B. Age 2



C. Age 7

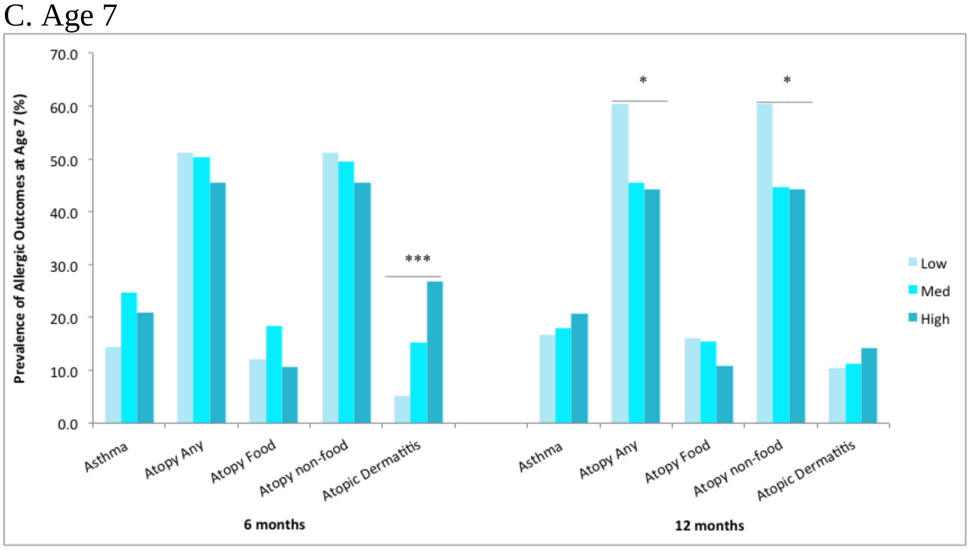


Figure 4 Prevalence of allergic outcomes in the CAPPS cohort at 1, 2 and 7 years of age according to allergenic food diversity at 6 months (low=0 foods, medium=1 foods, high=2-6 foods) and 12 months (low=1-2 foods, medium=3 foods, high=4-6 foods). Comparisons by chi-squared test for differences across food diversity groups: ***P<0.001, **P<0.01, *P<0.05.

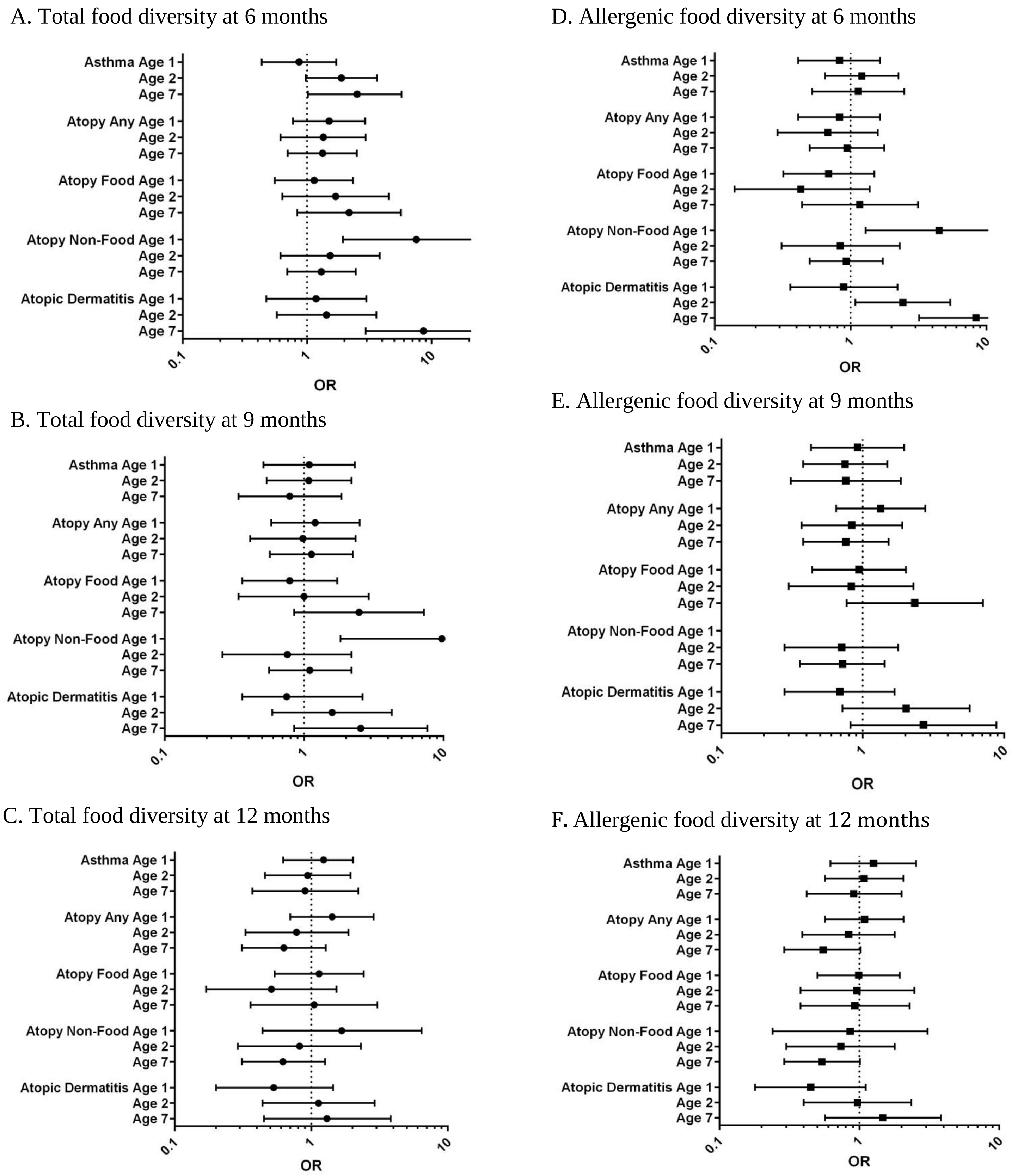


Figure 5. Effect of food diversity in the first year of life on allergic disease outcomes at 1, 2 and 7 years of age in the CAPPS cohort. Multiple logistic regression was used to determine the odds ratio (OR) and 95% confidence interval for high vs. low food diversity with adjustment for study group, study site, maternal food allergy and exclusive breastfeeding at 4 months. Food diversity was evaluated at 6 (A&D), 9 (B&E) and 12 (C&F) months and calculated using all foods (A,B,C) or allergenic foods only (soy, wheat, egg, dairy, seafood and peanuts; D,E,F) as shown in Table 1

Tables

Table 1. Classification of food diversity scores. Frequencies of food introduced at 6, 9 and 12 months were used to create low, medium and high categories of food diversity with approximately equal group sizes.

