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Nutrition and Bone Density in Boys with Autism Spectrum Disorder

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Abstract

Background—Boys with autism spectrum disorder (ASD) have lower bone mineral density (BMD) than typically developing controls (TDC). Differences in diet and exercise may contribute to low BMD.

Objectives—To examine macro- and micro-nutrient intake and self-reported physical activity in boys with ASD compared to TDC and the relationship of these variables with BMD.

Design/Methods—Cross-sectional study of 49 boys (25 ASD, 24 TDC) assessed for three-day food records and physical activity records, and BMD of the whole body less head, hip and spine using dual energy X-ray absorptiometry. Fasting levels of 25(OH) vitamin D and calcium were obtained.

Participants—Adolescent boys, ages 8–17 years, recruited from a clinic population (ASD) or community advertisements (ASD and TDC) matched for age.

Results—ASD participants were approximately 9 months younger than TDC participants on average. Body mass index and serum vitamin D and calcium levels were similar. Boys with ASD consumed 16% fewer calories, with a larger percentage obtained from carbohydrates, and 37% less animal protein and 20% less fat than TDC. A lower proportion of ASD participants were categorized as “very physically active” (27% vs. 79%, $p<0.001$). BMD Z-scores were 0.7 to 1.2 standard deviations lower in ASD than TDC at all locations. Higher animal protein, calcium and phosphorus intake was associated positively with bone density measures in boys with ASD.

Conclusion—Compared to TDC, boys with ASD had lower protein, calcium and phosphorus intake, activity levels and BMD Z-scores at the lumbar spine, femoral neck, total hip and whole body less head. Protein, calcium and phosphorus intake were associated positively with BMD.

Keywords

Autism Spectrum Disorder; Nutrient intake; Bone Mineral Density; Physical Activity

1. Introduction

Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder behaviorally characterized by impairments in social interactions and communication and atypical, restricted and repetitive patterns of behaviors with rates of up to 1 in 68 children in the United States.¹ Nutrition management of children with ASD is a challenge because children frequently have a restricted diet, often self-imposed and limited by taste or texture.² Their diet may also be limited by medical illness or parent choice of a restricted food type such as gluten-free and/or casein-free diets.^{3,4} Furthermore, concurrent gastrointestinal diseases in children with ASD may affect absorption of nutrients.⁵

Peak bone mass is an important determinant of future bone health.⁶ The childhood years are critical for development of bone mass, which depends upon many factors including genetics, nutrition, weight bearing activity, hormonal status, medication use and medical disease.⁷ Because of a restricted diet, insufficient vitamin D intake,^{8–10} gastrointestinal disease,^{5,11} chronic use of medications including anti-epileptics,^{12,13} antipsychotics¹⁴ and selective serotonin reuptake inhibitors,¹⁵ as well as hypotonia¹⁶ and lower physical activity levels,¹⁷ children with ASD have many risk factors for low bone mineral density (BMD). In cross-sectional studies examining BMD in ASD and typically developing age-matched controls (TDC), we have previously reported decreased BMD at the spine, hip and femoral neck in peripubertal boys with ASD compared to TDC,^{10,18} and other authors have also described low BMD Z-scores and low bone cortical thickness in ASD.^{19–22} Low peak bone mass could lead to increased fracture risk. Further, studies report higher odds of hip and spine fractures in children and adults with ASD.^{23,24} In a secondary analysis of the primary study, we now seek to learn whether differences in diet and activity contribute to lower bone mineral density in boys with autism spectrum disorder.

2. Subjects and Methods

2.1 Subjects

A total of 38 males (19 ASD and 19 TDC) between the ages of 8 to 17 years were enrolled at study initiation for the cross-sectional study in 2011¹⁰ and returned for a follow-up outpatient visit in 2015. At the time of the second visit, 13 additional participants (6 ASD and 7 TDC) were enrolled. Upon analysis, 2 TDC siblings were excluded due to abnormally low levels of serum 25-hydroxy vitamin D (25(OH)D) (<15 ng/mL), suggesting that they were no longer TDC and had a possible condition with the potential to affect bone metabolism. Therefore, a total of 49 participants (25 ASD and 24 TDC, including 2–3 siblings from each of 5 families) were available for cross-sectional analyses. Data for this secondary analysis were primarily obtained from participants' 2015 outpatient study visit (N=38). If data were not available at the 2015 visit, but were available from the 2011 visit, data from their 2011 visit (N=11) were used.

