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The prevalence of gluten free diet use among preschool children with autism spectrum disorder

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Abstract

Our objective was to estimate prevalence of current or ever use of a gluten free diet (GFD) in children aged 30–68 months with autism spectrum disorder (ASD) and population controls (POP); and to identify characteristics associated with ever having used GFD among children with ASD. We used data from the Study to Explore Early Development (SEED), a multi-site, case-control study of children with ASD. Caregivers reported GFD use by their children through structured questionnaires about diet patterns, gastrointestinal issues, and ASD-specific treatments. Prevalence was estimated and compared using log-Poisson regression, adjusting for confounders. In children with ASD, we examined whether child or mother's gastrointestinal conditions or child's phenotypic traits were associated with ever trying a GFD. In SEED, 71 children with ASD (11.1% prevalence after adjustment) were on a GFD at time of the study and 130 (20.4%) had ever used a GFD, a greater percentage than in POP children (N=11, 0.9% current use). Of current users with ASD, 50.7% had a dietary intervention that was prescribed by a medical professional. Among children with ASD, child gastrointestinal conditions and developmental regression were positively and independently associated with having ever used a GFD. Current use and ever use of a GFD were prevalent in children with ASD identified in SEED. GFD usage was associated with gastrointestinal issues and child phenotype. Clinicians may consider advising parents on how best to use these diets in the context of the child's GI presentation and current scientific knowledge about effectiveness in relation to ASD symptoms.

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Keywords

Gluten free diet; autism spectrum disorder; prevalence; alternative therapy; gastrointestinal conditions

Introduction

Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by social communication deficits and repetitive and restrictive behaviors and interests (American Psychiatric Association, 2013). Most interventions for ASD are behaviorally based, but there is growing interest in dietary therapies that families believe may improve behavioral outcomes (Herbert & Buckley, 2013; Valicenti-McDermott et al., 2014; Whiteley, 2015). These therapies may reduce burden of other co-occurring conditions, such as gastrointestinal (GI) issues or conditions, which are prevalent in people with ASD (estimates range from 4.2 to 96.8%) (Holingue, Newill, Lee, Pasricha, & Daniele Fallin, 2017). One such dietary therapy is a gluten free diet (GFD), which eliminates gluten, a protein found in wheat, barley, rye, and similar species and hybrids.

Because empiric evidence on the effectiveness of GFDs as an intervention for behavioral symptoms of ASD is weak and studies are few (Elder, Kreider, Schaefer, & de Laosa, 2015; Lange, Hauser, & Reissmann, 2015; Millward, Ferriter, Calver, & Connell-Jones, 2008; Sathe, Andrews, McPheeters, & Warren, 2017), it is important to understand which children (specifically of those without indications for a GFD like celiac disease) receive this type of alternative therapy as a way to better understand factors that influence the use of alternative therapies. The objective of this study was to estimate the prevalence proportion of current use or ever use of a GFD among children with ASD enrolled in the Study to Explore Early Development (SEED). Secondary objectives were to determine whether GFD use was associated with child traits like developmental regression, autism severity, and intellectual disability (ID), or with GI issues.

Methods

Design and participant ascertainment

SEED is a multi-site, community based, case-control study of ASD etiology and phenotypic correlates (Schendel et al., 2012). From 2007 to 2012, data were collected on children aged 30 to 68 months who were born between September 1, 2003 and August 31, 2006 in one of six sites (California, Colorado, Georgia, Maryland, North Carolina, and Pennsylvania). Each site's institutional review board and the Centers for Disease Control and Prevention review board approved the study protocol.

Children with ASD were identified through health and education agencies that provided diagnosis and services for children with ASD and other developmental disabilities or delays, and were invited to enroll in the study. ASD case status was confirmed by comprehensive evaluation (described below) as part of the study protocol. In addition, a sample of children born in the same years and regions were recruited from randomly sampled birth records to serve as population controls (POP)(Schendel et al., 2012).