A. Total food diversity (vegetables, fruit, meat, dairy, egg, rice, soy, other cereals, wheat, peanut, seafood).

Age	# of Total Foods Introduced	Frequency	%	Total Food Diversity Score
6 months	0	16	3.19	Low
	1	91	18.13	
	2	81	16.14	
	3	80	15.94	Medium
	4	76	15.14	
	5	77	15.34	High
	6	42	8.37	
	7	31	6.18	
	8	5	1	
	9	1	0.2	
	10	1	0.2	
	11	1	0.2	
9 months	0	1	0.2	Low
	1	1	0.2	
	2	2	0.4	
	3	33	6.57	
	4	61	12.15	
	5	104	20.72	
	6	111	22.11	Medium
	7	67	13.35	
	8	69	13.75	High
	9	36	7.17	
	10	13	2.59	
	11	4	0.8	
12 months	4	1	0.2	Low
	5	7	1.39	
	6	36	7.17	
	7	130	25.9	
	8	121	24.1	Medium
	9	86	17.13	
	10	82	16.33	High
	11	39	7.77	

B. Allergenic food diversity (soy, wheat, egg, dairy, seafood, peanuts).

Age	# of Allergenic Foods Introduced	Frequency	%	Allergenic Food Diversity Score
6 months	0	259	51.59	Low
	1	154	30.68	Medium
	2	67	13.36	High
	3	17	3.39	
	4	3	0.6	
	5	1	0.2	
	6	1	0.2	
9 months	0	78	15.54	Low
	1	172	34.26	Medium
	2	118	23.51	High
	3	70	13.94	
	4	46	9.16	
	5	14	2.79	
	6	4	0.8	
12 months	1	29	5.78	Low
	2	127	25.3	
	3	130	25.9	Medium
	4	90	17.93	High
	5	86	17.13	
	6	40	7.97	

Table 2. Food diversity at 6, 9, and 12 months according to demographic factors in the CAPPS cohort. Univariate associations between food diversity and covariates were determined by chi-squared test to identify potential confounders.

A. Total food diversity

		Total Food Diversity at 6 months (%)				Total Food Diversity at 9 months (%)				Total Food Diversity at 12 months (%)			
	N (%)	Low (0-2 foods)	Medium (3-4 foods)	High (5-11 foods)	p value	Low (0-5 foods)	Medium (6-7 foods)	High (8-11 foods)	p value	Low (0-7 foods)	Medium (8-9 foods)	High (10-11 foods)	p value
		N=188	N=156	N=158		N=202	N=178	N=122		N=174	N=207	N=121	
all		37.5	31.1	31.5		40.2	35.5	24.3		34.7	41.2	24.1	
Sex	502												
male	259 (51.6)	34.0	32.1	34.0	0.23	39.0	37.8	23.2	0.51	36.7	40.2	23.2	0.61
female	243 (48.4)	41.2	30.0	28.8		41.6	32.9	25.5		32.5	42.4	25.1	
Study Group	501												
control	245 (48.9)	13.1	32.2	54.7	<0.0001	13.5	39.6	46.9	<0.0001	11.8	44.5	43.7	<0.0001
intervention	256 (51.1)	60.9	30.1	9.0		66.0	31.3	2.7		56.3	38.3	5.5	
Study Site	501												
Vancover	257 (51.3)	36.6	31.1	32.3	0.87	41.6	29.6	28.8	0.009	32.7	36.2	31.1	0.0007
Winnipeg	244 (48.7)	38.5	31.2	30.3		38.9	41.4	19.7		36.5	46.7	16.8	
Exclusive Breastfeeding 4m	500												
yes	181 (36.2)	48.6	29.3	22.1	0.0002	48.1	32.0	19.9	0.02	42.5	37.6	19.9	0.02
no	319 (63.8)	31.4	32.0	36.7		35.7	37.6	26.7		30.1	43.6	26.3	
Maternal Education	498												
college, university, trade school	386 (77.5)	35.5	32.9	31.6	0.16	38.6	36.5	24.9	0.31	33.7	39.9	26.4	0.12
no post sec education	112 (22.5)	44.6	25.0	30.4		46.4	30.4	23.2		37.5	45.5	17.0	
Maternal Food Allergy history	498												
yes	164 (32.9)	35.4	39.0	25.6	0.021	39.6	43.3	17.1	0.006	37.2	45.7	17.1	0.03
no	334 (67.1)	38.6	27.3	34.1		40.7	31.1	28.1		33.2	38.9	27.8	
Paternal Food Allergy history	487												
yes	134 (27.5)	36.6	32.1	31.3	0.93	40.3	32.8	26.9	0.75	31.3	44.0	24.6	0.67
no	353 (72.5)	38.2	30.6	31.2		39.9	36.0	24.1		35.4	40.2	24.4	
Maternal Asthma history	498												
yes	212 (42.6)	36.8	34.0	29.3	0.47	43.4	36.8	19.8	0.11	37.3	41.5	21.2	0.33
no	286 (57.4)	38.1	29.0	32.9		38.1	33.9	28.0		32.5	40.9	26.6	
Paternal Asthma history	484												
yes	181 (37.4)	39.8	28.7	31.5	0.68	40.9	36.5	22.7	0.69	32.6	44.2	23.2	0.57
no	303 (62.6)	36.6	32.3	31.0		39.6	34.3	26.1		35.3	39.3	25.4	
Smokers in home	502												
yes	111 (22.1)	36.9	25.2	37.8	0.18	35.1	40.5	24.3	0.38	29.7	45.1	25.2	0.45
no	391 (77.9)	37.6	32.7	29.7		41.7	34.0	24.3		36.1	40.2	23.8	

N=sample size. Comparisons by chi squared test; significant p values (<0.05) are highlighted.