All children had a body mass index (BMI) z score between –1.88 and +1.88 for age, based on standard charts.²⁵ Children with ASD met Diagnostic and Statistical Manual of Mental Disorders (DSM)-IV²⁶ and Autism Diagnostic Observation Schedule criteria for an ASD.^{27,28} The control group was recruited through advertisement in primary care providers' offices, the internet, advertisement within the hospital, and word of mouth. Exclusion criteria for all participants included use of medications that affected bone metabolism including testosterone, estrogen/progesterone or glucocorticoids (except inhaled glucocorticoids), and use of anticonvulsant medications such as diphenylhydantoin, phenobarbital, topiramate, carbamazepine and valproic acid. Children with a known disease affecting bone such as Crohn's disease, celiac, thyroid and renal disease or evidence of impaired vitamin D metabolism based on lab results were also excluded. Studies were performed at a clinical research center as outpatients. The Institutional Review Board of Partners HealthCare System approved this study. Informed assent and consent were obtained from subjects and their parents, respectively.

2.2 Experimental Protocol

All participants had a history and physical examination performed at the outpatient visit at the clinical research center, including self-report of pubertal (Tanner) stage using standardized pictures. Parents helped with collection of food records, puberty and exercise assessment during the week before the visit. Daily nutrient intake and average food group serving count was assessed by Clinical Research Center dietitians using a 3-day food record and the Minnesota Nutrition Data System for Research (NDSR) software versions 2009 and 2014 (Nutrition Coordinating Center, University of Minnesota, Minneapolis, MN) which parents completed on the week prior to visit. Food records were collected from 79% of subjects on two weekdays and one weekend day and from 13% on three weekdays and 5% from two weekend days and one weekday. Final calculations were completed using NDSR version 2014 for all visits. Two activity questionnaires were utilized: The Oxford Physical Activity Questionnaire (OPAQ) and the Youth Physical Activity Survey (YPAS). The OPAQ is validated for adolescents, and while the YPAS is not validated, it contains activities that are more appropriate to the ASD population (e.g., rocking, spinning, full body tantrums).^{29,30}

BMD was measured using dual energy x-ray absorptiometry (DXA) (Hologic Discovery A, Software Version: APEX 4.0.2, Bedford, MA USA) at the total hip, femoral neck, and lumbar spine (L1-4). During the 2015 visit, whole body and whole body less head (WBLH) BMD was also measured (not available for participants assessed in 2011). Z-scores based on age-, sex-, and race-specific pediatric norms from Hologic were reported. DXA was also used for measures of body composition (lean and fat mass). Additional anthropometric measurements were completed at this outpatient visit using standardized techniques (Lohman). Height (cm) was measured without shoes in triplicate using a wall-mounted Harpenden stadiometer (Holtain, Ltd, UK) and weight (kg) was measured in light clothing, without shoes, using a calibrated Tanita BWB 800S digital scale (Tanita Corporation of America Inc. Arlington Heights, Ill).

2.3 Statistical Analysis

Data were analyzed using Statistical Analysis Software (SAS) (version 9.4, SAS Institute, Cary, NC). Continuous variables were assessed for normality, and transformations were performed to approximate normality as appropriate. Generalized estimating equations (GEE) were used to compare ASD vs. TDC participants to account for correlation among siblings as our sample included 5 sets of 2–3 siblings. Separate models were used to adjust for age and age plus physical activity. Estimates are reported for the mean age and log-transformed OPAQ physical activity levels. GEE was also used to test linear associations of nutrition parameters with body composition and BMD. All continuous data are reported as model-estimated means and standard errors and all categorical data are reported as model-estimated rates and 95% confidence intervals. Macronutrients are reported as grams per kilogram body weight. To account for effects of season on 25(OH)D formation, adjustments were made for the sine of day of year* π /365 in analyses of 25(OH)D levels. Hypotheses were tested at a two-tailed 0.05 significance level. We report p-values both unadjusted for multiple comparisons and after a step-down Bonferroni adjustment.

3. Results

Clinical Characteristics

Table 1 shows the clinical characteristics of ASD and TDC participants. Compared to TDC participants, ASD participants were approximately 9 months younger on average, although this difference was not significant. The two groups were similar with respect to BMI and biochemical measurements (serum vitamin D and serum calcium).