Developmental assessment

The child's primary caregiver (the mother in 98% of participating families) completed the Social Communication Questionnaire (SCQ)(Rutter, Bailey, & Lord, 2003) during the enrollment phone call, and all children were asked to complete a general developmental evaluation that included the Mullen Scales of Early Learning (MSEL)(Mullen, 1995). To confirm ASD, children who screened positive on the SCQ (using a score ≥11 to indicate risk for ASD, which improves case finding in younger children) (Wiggins, Bakeman, Adamson, & Robins, 2007), had a past diagnosis of ASD, or were suspected to have ASD by a study clinician during the general developmental evaluation, were invited to participate in a full ASD evaluation.

During the full ASD evaluation, clinicians completed the Autism Diagnostic Interview-Revised (ADI-R)(Rutter, Le Couteur, & Lord, 2003) with the child's primary caregiver and the Autism Diagnostic Observation Schedule-2 (ADOS)(Lord, Rutter, DiLavore, & Risi, 2012) with the child. An algorithm based on standard scoring for those measures was used to determine final case status as described in Wiggins et al, 2015 (Wiggins et al., 2015). Developmental regression, or a loss of previously acquired skills, was determined from the developmental regression item in the ADI-R. Child ASD severity was calculated using the ADOS total score, ADOS language level, and age at the evaluation (Wiggins et al., 2017). The ten-point scale was dichotomized into 'less severe' (scores of 4-7) and 'more severe' (scores of 8-10). Intellectual Disability (ID) was determined if a child scored ≤70 on the composite score of the MSEL (Mullen, 1995).

Gluten free diet

We defined a GFD as the purposeful restriction of gluten or carbohydrates from a child's diet. We included diets that eliminate carbohydrates since they remove gluten by definition, although not all GFDs exclude all carbohydrates. Diets that eliminate casein, a protein found in dairy, are also common in conjunction with a GFD; however, our operational definition was based on any GFD, regardless of other dietary restrictions.

Current use—We determined GFD use at time of study participation (current use) by a GI-specific questionnaire asking all primary caregivers (both ASD cases and POP controls) if the child was currently on a restricted diet. If they answered yes, they were asked to describe the restrictions in an open-ended question. They were also asked whether the child's diet was self-restricted, parent-restricted, or medically prescribed (although data were not collected to confirm that the prescribed diet was a GFD or who prescribed or suggested the diet). Text responses were manually examined and if the text indicated GFD or a synonym (for example, 'no gluten') then children were classified as currently on a GFD.

Ever use—Caregivers of children with ASD completed an additional questionnaire on ASD-specific therapies and interventions and were asked 'what special diet, vitamins, food supplements, alternative treatments, or interventions has your child ever received?' We examined data from the text fields for any indication of a GFD. We combined past and current use to form an ever use GFD variable for the children with ASD.

Other data collection

Demographic data were collected by caregiver interview and from the child's birth certificate. Family medical history, including maternal history of any GI issues or of physician-diagnosed GI disorders (i.e., 'Did the mother ever have/or has the condition: gastrointestinal disorders' [yes/no]) and child's history of immune-related GI ('had the child ever had a diagnosis of celiac disease or non-celiac gluten sensitivity'), was ascertained through self-completed questionnaires. To identify children with GI problems, we used the caregiver's report that the child currently or in the past had GI issues on a regular basis (specifically, vomiting, constipation, diarrhea, loose stool, painful stool, abdominal pain, gas, or other occurring more than twice a month [yes/no for each issue.

Our primary analysis included all children who had SEED-confirmed ASD or were POP controls that provided data on current dietary practices (N=1481). To examine ever use of a GFD, our sample was restricted to children with ASD who had additional data reflecting use of GFD prior to study participation.

Prevalence proportions for the ASD group and POP group for current use and the ASD group for ever use of GFDs were modeled using multi-level log Poisson regression. We ran a crude model (with site as a random intercept since it is a design variable) and a model that used inverse probability weights (Rothman, Greenland S., & Lash T.L., 2008) to adjust for confounders identified a priori (maternal age, race, ethnicity, education, and child year of birth), keeping site as a random intercept. Based on minimal missing covariate data (<1%) we ran complete case analyses. Because a child could have received the first diagnosis of ASD in SEED, and these children might have different dietary experiences than those with a previous history of the diagnosis, we additionally ran a sensitivity analysis restricted to children who had a history of an ASD diagnosis.