B. Allergenic food diversity

	N (%)	Allergenic Food Diversity at 6 months (%)				Allergenic Food Diversity at 9 months (%)				Allergenic Food Diversity at 12 months (%)			
		Low (0 foods)	Medium (1 food)	High (2-6 foods)	p value	Low (0 foods)	Medium (1 food)	High (2-6 foods)	p value	Low (1-2 foods)	Medium (3 foods)	High (4-6 foods)	p value
		N=259	N=154	N=89		N=78	N=172	N=252		N=156	N=130	N=216	
all		51.6	30.7	17.7		15.5	34.3	50.2		31.1	25.9	43.0	
Sex	502												
male	259 (51.6)	48.7	33.2	18.2	0.36	14.7	35.9	49.4	0.69	33.2	26.3	40.5	0.45
female	243 (48.4)	54.7	28.0	17.3		16.5	32.5	51.0		28.8	25.5	45.7	
Study Group	501												
control	245 (48.9)	33.5	36.3	30.2	<0.0001	4.5	18.4	77.1	<0.0001	9.4	18.0	72.7	<0.0001
intervention	256 (51.1)	69.1	25.0	5.9		26.2	49.2	24.6		51.6	33.6	14.8	
Study Site	501												
Vancouver	257 (51.3)	58.8	26.5	14.8	0.005	18.3	32.3	49.4	0.21	27.2	24.9	47.9	0.07
Winnipeg	244 (48.7)	44.3	34.8	20.9		12.7	36.1	51.2		34.8	27.1	38.1	
Exclusive Breastfeeding 4m	500												
yes	181 (36.2)	62.4	22.1	15.5	0.0009	18.8	40.9	40.3	0.004	37.6	26.0	36.5	0.04
no	319 (63.8)	45.5	35.4	19.1		13.8	30.4	55.8		27.6	25.7	46.7	
Maternal Education	498												
college, university, trade school	386 (77.5)	52.3	29.0	18.7	0.44	15.0	35.0	50.0	0.81	30.0	26.7	43.3	0.66
no post sec education	112 (22.5)	50.0	34.8	15.2		17.0	32.1	50.9		33.9	23.2	42.9	
Maternal Food Allergy history	498												
yes	164 (32.9)	52.4	32.9	14.6	0.37	14.6	38.4	47.0	0.41	32.3	30.5	37.2	0.12
no	334 (67.1)	51.5	29.0	19.5		15.9	32.3	51.8		30.2	23.7	46.1	
Paternal Food Allergy history	487												
yes	134 (27.5)	49.3	29.9	20.9	0.52	16.4	32.8	50.8	0.91	27.6	28.4	44.0	0.63
no	353 (72.5)	53.5	29.8	16.7		15.6	34.8	49.6		31.7	25.2	43.1	
Maternal Asthma history	498												
yes	212 (42.6)	52.4	33.5	14.2	0.13	16.5	37.7	45.8		33.5	25.9	40.6	0.5
no	286 (57.4)	51.4	28.0	20.5		14.7	31.8	53.5	0.23	29.0	25.9	45.1	
Paternal Asthma history	484												
yes	181 (37.4)	55.3	27.6	17.1	0.63	15.5	33.2	51.4	0.9	27.6	30.9	41.4	0.15
no	303 (62.6)	50.8	31.0	18.2		16.2	34.8	49.2		32.3	23.1	44.6	
Smokers in home	502												
yes	111 (22.1)	44.1	34.2	21.6	0.19	13.5	23.4	63.1	0.007	25.2	24.3	50.5	0.17
no	391 (77.9)	53.7	29.7	16.6		16.1	37.3	46.6		32.7	26.3	40.9	

N=sample size. Comparisons by chi squared test; significant p values (<0.05) are highlighted.

Table 3. Prevalence of allergic disease outcomes at ages 1, 2 and 7 years in the CAPPS cohort according to food diversity at 6, 9 and 12 months.

A. Total food diversity

Outcomes	N (%)	Total Food Diversity at 6 months (% with outcome)				Total Food Diversity at 9 months (% with outcome)				Total Food Diversity at 12 months (% with outcome)			
		Low (0-2 foods)	Medium (3-4 foods)	High (5-11 foods)	p value	Low (0-5 foods)	Medium (6-7 foods)	High (8-11 foods)	p value	Low (0-7 foods)	Medium (8-9 foods)	High (10-11 foods)	p value
		N=188	N=156	N=158		N=202	N=178	N=122		N=174	N=207	N=121	
Asthma													
age 1	88 (17.7)	16.6	18.1	19.0	0.84	14.9	20.0	19.3	0.39	15.0	18.6	20.3	0.47
age 2	112 (23.3)	17.9	23.2	30.2	0.032	20.4	24.9	26.3	0.42	20.4	26.3	22.8	0.41
age 7	71 (18.6)	10.3	24.2	23.5	0.005	16.3	20.9	20.0	0.56	16.2	20.7	18.8	0.61
Atopy - any													
age 1	107 (22.0)	18.4	25.8	22.8	0.25	19.1	26.3	20.9	0.23	19.5	22.8	24.6	0.56
age 2	70 (14.8)	14.6	14.1	15.8	0.92	15.0	15.7	13.3	0.86	14.6	16.8	11.5	0.44
age 7	185 (50.0)	45.7	61.2	43.5	0.012	49.7	54.0	44.1	0.37	59.2	44.0	46.3	0.028
Atopy food													
age 1	91 (18.7)	16.2	24.5	16.1	0.093	18.6	21.6	14.8	0.35	18.3	19.3	18.4	0.97
age 2	44 (9.3)	7.9	9.4	11.0	0.63	8.8	10.2	8.9	0.87	8.5	11.7	6.2	0.25
age 7	51 (13.8)	10.1	20.7	11.3	0.034	11.3	18.3	11.9	0.2	15.4	14.5	10.0	0.52
Atopy non-food													
age 1	22 (4.5)	2.7	2.7	8.7	0.013	1.5	6.4	7.0	0.027	4.1	3.5	7.0	0.33
age 2	50 (10.6)	10.7	11.4	9.6	0.88	12.4	10.8	7.1	0.34	12.2	11.2	7.1	0.37
age 7	184 (49.7)	45.7	60.3	43.5	0.019	49.7	53.2	44.1	0.43	59.2	43.4	46.3	0.022
Atopic Dermatitis													
age 1	47 (9.5)	9.1	9.7	9.8	0.97	10.0	8.6	10.1	0.87	10.4	9.8	7.6	0.72
age 2	52 (10.9)	8.5	12.6	12.2	0.42	8.2	13.1	12.4	0.28	9.0	11.7	12.4	0.62
age 7	46 (12.07)	4.8	12.5	20.9	0.0004	6.6	18.6	12.9	0.007	10.3	13.4	12.5	0.71

N=sample size. Comparisons by chi squared test; significant p values (<0.05) are highlighted.