Macronutrient Intake

Table 2 compares daily macronutrient intake in ASD vs. TDC participants, adjusting for age. In this sample, ASD participants consumed approximately 16% fewer calories overall compared to TDC, both with and without the inclusion of supplements. Food intake alone was proportionally higher for calories obtained from carbohydrates, and lower for calories obtained from proteins. ASD participants consumed 37% less animal protein than TDC, and 28% less protein overall than TDC, while vegetable protein intake did not differ between groups. ASD participants consumed 20% fewer grams of total fat (mostly from a reduction in saturated fatty acids), while monounsaturated and polyunsaturated fatty acid intake was similar across groups. Fiber consumption did not differ between groups. After controlling for physical activity in addition to age, neither consumption of carbohydrates nor consumption of total fat differed between study groups. Our findings were similar for macronutrient intake from food and supplements.

Micronutrient Intake

Table 3 compares daily micronutrient intake in ASD vs. TDC participants, adjusting for age. Evaluating food intake alone, boys with ASD consumed significantly less calcium, iron, phosphorous, selenium, vitamins A, riboflavin, niacin, B6, B12 and dietary folate equivalents, with deficiencies ranging from 19 to 35%. Marginal deficiencies were also observed in copper, magnesium, thiamin and vitamin D ($p < 0.15$). With the inclusion of supplements, the two study groups were more similar in their micronutrient intake, except for persisting deficiencies in calcium, phosphorous, selenium, and riboflavin in the ASD group. After controlling for physical activity in addition to age, the differences in calcium, iron, and vitamins A and B12 consumption from food were no longer significant, but estimated deficits in the ASD group still ranged from 21 to 30%.

Activity Levels

Only 27% of ASD participants were classified as ‘very active’ per the Youth Physical Activity Survey, compared to 79% of TDC participants (Table 1).

Bone Density Measures

Table 1 also shows BMD measures in the study groups. Mean BMD Z-scores were more than 0.7 standard deviations lower in ASD than TDC at the lumbar spine (0.97), femoral neck (1.21), total hip (0.98), whole body (0.80), and WBLH (0.71). These bone density differences held across groups after controlling for Tanner stage and bone age.^{21,22}

Associations of Nutrient Intake with Bone Mineral Density

Associations between nutrition parameters and BMD in ASD and TDC groups were explored separately. Higher animal protein intake was associated with higher BMD Z-scores in ASD participants only, while higher vegetable protein intake was associated with higher femoral neck BMD Z-scores in TDC participants only. Total and monounsaturated fat was positively associated with femoral neck BMD Z-scores in the TDC group. Calcium and phosphorus intake from diet and supplements such as vitamins, minerals, high protein drinks were positively associated with all measures of BMD in boys with ASD, but not TDC.

4. Discussion

We observed that boys with ASD consume fewer calories, more carbohydrates, and less protein and fat than TDC, and higher animal protein, calcium and phosphorus intake was associated positively with bone density measures in boys with ASD. We confirmed lower physical activity levels and markedly lower BMD Z-scores in boys with ASD compared to TDC. Our results support past research that identify restricted diets and decreased physical activity as risk factors for low BMD in children with ASD.^{4,10} While most past research has focused on the impact of calcium and vitamin D intake on bone health, other nutrients may play a critical role as well.

Diet

Animal protein intake was associated with higher BMD Z-scores in ASD participants only, while vegetable protein was associated with higher femoral neck BMD Z-scores in TDC participants only. Although there have been limited studies examining associations of protein intake and BMD in children, and findings regarding the effect of dietary protein on bone metabolism are mixed, results from a prospective study by Alexy et.al, indicate a positive association between dietary protein intake and bone variables in prepubescent and pubescent children as assessed by peripheral quantitative computed tomography (pQCT) of the forearm.³¹ Protein intakes in the study by Alexy et al. (g/kg/day) were similar to those observed in our study participants and higher than the Recommended Dietary Allowance proposed by the National Institute of Medicine (IOM), i.e., 0.95 g/kg/day for males 9–13 years and 0.85 g/kg/day for males 14–18 years (IOM).³² Similarly, several adult studies have observed a positive association between dietary protein and bone health.^{33–35} In a supplemental review by Heaney et.al (part of The Protein Summit in 2008, which focused on dietary protein and bone health), the authors suggested that in the setting of adequate dietary calcium, higher protein diets may be associated with increased bone mass (bone mineral content) and decreased risk for fractures.³³ High protein diets lead to increased intestinal absorption of calcium, increased levels of circulating insulin like growth factor-1 (IGF-1), and decreased serum parathyroid hormone (PTH) levels, even though the renal acid load leads to bone resorption and increased calcium loss.^{33,35} Low-protein diets, in contrast, may negatively affect skeletal health through impaired calcium absorption.³⁶