Among the ASD group, we ran multi-level log Poisson models, similarly weighted as in our prior model to control for confounding, to compare prevalence of ever use of GFD by the child's developmental and family health characteristics: ID, developmental regression, ASD severity, child GI issues, and maternal GI issues. Because time and duration of GFD were not collected, we evaluated GFD use in association with phenotypic traits more likely to be stable with time. We evaluated the association between child and maternal GI issues and GFDs because GFD is often used to treat GI issues. We also stratified these analyses by whether the child had a history of GI issues to examine whether factors associated with GFD diet use were differentially associated with GI issues.

Results

We had adequate data to assess a child's GFD use for 689 (95%) of the 722 children with ASD and 759 (77%) of 986 POP children. POP mothers without data were of similar race and slightly less educated compared to POP mothers with data. Among children with ASD, 130 (18.8%) had ever use of a GFD and 71 had current use (10.3%). Of those current users, 34 indicated current use only and 37 indicated both past and current use. In the ASD group, those with current or ever GFD use were more likely to have mothers who were white (77.5% of mothers of ever users compared to 58.2% of mothers of never users) or have a

bachelor's degree or higher (65.1% of mothers of ever users compared to 48.6% of mothers of never users) than never users (Table 1). For children with ASD, 98% of ever users and 82% of those who never used a GFD had a past diagnosis of ASD at SEED enrollment. Of children with ASD who were current users of a GFD, 36 (50.7%) were on a diet that was medically prescribed. Forty children with ASD who were not current using a GFD (6.4%) were on a medically prescribed diet at study entry. We did not have information on what type of professional prescribed the diet. In contrast, 11 POP children (1.1%) had current use of a GFD. Of theses 11, 88.9% had white mothers, 72.7% were males, 44.4% had mothers with a bachelor's degree or higher, and none had ID. Among POP children who did not indicate current use of a GFD, 74.9% had white mothers, 64.9% had mothers with a bachelor's degree or higher and 90.4% were not Hispanic. In our sample, no children had celiac disease based on parental report.

Among children with ASD, 11.1% were current users of a GFD after adjusting for confounding (95% confidence interval [CI]: 8.2, 14.8) (Table 2). By comparison, 0.9% of POP children were current users in our adjusted model (95% CI: 0.5, 1.8). The adjusted prevalence estimate for ever use among children with ASD was 20.4% (95% CI: 17.3, 24.1). In a sensitivity analysis limited to just children with past ASD diagnosis results were similar to our full sample results; current use was 12.9% (95% CI: 9.2, 18.0) and ever use was 23.7% (95 CI: 19.1, 29.0).

Ever use of GFD was associated with developmental regression (prevalence ratio (PR): 1.70, 95% CI: 1.23, 2.36) and child GI issues (PR 2.95, 95% CI: 2.31, 3.77) (Table 3). GFD was not associated with child ID, ASD severity, or maternal GI issues. However, among children with ASD and GI issues, ASD severity was associated with ever use of a GFD (PR 1.43; 95% CI 1.01, 2.02) (Figure 1), while severity was not associated with ever use among children without GI issues (PR 1.11; 95% CI: 0.54, 2.29). In contrast, PRs for developmental regression were larger among children with ASD without GI issues (PR 2.53; 95% CI: 1.69, 3.79) compared to those with GI issues (PR 1.57, 95% CI: 1.08, 2.28). Maternal GI issues and ID were not associated with use of a GFD in either stratum of child GI issues.

Discussion

GFDs were common in preschool aged children with ASD in SEED with 20.4% of having ever used a GFD and 11.1% using a GFD at study entry. Current use was significantly more prevalent among ASD cases compared to POP controls who had a prevalence of 0.9%. Among children with ASD, 55% of those who had ever used a GFD remained on GFD at the time of study participation. GFD use was associated with child GI issues and developmental regression.