B. Allergenic* food diversity

Outcomes	N (%)	Total Food Diversity at 6 months (% with outcome)				Total Food Diversity at 9 months (% with outcome)				Total Food Diversity at 12 months (% with outcome)			
		Low (0-2 foods)	Medium (3-4 foods)	High (5-11 foods)	p value	Low (0-5 foods)	Medium (6-7 foods)	High (8-11 foods)	p value	Low (0-7 foods)	Medium (8-9 foods)	High (10-11 foods)	p value
		N=188	N=156	N=158		N=202	N=178	N=122		N=174	N=207	N=121	
Asthma													
age 1	88 (17.7)	16.6	18.1	19.0	0.84	14.9	20.0	19.3	0.39	15.0	18.6	20.3	0.47
age 2	112 (23.3)	17.9	23.2	30.2	0.032	20.4	24.9	26.3	0.42	20.4	26.3	22.8	0.41
age 7	71 (18.6)	10.3	24.2	23.5	0.005	16.3	20.9	20.0	0.56	16.2	20.7	18.8	0.61
Atopy - any													
age 1	107 (22.0)	18.4	25.8	22.8	0.25	19.1	26.3	20.9	0.23	19.5	22.8	24.6	0.56
age 2	70 (14.8)	14.6	14.1	15.8	0.92	15.0	15.7	13.3	0.86	14.6	16.8	11.5	0.44
age 7	185 (50.0)	45.7	61.2	43.5	0.012	49.7	54.0	44.1	0.37	59.2	44.0	46.3	0.028
Atopy food													
age 1	91 (18.7)	16.2	24.5	16.1	0.093	18.6	21.6	14.8	0.35	18.3	19.3	18.4	0.97
age 2	44 (9.3)	7.9	9.4	11.0	0.63	8.8	10.2	8.9	0.87	8.5	11.7	6.2	0.25
age 7	51 (13.8)	10.1	20.7	11.3	0.034	11.3	18.3	11.9	0.2	15.4	14.5	10.0	0.52
Atopy non-food													
age 1	22 (4.5)	2.7	2.7	8.7	0.013	1.5	6.4	7.0	0.027	4.1	3.5	7.0	0.33
age 2	50 (10.6)	10.7	11.4	9.6	0.88	12.4	10.8	7.1	0.34	12.2	11.2	7.1	0.37
age 7	184 (49.7)	45.7	60.3	43.5	0.019	49.7	53.2	44.1	0.43	59.2	43.4	46.3	0.022
Atopic Dermatitis													
age 1	47 (9.5)	9.1	9.7	9.8	0.97	10.0	8.6	10.1	0.87	10.4	9.8	7.6	0.72
age 2	52 (10.9)	8.5	12.6	12.2	0.42	8.2	13.1	12.4	0.28	9.0	11.7	12.4	0.62
age 7	46 (12.07)	4.8	12.5	20.9	0.0004	6.6	18.6	12.9	0.007	10.3	13.4	12.5	0.71

N=sample size. Comparisons by chi squared test; significant p values (<0.05) are highlighted. *Allergenic foods are: soy, wheat, egg, dairy, seafood, peanuts.

Table 4 Crude and adjusted** associations (OR with 95% CI) between food diversity at 6, 9 and 12 months and allergic disease outcomes at 1, 2 and 7 years in the CAPPS cohort.