The source as well as the quantity of dietary protein affects bone health. Sources of animal protein may have a more positive effect on bone health than vegetable protein (in particular, soy), possibly due to the impact of soy on serum IGF-1 levels.^{36,37} Protein intakes

associated with normal calcium metabolism in adults range from 1–1.5 gm/kg whereas at lower levels, 0.8 gm/kg – 1 gm/kg, intestinal calcium absorption is reduced, and parathyroid hormone levels increase, causing the release of calcium from bone.³⁶ In our study, participants with ASD consumed 37% less animal protein compared to TDC, and those with higher animal protein intakes had higher BMD z-scores. Several studies have suggested that diets should focus on increasing the intake of fruits and vegetables high in potassium and magnesium, alkalizing minerals that possibly reduce dietary acid load and decrease urinary calcium excretion, instead of restricting protein sources.^{31,33}

Our data confirm reports of micronutrient inadequacies in the diets (food alone) of boys with ASD and that vitamin supplementation does not correct several of these inadequacies.⁴ In particular, we report that boys with ASD consumed significantly less calcium, iron, phosphorous, selenium, vitamin A, several B vitamins, and dietary folate equivalents than TDC. Diets were marginally deficient in copper, magnesium and vitamin D. With supplementation, deficiencies persisted in selenium and riboflavin as well as two minerals important to bone health, calcium and phosphorus. These nutrients (selenium, riboflavin, calcium and phosphorus) are commonly found in animal protein, in particular dairy products. This is similar to results of a cross-sectional study in children with ASD by Stewart et al. in 2015, where after supplementation, inadequacies in dietary calcium were not corrected in 40 – 55% of the children with ASD.⁴ In contrast to other studies, we found that vitamin D intake was similar across the groups after supplementation. When translated into categories of food groups consumed, our data showed that participants with ASD consumed significantly less dairy than TDC. Boys with ASD consumed (mean number of servings 2.92 vs 6.93, $p = 0.003$) compared to TDC contributing not only to the lack of dietary protein, but also to the lack of calcium and phosphorus. This is relevant in that calcium and phosphorus intake were consistent predictors of all BMD measures in children with ASD. There was no significant difference between intakes of non-dairy alternatives between the two groups.

Our study suggests that dietary recommendations in children with ASD should focus on higher protein intake (greater than the current RDA recommendations) and adequate intake of calcium and phosphorus.

Activity

Physical activity and mechanical loading can directly impact BMD in children, and children with ASD may be at risk for lower BMD than typically developing children early in life because of lower levels of physical activity.^{7,17,20} In this study, children with ASD were found to be engaged in activities classified as “very active” significantly less than TDC children. Other studies have found similar results where children with ASD have a high ratio of screen time to physical activity (1:3 minutes – 69 minutes/day active and 251 minutes/day media time²⁰). These values, similar to the “very active” designation used in the questionnaires in this study, are subjective to the parent’s or guardian’s perception. Furthermore, these questionnaires define “very active” as participating in organized sports teams, which may dissuade parents or guardians from considering other activities that are very active but not part of an organized sports team. For example, the OPAQ only asks for

information regarding time spent playing sports on an organized team or in Physical Education class, where the YPAS offers options of other activities that could be classified as very active that are not considered team sports (tantrums, spinning, jumping, trampolining, climbing hills). These questionnaires may not show an accurate comparison for children with autism due to potential social aspect that may make it difficult to participate in organized sports. These factors need to be taken into consideration when validating physical activity questionnaires for this population.

While low BMD and increased fracture risk has been reported in children with other chronic diseases and those with physical limitations, these populations differ from children with ASD in many ways. For example, children with ASD are very different from undernourished children with eating disorders. In contrast to children with low weight eating disorders, the BMI of the ASD participants in this study was comparable and if anything, higher than that of the TDC. Also, in contrast to our participants with ASD, children with eating disorders tend to do better than controls for intake of calcium and vitamin D.³⁸ Children with inflammatory bowel disorders and low bone density are often of lower weight than controls, and/or have evidence of significant inflammation and/or malabsorption that may impact their bones. They may also be hypogonadal, and on medications that impact bone directly (such as glucocorticoids). This is in contrast to children with ASD, who may have some GI issues, but not to the extent seen in children with inflammatory bowel disorders.^{39–42} They were also not hypogonadal or typically on medications that have such significant impact on bone. Children with diabetes are now being recognized to have low BMD,^{43,44} however, this is associated with poor glycemic control, inflammation and possibly advanced glycation end products. None of our participants had evidence of hyperglycemia. Further, children with cerebral palsy and conditions associated with limited mobility have reduced BMD and increased fracture risk from nutritional issues, reduced weight bearing, hypotonia and possibly use of medications that may impact bone directly (such as glucocorticoids), or by impacting vitamin D metabolism.⁴⁵ While our participants reported lower physical activity levels compared to controls, they were all ambulatory and did not have the physical impairment observed in children with cerebral palsy. We also excluded children with ASD who were on medications that may impact bone directly or vitamin D metabolism.