When comparing these results to past estimates of GFD prevalence, it is important to account for differences in methods and child age. An online survey conducted in 2011 in Southern Virginia of 194 parents of children with ASD found 54.8% had ever initiated a GFD for their child (Hopf, Madren, & Santianni, 2016). The survey sampled from members of autism community organizations asking whether they used any diet modifications or restrictions for their child. If the answer was yes, they were asked whether the modification

or restriction was a gluten free-casein free diet, or a GFD. Average child age was 9.9 years (standard deviation of 4.4 years)(Hopf et al., 2016). The estimate for GFD use may have been higher because these children were older and had more time to try this type of diet. Another survey sampled 246 parents of children with ASD recruited through regional databases and parent support organizations and forums in the United Kingdom between 2009 and 2010 and estimated that GFDs had been used by 31% of children aged 3-5 years (Winburn et al., 2014). Participation from specific parent forums or databases may reflect parents with similar approaches in trying therapies or, the group may have had shared communication about intervention effectiveness.

The results of our study of children aged 3–5 years reflect a broader sample from multiple sites, which adds demographic and phenotypic diversity. Because SEED recruited from a variety of clinical and educational sources, this estimate of GFD prevalence may reflect a broader population of individuals with ASD in this age category than would sampling from a particular setting or region. While SEED is unable to ascertain response proportions from the multi-source community sample, we adjusted analyses to control for potential socioeconomic differences in factors. Additional strengths of our study were the confirmation of ASD case status through gold standard developmental evaluation, and a sampling strategy that both confirmed case status and identified previously undiagnosed children, thus reducing potential for ASD misclassification that might reflect biases in access to health care and ASD case ascertainment.

Our study focused specifically on patterns of GFD use but was unable to assess the effectiveness of GFD for managing either ASD or GI symptoms. Prevalence of GFD use may be elevated as compared to POP controls because parents believe that reducing discomfort from GI issues can improve child behavior. GI issues in children with ASD are common (Hsiao, 2014; Ibrahim, Voigt, Katusic, Weaver, & Barbaresi, 2009) and GFDs are frequenty used as an alternative therapy for non-celiac GI issues, with some indication of success for irritable bowel syndrome (El-Chammas & Danner, 2011; Reilly, 2016). Our results showed a strong association between GFD and child history of GI issues, which may suggest that GFDs are tried in an attempt to alleviate these symptoms. The high prevalence of GI issues among children with ASD and the relative ease with which a parent can implement a dietary intervention may be a factor in the prevalence of GFDs. Although often expensive and hard to maintain (Elder et al., 2015), a GFD does not need a medical prescription or specialized training.

Reported celiac disease or gluten intolerance is no higher in children less than 10 years old with ASD than population controls (Ludvigsson, Reichenberg, Hultman, & Murray, 2013), but it has been hypothesized that a genetic condition among children with ASD might lead to a ‘leaky gut’ where gluten or casein creates an excess of peptides, causing behavioral symptoms common to ASD (Campbell et al., 2009; Elder et al., 2015; Reichelt & Knivsberg, 2009). Knowing that ASD behaviors may be related to the gut microbiome (Mangiola et al., 2016), parents or clinicians may decide to try this diet on children with ASD, regardless of the results of tests for these peptides. As yet, there have been only a few randomized controlled trials assessing effectiveness of a GFD as a tool to reduce behavioral symptoms, and among the studies that have been done, results lean toward no effect (Elder

et al., 2015; Hyman et al., 2016; Mari-Bauset, Zazpe, Mari-Sanchis, Llopis-Gonzalez, & Morales-Suarez-Varela, 2014; Millward et al., 2008; Navarro et al., 2015); however, few have addressed GI issues as a modifier in these trials (Elder et al., 2015). In our study, 50.7% of children with ASD who were current users of a GFD were on a diet that was prescribed by a medical professional (although data were not collected to confirm that the diet indicated was a GFD nor who was the prescriber). This percentage of children with a prescribed diet is high, given the lack of evidence supporting the efficacy of GFD use for reduction of ASD symptoms or GI symptoms in children with ASD. More information is needed to understand how these diets are discussed between clinicians and parents, given the often-difficult nature of diagnosing GI conditions in children with ASD (Buie et al., 2010) and the popularity of complementary treatments among parents (Valicenti-McDermott et al., 2014). Based on the current lack of knowledge and the uncertainty about efficacy communicating this uncertainty is important when GFD is discussed between parents and medical professionals.