A. Total food diversity

Outcome / Age (years) / Model	N	Total Food Diversity at 6 months (%): Low (reference) (0-2 foods)	Medium (3-4 foods)	High (5-11 foods)	Continuous (per food)	Total Food Diversity at 9 months (%): Low (reference) (0-5 foods)	Medium (6-7 foods)	High (8-11 foods)	Continuous (per food)	Total Food Diversity at 12 months (%): Low (reference) (0-7 foods)	Medium (8-9 foods)	High (10-11 foods)	Continuous (per food)
Asthma													
Age 1													
Crude	495	1	1.11 (0.63-1.95)	1.18 (0.67-2.06)	1.01 (0.90-1.13)	1	1.43 (0.83-2.44)	1.37 (0.75-2.48)	1.08 (0.95-1.22)	1	1.29 (0.75-2.23)	1.44 (0.78-2.67)	1.12 (0.96-1.32)
Adjusted	489	1	0.98 (0.54-1.80)	0.86 (0.43-1.71)	0.93 (0.81-1.08)	1	1.22 (0.67-2.20)	1.09 (0.51-2.32)	1.02 (0.87-1.20)	1	1.11 (0.62-2.02)	1.23 (0.58-2.61)	1.08 (0.89-1.32)
Age 2													
Crude	479	1	1.39 (0.81-2.37)	**1.99 (1.18-3.34)**	**1.11 (1.00-1.24)**	1	1.29 (0.79-2.11)	1.39 (0.81-2.40)	1.06 (0.95-1.20)	1	1.39 (0.85-2.28)	1.16 (0.65-2.06)	1.05 (0.91-1.21)
Adjusted	473	1	1.33 (0.74-2.39)	1.88 (0.97-3.64)	1.08 (0.95-1.23)	1	1.05 (0.60-1.82)	1.08 (0.54-2.18)	0.99 (0.85-1.15)	1	1.17 (0.68-2.03)	0.94 (0.46-1.93)	0.97 (0.81-1.17)
Age 7													
Crude	380	1	**2.77 (1.40-5.44)**	**2.66 (1.34-5.28)**	1.12 (0.99-1.27)	1	1.36 (0.75-2.46)	1.29 (0.66-2.52)	1.10 (0.96-1.27)	1	1.36 (0.75-2.45)	1.20 (0.58-2.47)	1.05 (0.88-1.26)
Adjusted	376	1	**2.44 (1.18-5.05)**	**2.52 (1.01-5.74)**	1.08 (0.92-1.26)	1	0.85 (0.43-1.67)	0.79 (0.34-1.85)	1.00 (0.83-1.21)	1	0.93 (0.47-1.85)	0.90 (0.37-2.21)	0.94 (0.74-1.20)
atopy - any													
Age 1													
Crude	485	1	1.55 (0.92-2.60)	1.31 (0.77-2.24)	1.05 (0.94-1.16)	1	1.51 (0.93-2.47)	1.12 (0.63-1.98)	1.05 (0.94-1.18)	1	1.22 (0.74-2.01)	1.34 (0.76-2.38)	1.04 (0.90-1.21)
Adjusted	483	1	1.61 (0.92-2.83)	1.50 (0.77-2.92)	1.06 (0.93-1.22)	1	1.61 (0.94-2.76)	1.20 (0.58-2.50)	1.08 (0.93-1.26)	1	1.26 (0.74-2.16)	1.42 (0.70-2.86)	1.05 (0.87-1.26)
Age 2													
Crude	473	1	0.96 (0.52-1.79)	1.09 (0.59-2.01)	0.97 (0.85-1.10)	1	1.06 (0.59-1.88)	0.87 (0.45-1.71)	0.99 (0.86-1.13)	1	1.18 (0.67-2.09)	0.76 (0.37-1.56)	0.95 (0.80-1.14)
Adjusted	471	1	1.01 (0.52-1.98)	1.35 (0.61-2.96)	0.97 (0.83-1.14)	1	1.07 (0.56-2.03)	0.98 (0.41-2.34)	1.01 (0.84-1.22)	1	1.18 (0.64-2.18)	0.78 (0.33-1.87)	0.97 (0.78-1.21)
Age 7													
Crude	369	1	**1.88 (1.14-3.10)**	0.92 (0.56-1.51)	0.97 (0.88-1.07)	1	1.19 (0.74-1.90)	0.80 (0.47-1.36)	0.97 (0.87-1.09)	1	**0.54 (0.34-0.87)**	0.59 (0.34-1.04)	**0.84 (0.73-0.98)**
Adjusted	365	1	**2.18 (1.26-3.77)**	1.33 (0.70-2.51)	1.03 (0.91-1.17)	1	1.34 (0.79-2.27)	1.13 (0.57-2.24)	1.05 (0.91-1.22)	1	**0.52 (0.31-0.88)**	0.63 (0.31-1.28)	0.86 (0.71-1.03)
Atopy food													
Age 1													
Crude	485	1	1.68 (0.98-2.87)	0.99 (0.55-1.78)	1.00 (0.89-1.12)	1	1.21 (0.73-2.01)	0.76 (0.41-1.42)	0.98 (0.86-1.11)	1	1.07 (0.63-1.80)	1.01 (0.54-1.86)	0.99 (0.84-1.15)
Adjusted	483	1	1.73 (0.97-3.09)	1.14 (0.55-2.33)	1.03 (0.89-1.18)	1	1.20 (0.68-2.11)	0.79 (0.36-1.73)	1.00 (0.85-1.17)	1	1.11 (0.64-1.94)	1.14 (0.54-2.42)	1.01 (0.83-1.23)
Age 2													
Crude	473	1	1.22 (0.56-2.64)	1.44 (0.68-3.06)	1.00 (0.86-1.17)	1	1.19 (0.59-2.41)	1.01 (0.45-2.29)	1.03 (0.87-1.22)	1	1.42 (0.71-2.87)	0.71 (0.28-1.81)	0.94 (0.76-1.17)
Adjusted	471	1	1.27 (0.55-2.94)	1.69 (0.63-4.53)	0.98 (0.81-1.20)	1	1.25 (0.57-2.75)	1.00 (0.34-2.91)	1.04 (0.83-1.30)	1	1.31 (0.62-2.76)	0.51 (0.17-1.53)	0.88 (0.67-1.15)
Age 7													
Crude	369	1	**2.31 (1.13-4.71)**	1.13 (0.51-2.51)	0.99 (0.85-1.14)	1	1.75 (0.90-3.41)	1.06 (0.47-2.41)	1.03 (0.88-1.21)	1	0.93 (0.49-1.78)	0.61 (0.26-1.46)	0.91 (0.74-1.13)
Adjusted	365	1	**2.78 (1.30-5.93)**	2.17 (0.83-5.67)	1.11 (0.93-1.33)	1	**2.12 (1.01-4.44)**	2.48 (0.85-7.26)	1.23 (0.98-1.56)	1	1.03 (0.50-2.13)	1.05 (0.36-3.04)	1.05 (0.79-1.39)
Atopy non-food													
Age 1													
Crude	485	1	0.98 (0.26-3.71)	**3.44 (1.20-9.89)**	**1.28 (1.05-1.57)**	1	**4.49 (1.23-16.38)**	**4.89 (1.27-18.80)**	**1.33 (1.06-1.68)**	1	0.83 (0.29-2.42)	1.75 (0.62-4.96)	1.08 (0.80-1.44)
Adjusted	483	1	1.41 (0.36-5.62)	**7.52 (1.94-29.26)**	**1.46 (1.12-1.89)**	1	**6.94 (1.82-26.52)**	**9.73 (1.82-52.13)**	**1.59 (1.15-2.20)**	1	0.90 (0.29-2.78)	1.67 (0.44-6.43)	1.03 (0.72-1.49)
Age 2													
Crude	473	1	1.08 (0.54-2.16)	0.89 (0.43-1.84)	0.94 (0.81-1.10)	1	0.86 (0.45-4.65)	0.54 (0.23-1.25)	0.90 (0.77-1.06)	1	0.91 (0.48-1.73)	0.55 (0.23-1.29)	0.88 (0.72-1.07)
Adjusted	471	1	1.32 (0.63-2.77)	1.53 (0.61-3.83)	1.03 (0.86-1.24)	1	0.92 (0.45-1.89)	0.76 (0.26-2.18)	0.97 (0.78-1.21)	1	1.04 (0.52-2.07)	0.82 (0.29-2.30)	0.97 (0.75-1.26)
Age 7													
Crude	369	1	**1.81 (1.10-2.99)**	0.92 (0.56-1.51)	0.97 (0.88-1.07)	1	1.15 (0.72-1.84)	0.80 (0.47-1.36)	0.97 (0.87-1.09)	1	**0.53 (0.33-0.84)**	0.59 (0.34-1.04)	**0.84 (0.73-0.98)**
Adjusted	365	1	**2.07 (1.20-3.58)**	1.30 (0.69-2.46)	1.03 (0.91-1.17)	1	1.27 (0.75-2.15)	1.10 (0.56-2.18)	1.05 (0.90-1.22)	1	**0.50 (0.29-0.84)**	0.62 (0.31-1.26)	0.85 (0.71-1.03)
Atopic Dermatitis													
Age 1													
Crude	495	1	1.07 (0.52-2.22)	1.09 (0.52-2.26)	1.03 (0.89-1.19)	1	0.85 (0.42-1.71)	1.02 (0.48-2.16)	1.01 (0.86-1.18)	1	0.94 (0.48-1.83)	0.71 (0.31-1.64)	0.86 (0.70-1.06)
Adjusted	489	1	1.10 (0.50-2.43)	1.18 (0.47-2.98)	1.05 (0.87-1.26)	1	0.90 (0.42-1.95)	0.75 (0.36-2.63)	1.00 (0.82-1.24)	1	0.88 (0.43-1.81)	0.53 (0.20-1.44)	0.77 (0.60-1.00)
Age 2													
Crude	476	1	1.56 (0.76-3.18)	1.50 (0.73-3.08)	**1.16 (1.01-1.33)**	1	1.69 (0.85-3.33)	1.58 (0.74-3.38)	1.16 (0.99-1.36)	1	1.33 (0.67-2.64)	1.42 (0.66-3.08)	1.05 (0.87-1.28)
Adjusted	470	1	1.39 (0.63-3.05)	1.43 (0.57-3.59)	1.19 (0.99-1.42)	1	1.72 (0.81-3.69)	1.59 (0.59-4.27)	1.20 (0.97-1.48)	1	1.19 (0.57-2.48)	1.13 (0.44-2.91)	0.98 (0.77-1.26)
Age 7													
Crude	380	1	**2.82 (1.11-7.16)**	**5.20 (2.15-12.57)**	**1.31 (1.13-1.52)**	1	**3.22 (1.51-6.86)**	2.10 (0.87-5.05)	**1.23 (1.04-1.46)**	1	1.35 (0.66-2.75)	1.25 (0.53-2.95)	1.11 (0.90-1.38)
Adjusted	376	1	**3.20 (1.20-8.48)**	**8.58 (2.96-24.86)**	**1.44 (1.18-1.76)**	1	**2.88 (1.26-6.56)**	2.55 (0.85-7.63)	**1.34 (1.05-1.70)**	1	1.11 (0.49-2.51)	1.30 (0.45-3.81)	1.15 (0.86-1.53)