Limitations

Because of the use of self-reported food and activity diaries, known bias and imprecision may exist in recorded information.^{46–48} Data, in particular energy intake, may be underestimated and should be interpreted with caution.⁴⁹ People are better at reporting what they have not done in terms of physical activity rather than what they have done because the concept of not doing something is more definitive in ones' memory, whereas a reactivity response may occur where people report actual activity by over-reporting. Our food and activity diaries, although reviewed by a trained research dietitian, were completed either by the parent or in some cases, the study participant. Children attending school during the collection of data may have incomplete diaries due to limited knowledge of portion size estimation, school food service menu and physical education class details. Further, in order to maximize numbers of participating children, we included siblings, and as a consequence had to control for covariance between siblings using statistical methods.

Conclusion

Boys with ASD had lower BMD Z-scores at the lumbar spine, femoral neck, total hip and whole body than TDC. Protein, calcium and phosphorus intake were lower in ASD than TDC and were associated positively with BMD measures. Future studies, including those studying females with ASD, and interventional studies that focus on diet and exercise in ASD, are needed. Better understanding of activities suitable for children with ASD and their impact on bone would permit better guidance regarding recommendations. Our study suggests that encouraging diets higher in fortified dairy and animal protein, as well as increased high-level exercise (particularly bone loading activities) may improve bone health. It is thus important for practitioners to assess dietary intake of fortified dairy and animal protein in patients, and to recommend sufficient servings to provide at least the recommended dietary allowance of these ingredients in diet. For those patients on a dairy free diet, supplements may be necessary to optimize intake of calcium and phosphorus.

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Research Snapshot

Research Question

Do differences in diet and activity contribute to lower bone mineral density in boys with autism spectrum disorder?

Key Findings

In this cross-sectional study of 49 boys (24 of which are controls), study participants were assessed for bone mineral density, three-day food records, and physical activity. Boys with autism spectrum disorder (ASD) consumed 16% fewer calories and 37% less animal protein than controls, were less active and had lower BMD-Z scores. Protein, calcium and phosphorus intake were lower in ASD than typically developing controls (TDC) and were associated positively with bone mineral density (BMD).

Table 1

Clinical characteristics and body composition and Bone Mineral Density (BMD) in boys with Autism Spectrum Disorder (ASD) and typically developing controls (TDC)

Variable	ASD Mean (SE) or Rate (95% CI)	Control Mean (SE) or Rate (95% CI)	ASD vs. Control Difference (95% CI) or OR (95% CI)	P-Value
Age (years)	12.72 (0.50)	13.50 (0.48)	-0.78 (-2.14, 0.58)	0.26
Height Z-Score	0.29 (0.21)	0.71 (0.26)	-0.42 (-1.07, 0.23)	0.20
Weight Z-Score	0.35 (0.20)	0.31 (0.17)	0.04 (-0.46, 0.53)	0.89
BMI Z-Score	0.18 (0.22)	-0.07 (0.19)	0.24 (-0.32, 0.81)	0.40
Lean dry mass (kg)	7.66 (0.34)	8.42 (0.30)	-0.76 (-1.64, 0.11)	0.088
Fat mass (kg)	15.46 (2.19)	12.28 (1.55)	3.18 (-2.06, 8.41)	0.23
Lumbar Spine Bone Mineral Density (BMD) Z-Score	-0.94 (0.22)	0.02 (0.18)	-0.97 (-1.52, -0.41)	<.001
Femoral Neck BMD Z-Score	-1.56 (0.19)	-0.35 (0.18)	-1.21 (-1.72, -0.70)	<.001
Total Hip BMD Z-Score	-0.92 (0.25)	0.06 (0.22)	-0.98 (-1.62, -0.33)	0.003
Whole Body BMD Z-Score	-1.29 (0.20)	-0.49 (0.18)	-0.80 (-1.32, -0.28)	0.003
Whole body less head z-scores	-1.19 (0.22)	-0.48 (0.19)	-0.71 (-1.28, -0.14)	0.014
Serum Calcium (mg/dL)	9.66 (0.06)	9.65 (0.05)	0.01 (-0.15, 0.16)	0.92
Serum Vitamin D (ng/mL) (Adjusting for seasonality)	25.74 (1.35)	28.79 (2.92)	-3.06 (-9.80, 3.69)	0.37
Log Oxford Physical Activity Questionnaire Mets	7.42 (0.22)	8.13 (0.17)	-50.56% (-68.93%, -21.32%)	0.003
Youth Physical Activity Level: Very Active	27.3% (12.8, 48.9%)	79.2% (59.3, 90.8%)	OR=0.1 (0.0, 0.4)	<.001