We found that developmental regression was associated with ever use of a GFD. A study by Gadow et al. (2017) found that children with developmental regression were more likely to have a severe ASD presentation, and Patten et al. (Patten, Baranek, Watson, & Schultz) found that children with more severe presentations had tried more interventions. In our study, ever use of GFD was more likely in children with developmental regression and no GI issues than in children with developmental regression and GI issues. Despite limited scientific evidence for efficacy or effectiveness, parents often report that GFDs help improve child ASD symptoms such as social communication and interaction (Hopf et al., 2016; Winburn et al., 2014). It is possible that parents who report improvement in their child pass this information through social and support networks to other parents of children with ASD, increasing GFD usage. Although we did not have data on what motivated GFD usage, these results suggest that there could be at least three reasons for using this diet: 1) to reduce GI symptoms, 2) to reduce ASD specific symptoms, or 3) both.

Our study had some limitations that temper our conclusions. We did not collect data on date a GFD was initiated and length of time that it was used. This prevented us from exploring factors that preceded GFD use or average duration. Because data were collected at one point in time, we were unable to examine the impact of the GFD on child GI issues or ASD symptoms, or whether the parent found a GFD helpful. Further, data on child GI issues and GFD diet usage came from parent reports. Studies have reported wide ranges of GI issues in children with ASD that depends largely on method of data collection (Holingue et al., 2017; McElhanon, McCracken, Karpen, & Sharp, 2014). Our sample consisted of children who were 3–5 years old between 2007 and 2012. Our findings may not be generalizable to older children who may have more influence on their diet, or have had more time to try interventions, or to develop gluten intolerance. Because of this young age range, we were not able to evaluate the association between co-occurring conditions that may develop later in life, like epilepsy or obesity, and GFD initiation. Although we adjusted for the child's year of birth and had a narrow age range, children differed in the amount of time that they could have used a GFD. Lastly, the time frame of our data collection may not have captured the boom in GFDs in the general population in the early 2010s (Reilly, 2016).

Despite these limitations, SEED collected extensive data, allowing examination of GFD use and various developmental characteristics important for refining smaller ASD subgroups, which may be more or less likely to try or to benefit from particular therapies. Our sample was from a multi-site community-based study with confirmed ASD diagnosis, reducing potential biases associated with self-selection from online surveys or clinic-only samples. This study estimated prevalence for both current use and ever use, which provides insight into the frequency with which parents try and then abandon GFDs. Additional research is needed regarding effectiveness of the GFD and why parents who try the diet choose to continue or discontinue it.

More than 20% of young children with ASD have been tried on a GFD. Despite a lack of rigorous evidence that GFDs broadly impact ASD symptoms, this diet may still be used in an attempt to reduce GI or ASD symptoms. Children with ASD who had parent-reported developmental regression or GI issues were more likely to have used a GFD, yet developmental regression was more strongly associated with GFD when a child did not have GI issues. GFDs are necessary for treating celiac disease and may be appropriate for children with other GI issues, but effectiveness for treating ASD or other conditions deserves further study so that parents can make informed decisions about whether their child may benefit from this diet. Because GFD use is high and efficacy is uncertain, more information about the effect of a GFD on GI and ASD symptoms is needed so that clinicians can better advise parents of children with ASD.

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Lay summary

Gluten free diets are commonly used as an alternative therapy for autism spectrum disorder (ASD); however, the effectiveness is still uncertain which makes it important to know who tries this type of diet. We found that one in five preschool aged children with ASD had ever used a gluten free diet. Children with gastrointestinal conditions and developmental regression were more likely to have tried a gluten free diet.