**Adjusted for study group, study site, maternal food allergy, and exclusive breastfeeding at 4 months.
Odds ratios generated by multiple regression analyses with low food diversity as the reference group, or with food diversity as a continuous variable.
Significant associations (p<0.05) are highlighted. N=sample size, OR=odds ratio, CI=confidence interval.

B. Allergenic* food diversity

Outcome Age (years) Model	N	Allergenic Food Diversity at 6 months (%) Low (reference) (0 foods)	Medium (1 food)	High (2-6 foods)	Continuous (per food)	Allergenic Food Diversity at 9 months (%) Low (reference) (0 foods)	Medium (1 food)	High (2-6 foods)	Continuous (per food)	Allergenic Food Diversity at 12 months (%) Low (reference) (1-2 foods)	Medium (3 foods)	High (4-6 foods)	Continuous (per food)
Asthma													
Age 1													
Crude	495	1	1.10 (0.65-1.86)	1.09 (0.58-2.05)	0.97 (0.75-1.25)	1	0.94 (0.46-1.95)	1.21 (0.62-2.37)	1.10 (0.93-1.30)	1	1.37 (0.73-2.58)	1.51 (0.86-2.66)	1.11 (0.95-1.32)
Adjusted	489	1	0.93 (0.53-1.62)	0.83 (0.41-1.65)	0.85 (0.64-1.13)	1	0.87 (0.42-1.82)	0.92 (0.43-1.96)	1.03 (0.84-1.27)	1	1.32 (0.69-2.53)	1.26 (0.62-2.54)	1.07 (0.86-1.32)
Age 2													
Crude	479	1	1.24 (0.76-2.02)	1.57 (0.90-2.74)	1.12 (0.90-1.40)	1	0.69 (0.36-1.33)	1.06 (0.58-1.92)	1.09 (0.93-1.28)	1	1.12 (0.63-1.99)	1.37 (0.83-2.26)	1.05 (0.90-1.22)
Adjusted	473	1	1.07 (0.64-1.81)	1.21 (0.65-2.25)	1.00 (0.78-1.28)	1	0.58 (0.29-1.13)	0.75 (0.38-1.49)	1.01 (0.83-1.22)	1	1.02 (0.56-1.87)	1.08 (0.57-2.06)	0.97 (0.79-1.18)
Age 7													
Crude	380	1	**1.94 (1.09-3.47)**	1.58 (0.77-3.21)	1.15 (0.87-1.51)	1	1.49 (0.65-3.38)	1.44(0.65-3.19)	1.07 (0.88-1.31)	1	1.08 (0.55-2.14)	1.30 (0.70-2.40)	1.06 (0.87-1.28)
Adjusted	376	1	1.55 (0.84-2.87)	1.14 (0.52-2.48)	0.98 (0.72-1.35)	1	1.12 (0.48-2.64)	0.76 (0.31-1.86)	0.93 (0.73-1.20)	1	0.87 (0.41-1.83)	0.91 (0.42-2.00)	0.96 (0.75-1.23)
Atopy any													
Age 1													
Crude	485	1	1.23 (0.76-1.98)	0.78 (0.41-1.46)	0.98 (0.78-1.25)	1	1.14 (0.58-2.23)	1.21 (0.64-2.29)	1.02 (0.87-1.20)	1	1.17 (0.67-2.07)	1.12 (0.67-1.87)	1.03 (0.88-1.21)
Adjusted	483	1	1.28 (0.77-2.13)	0.83 (0.41-1.65)	1.01 (0.78-1.31)	1	1.22 (0.62-2.42)	1.34 (0.65-2.78)	1.03 (0.84-1.26)	1	1.14 (0.64-2.04)	1.09 (0.57-2.07)	1.02 (0.83-1.25)
Age 2													
Crude	473	1	1.03 (0.59-1.81)	0.64 (0.30-1.39)	0.83 (0.61-1.12)	1	0.97 (0.46-2.05)	0.81 (0.40-1.68)	0.92 (0.76-1.12)	1	1.24 (0.65-2.36)	0.85 (0.46-1.57)	0.93 (0.77-1.12)
Adjusted	471	1	1.05 (0.58-1.91)	0.68 (0.29-1.58)	0.84 (0.60-1.17)	1	0.97 (0.45-2.08)	0.84 (0.37-1.91)	0.93 (0.73-1.19)	1	1.20 (0.62-2.33)	0.84 (0.39-1.79)	0.92 (0.72-1.17)
Age 7													
Crude	369	1	0.97 (0.61-1.54)	0.80 (0.45-1.40)	0.89 (0.71-1.11)	1	0.64 (0.34-1.18)	0.63 (0.35-1.15)	0.92 (0.78-1.08)	1	**0.55 (0.32-0.94)**	**0.52 (0.32-0.85)**	**0.84 (0.72-0.97)**
Adjusted	365	1	1.01 (0.62-1.65)	0.94 (0.50-1.76)	0.94 (0.73-1.21)	1	0.67 (0.35-1.28)	0.76 (0.38-1.52)	1.00 (0.82-1.23)	1	**0.53 (0.30-0.92)**	0.55 (0.29-1.02)	0.86 (0.70-1.04)
Atopy food													
Age 1													
Crude	485	1	1.21 (0.73-1.99)	0.64 (0.82-1.29)	0.94 (0.73-1.21)	1	1.20 (0.60-2.38)	0.91 (0.47-1.78)	0.92 (0.77-1.10)	1	1.01 (0.56-1.83)	0.93 (0.54-1.59)	0.96 (0.82-1.14)