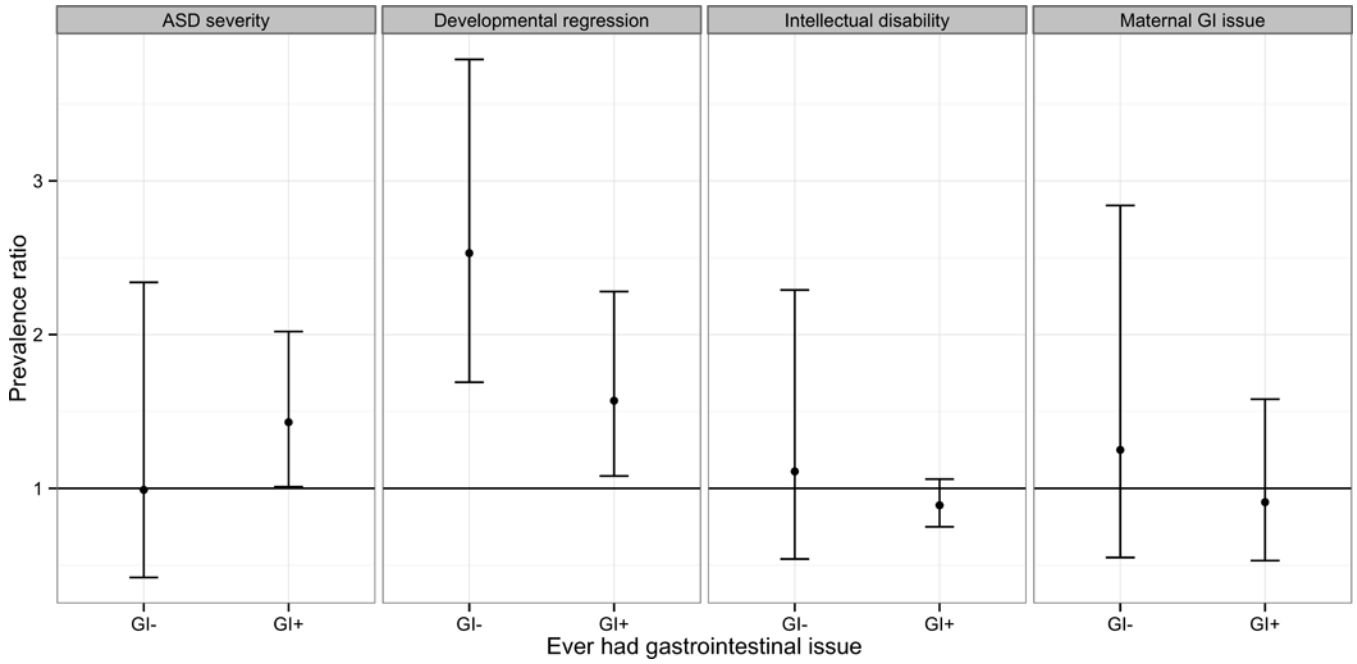

Figure 1.

Prevalence ratios between associated features and ever use of a gluten free diet by whether the child ever had gastrointestinal issues among children 3–5 years old with autism spectrum disorder in the Study to Explore Early Development GI+, child ever having gastrointestinal issue; GI-, child never having gastrointestinal issue; ASD, autism spectrum disorder Adjusted for maternal race/ethnicity, maternal education, and maternal age at clinic visit, child year of birth using inverse probability weights; site adjusted using random intercept

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Table 1

Distribution of demographic characteristics of children 3–5 years old in the Study to Explore Early Development, by gluten free diet use

	ASD cases			POP controls	
	Ever use N=130	Current use N=71	Never use N=559	Current use N=11	'Not current' N=748
	%	%	%	%	%
Maternal race					
White	77.5	78.6	58.2	88.9	74.9
Black	4.7	2.9	23.8	11.1	13.5
Asian	7.8	10.0	9.1	0.0	4.6
Other	10.1	8.6	9	0.0	7.0
Missing (n)	1	1		2	3
Maternal education					
Less than high school	2.3	1.4	6.1	0.0	3.1
High school	4.7	2.9	13.3	0/0	7.3
Associates or some college	27.9	25.7	32.1	33.3	24.7
Bachelor's degree	36.4	37.1	28.9	44.4	35.5
Master's degree	28.7	32.9	19.7	22.2	29.4
Missing (n)	1	1	1	2	4
Maternal ethnicity					
Hispanic	11.6	10.0	12.9	0	8.3
Not Hispanic	88.4	90.0	87.1	100	90.4
Missing (n)	1		3	2	13
Maternal age at enrollment (years)					
Mean	37.0	37.6	36.1	36.6	36.6
Standard deviation	4.6	4.6	5.7	6.5	5.5
Study Site					
California	23.1	19.7	14.9	9.1	16.9
Colorado	21.5	28.2	19.1	18.2	19.5
Georgia	12.3	8.5	21.1	18.2	18.9