Adjusted	483	1	1.24 (0.73-2.11)	0.69 (0.32-1.49)	0.98 (0.74-1.30)	1	1.23 (0.61-2.47)	0.94 (0.44-2.02)	0.93 (0.75-1.15)	1	1.00 (0.55-1.85)	0.99 (0.50-1.94)	0.98 (0.79-1.21)
Age 2													
Crude	473	1	1.02 (0.52-2.00)	0.43 (0.15-1.28)	0.73 (0.49-1.10)	1	0.83 (0.34-2.05)	0.81 (034-1.91)	0.94 (0.73-1.19)	1	1.44 (0.64-3.25)	1.12 (0.52-2.39)	0.94 (0.75-1.18)
Adjusted	471	1	1.03 (0.50-2.12)	0.43 (0.14-1.38)	0.72 (0.47-1.12)	1	0.90 (0.36-2.28)	0.83 (0.30-2.28)	0.90 (0.67-1.21)	1	1.34 (0.59-3.06)	0.96 (0.38-2.47)	0.85 (0.63-1.14)
Age 7													
Crude	369	1	1.67 (0.88-3.18)	0.87 (0.36-2.15)	0.96 (0.69-1.34)	1	2.06 (0.74-5.77)	1.75 (0.64-4.81)	0.99 (0.78-1.24)	1	0.97 (0.47-2.00)	0.64 (0.32-1.31)	0.87 (0.70-1.10)
Adjusted	365	1	1.74 (0.87-3.42)	1.17 (0.44-3.13)	1.07 (0.73-1.56)	1	1.99 (0.70-5.68)	2.33 (0.77-7.07)	1.19 (0.87-1.62)	1	1.00 (0.47-2.17)	0.93 (0.38-2.28)	1.01 (0.75-1.35)
Atopy non-food													
Age 1													
Crude	485	1	1.55 (0.55-4.36)	2.76 (0.97-7.85)	1.40 (0.96-2.04)	1	1.36 (0.14-13.25)	6.08 (0.80-46.33)	**1.43 (1.07-1.90)**	1	0.83 (0.26-2.68)	1.06 (0.39-2.84)	1.13 (0.83-1.53)
Adjusted	483	1	2.10 (0.70-6.28)	**4.48 (1.29-15.59)**	**1.60 (1.04-2.46)**	1	1.73 (0.18-17.08)	**13.43 (1.60-112.50)**	**1.72 (1.15-2.57)**	1	0.80 (0.24-2.63)	0.86 (0.24-3.07)	1.08 (0.73-1.62)
Age 2													
Crude	473	1	1.20 (0.63-2.27)	0.64 (0.25-1.61)	0.86 (0.61-1.22)	1	0.89 (0.39-2.01)	0.60 (0.27-1.34)	0.80 (0.62-1.02)	1	1.15 (0.56-2.34)	0.58 (0.28-1.20)	0.84 (0.68-1.05)
Adjusted	471	1	1.35 (0.68-2.66)	0.84 (0.31-2.31)	0.96 (0.65-1.41)	1	0.86 (0.38-1.98)	0.71 (0.28-1.78)	0.85 (0.63-1.15)	1	1.22 (0.59-2.53)	0.74 (0.30-1.79)	0.93 (0.70-1.23)
Age 7													
Crude	369	1	0.94 (0.59-1.49)	0.80 (0.45-1.40)	0.88 (0.70-1.11)	1	0.64 (0.63-1.18)	0.62 (0.34-1.13)	0.92 (0.78-1.08)	1	**0.53 (0.31-0.90)**	**0.52 (0.32-0.85)**	**0.84 (0.72-0.98)**
Adjusted	365	1	0.97 (0.60-1.58)	0.93 (0.50-1.73)	0.93 (0.72-1.20)	1	0.66 (0.35-1.26)	0.72 (0.36-1.43)	1.00 (0.81-1.22)	1	**0.50 (0.29-0.88)**	0.54 (0.29-1.01)	0.85 (0.70-1.04)
Atopic Dermatitis													
Age 1													
Crude	495	1	0.64 (0.31-1.33)	0.83 (0.36-1.89)	0.84 (0.59-1.21)	1	**0.34 (0.14-0.83)**	0.62 (0.30-1.30)	0.93 (0.74-1.17)	1	1.22 (0.58-2.55)	0.67 (0.32-1.40)	0.86 (0.69-1.08)
Adjusted	489	1	0.70 (0.33-1.50)	0.89 (0.36-2.22)	0.87 (0.59-1.28)	1	**0.37 (0.15-0.91)**	0.69 (0.28-1.68)	0.89 (0.67-1.18)	1	1.10 (0.52-2.34)	0.45 (0.18-1.11)	**0.74 (0.56-0.99)**
Age 2													
Crude	476	1	0.82 (0.40-1.700	**2.10 (1.05-4.17)**	1.18 (0.89-1.57)	1	1.07 (0.39-2.89)	1.80 (0.72-4.50)	1.12 (0.91-1.39)	1	1.67 (0.78-3.60)	1.29 (0.63-2.65)	1.05 (0.85-1.29)
Adjusted	470	1	0.82 (0.38-1.79)	**2.42 (1.08-5.42)**	1.20 (0.87-1.66)	1	1.17 (0.43-3.22)	2.03 (0.72-5.71)	1.11 (0.85-1.45)	1	1.42 (0.65-3.14)	0.97 (0.40-2.35)	0.96 (0.76-1.26)
Age 7													
Crude	380	1	**3.33 (1.48-7.49)**	**6.80 (2.95-15.66)**	**1.82 (1.34-2.48)**	1	1.43 (0.44-0.61)	2.93 (0.99-8.68)	1.25 (0.99-1.57)	1	1.10 (0.48-2.53)	1.41 (0.68-2.95)	1.08 (0.86-1.36)
Adjusted	376	1	**2.93 (1.25-6.89)**	**8.35 (3.20-21.76)**	**1.92 (1.33-2.78)**	1	1.32 (0.40-4.34)	2.69 (0.82-8.80)	1.31 (0.97-1.77)	1	0.99 (0.41-2.41)	1.47 (0.57-3.83)	1.12 (0.83-1.51)

**Adjusted for study group, study site, maternal food allergy, and exclusive breastfeeding at 4 months.
Odds ratios generated by multiple regression analyses with low food diversity as the reference group, or with food diversity as a continuous variable. Significant associations ($p<0.05$) are highlighted. N=sample size, OR=odds ratio, CI=confidence interval. **Allergenic foods are: soy, wheat, egg, dairy, seafood, peanuts.

Table 5. Summary of studies investigating early food diversity and allergic disease.

	CAPPS	PASTURE/EFRAIM	DIPP	LISA
Year of Birth	1995	2002-2005	1994	1997-1999
N	545	856	3781	2073
Population	high-risk	general	general	general
Setting	urban	rural	urban	urban
Country	Canada	Austria, Finland, France, Germany, Switzerland	Finland	Germany
Age at Food Diversity Assessment	6, 9, 12 months	6, 12 months	3, 6, 12 months	6, 12 months
Common Foods Evaluated	vegetables, fruit, meat, eggs, fish, dairy, wheat, other grains, soy, nuts	vegetables, fruit, meat, eggs, fish, dairy, cow's milk, cereal, soy, nuts	vegetables, fruit, meat, eggs, fish, cow's milk, cereal, wheat, other grains	vegetables, fruit, meat, eggs, fish, dairy, cereal, soy, nuts
Unique Foods Evaluated	rice	chocolate, cake, margarine, butter, bread, yogurt	potatoes	chocolate, cacao
Age at Outcome Assessment	age 1, 2, 7	age 6	age 5	age 6
Outcome Assessment	asthma, atopic sensitization, atopic dermatitis	asthma, allergic rhinitis, food allergy, atopic sensitization	atopic sensitization	asthma, allergic rhinitis, atopic sensitization, atopic dermatitis
Results	↑ food diversity at 6m is associated with ↑ risk asthma, atopy and atopic dermatitis; ↑ food diversity at 12m is associated with with ↓ risk for atopy	↑ food diversity is associated with ↓ risk in asthma, food allergy, food sesnsitization	↓ food diversity is associated with ↑ risk for food/non-food sensitization	↑ food diversity at 4m is associated with ↑ risk for atopic dermatitis, no association for others

CAPPS: Canadian Asthma Primary Prevention Study[35,36,40]
PASTURE/EFRAIM: Protection Against Allergy Study in Rural Environments[11]
DIPP: Finnish Type 1 Diabetes Prediction and Prevention[9]
LISA: Influences of Lifestyle-Related Factors on the Immune System and the Development of Allergies in Childhood[31]

Acknowledgments

I would like to thank Dr. Meghan Azad for initially agreeing to mentor and take me on as a student for this project. She has been nothing less than encouraging, patient and incredibly knowledgeable. She has been an exemplary supervisor whom I was fortunate to work with.

Thank you also to Dr. Moira Chan-Yeung, Dr. Edmond Chan and Dr. Allan B. Becker for providing access to CAPPS data, and for their valuable feedback and critical reading of the thesis. I would also like to thank all the families that participated in the CAPPS study, including students and staff involved.

Thank you to my entire Physician Assistant “family”: administration, advisors, preceptors and classmates for embarking with me on this crazy 2-year journey, which has allowed me the privilege of practicing medicine, the best job in the world.

Finally, I would like to thank my family: my parents Victor and Zeny, my in-laws Larry and Janice and *especially* Isaiah, Evan, Emmanuel and Andrew who provide unconditional love, continuous support and motivation, infinite patience and endless “study hugs” everyday. The greatest gift of encouragement was knowing that no matter how long I studied or how long I worked; there was someone, somewhere who couldn’t wait to see me.

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