	ASD cases			POP controls	
	Ever use N=130	Current use N=71	Never use N=559	Current use N=11	'Not current' N=748
	%	%	%	%	%
Maryland	17.7	16.9	14.1	27.3	13.3
North Carolina	13.9	15.5	15.6	9.1	18.0
Pennsylvania	11.5	11.3	15.2	18.2	13.4
Child year of birth †					
2003	8.5	11.3	8.8	0.0	5.4
2004	28.5	35.2	31.3	36.4	40.6
2005	41.5	38.0	38.3	54.5	44.8
2006	21.5	15.5	21.6	9.1	9.1
Child sex					
Male	86.2	87.3	80.9	72.7	53.2
Female	13.8	12.7	19.1	27.3	46.8
Previous ASD diagnosis					
Yes	98.4	100	82.5	–	–
No	1.6	0	17.5	–	–
Missing	1	–	4		
Child Social Communication Questionnaire Score					
Mean	18.2	18.3	17.1	5.6	4.2
Standard deviation	6.0	5.6	6.1	5.3	3.5

ASD, autism spectrum disorder; Current use, using a gluten free diet at time of study participation; Ever use, use of a gluten free diet either in the past or at study participation

† Children were born between September 1, 2003 and August 31, 2006

Table 2

Prevalence proportion of current use and ever use of a gluten free diet in children 3–5 years old in the Study to Explore Early Development

		Crude		Adjusted[†]	
	N	**Prevalence %**	**95% CI**	**Prevalence %**	**95% CI**
Current use					
ASD	71	10.1	7.4, 14.0	11.1	8.2, 14.8
POP	11	1.1	0.8, 1.6	0.9	0.5, 1.8
Ever use					
ASD	130	18.8	15.1, 23.3	20.4	17.3, 24.1

ASD, autism spectrum disorder; POP, Population controls; CI, confidence interval; ‘Current use,’ using a gluten free diet at time of study participation; Ever use, use of a gluten free diet either in the past or at study participation

Crude models adjusted only for site using a random intercept

[†]Adjustment for maternal race/ethnicity, maternal education, maternal age at clinic visit (with spline at 36 years), child year of birth using inverse probability weights, site adjusted using a random intercept

Table 3

Prevalence ratios for the relationship between associated features and ever use of a gluten free diet among children 3–5 years old with autism spectrum disorder in the Study to Explore Early Development

Associated Feature	Ever use N=130 %	Never use N=559 %	Prevalence Ratio	95% CI
Developmental regression				
Yes	42.3	25.6	**1.70**	**1.23, 2.36**
No	67.7	74.4	–	–
Intellectual disability				
Yes	61.5	62.3	0.92	0.77, 1.10
No	38.5	37.7	–	–
ASD severity				
>7	49.6	38.6	1.34	0.94, 1.91
<7	50.4	61.4	–	–
Missing (n)	5	10	–	–
Maternal gastrointestinal issues				
Yes	16.0	20.3	0.96	0.56, 1.65
No	84.0	79.7	–	–
Missing (n)	1	19	–	–
Child gastrointestinal issues				
Yes	78.3	47.0	**2.95**	**2.31, 3.77**
No	21.7	53.0	–	–
Missing (n)	1	29	–	–

GFD, gluten free diet; ASD, autism spectrum disorder; CI, confidence interval

Observations with missing data were dropped from the regression model

Adjustment for maternal race/ethnicity, maternal education, and maternal age at clinic visit, child year of birth using inverse probability weights; site adjusted using a random intercept