* Whole body and Whole body less head Z-scores were available for 16 ASD and 18 TDC.

Estimates and p-values are reported from a generalized estimating equation model that accounted for covariance among siblings

Table 2

Daily macronutrient intake in boys with Autism Spectrum Disorder (ASD) vs. typically developing controls (TDC).

	Results from models adjusting for age ¹					Results from models adjusting for age and physical activity ¹		
	ASD Mean (SE)	TDC Mean (SE)	ASD vs. TDC Difference (95% CI)	Nominal P-Value ²	Corrected P-Value ²	ASD vs. TDC Difference (95% CI)	Nominal P-Value ²	Corrected P-Value ²
Intake from Food Only								
Energy (kcal)	2040 (95.7)	2430 (120.3)	-16.07% (-26.48%, -4.17%)	0.010	0.22	-11.26% (-23.38%, 2.78%)	0.11	>.99
Total Carbohydrate (g/kg)	5.34 (0.40)	5.88 (0.38)	-9.17% (-25.49%, 10.71%)	0.34	>.99	-17.79% (-33.01%, 0.90%)	0.061	>.99
Calories from Carbohydrate (%)	52.65 (1.34)	48.87 (1.23)	3.78 (0.33, 7.23)	0.032	0.61	1.78 (-2.92, 6.48)	0.46	>.99
Total Protein (g/kg)	1.41 (0.09)	1.95 (0.13)	-27.77% (-39.43%, -13.87%)	<.001	0.008	-34.44% (-46.96%, -18.97%)	<.001	0.003
Calories from Protein (%)	14.15 (0.46)	16.85 (0.72)	-2.70 (-4.39, -1.02)	0.002	0.043	-3.02 (-4.65, -1.39)	<.001	0.007
Animal Protein (g/kg)	0.83 (0.07)	1.33 (0.11)	-37.46% (-50.01%, -21.76%)	<.001	0.001	-42.46% (-55.85%, -25.02%)	<.001	0.001
Vegetable Protein (g/kg)	0.52 (0.05)	0.58 (0.04)	-9.85% (-28.35%, 13.42%)	0.38	>.99	-16.61% (-34.16%, 5.63%)	0.13	>.99
Total Fat (g/kg)	1.50 (0.11)	1.87 (0.14)	-19.51% (-33.78%, -2.16%)	0.029	0.59	-19.82% (-36.57%, 1.36%)	0.065	>.99
Calories from Fat (%)	33.18 (1.20)	34.22 (0.98)	-1.05 (-4.01, 1.92)	0.49	>.99	1.27 (-2.87, 5.42)	0.55	>.99
Total Saturated Fatty Acids (SFA) (g/kg)	0.47 (0.04)	0.67 (0.06)	-29.51% (-43.68%, -11.77%)	0.002	0.056	-26.88% (-44.06%, -4.42%)	0.022	0.52
Calories from SFA (%)	10.59 (0.57)	12.36 (0.48)	-1.77 (-3.23, -0.31)	0.017	0.37	-0.65 (-2.25, 0.95)	0.43	>.99
Total Monounsaturated Fatty Acids (MUFA) (g/kg)	0.52 (0.04)	0.64 (0.05)	-18.07% (-33.56%, 1.04%)	0.062	>.99	-16.34% (-36.31%, 9.87%)	0.20	>.99
Calories from MUFA (%)	11.85 (0.67)	11.79 (0.47)	0.06 (-1.53, 1.64)	0.94	>.99	1.22 (-1.21, 3.65)	0.32	>.99
Total Polyunsaturated Fatty Acids (PUFA) (g/kg)	0.36 (0.03)	0.37 (0.03)	-4.46% (-23.90%, 19.96%)	0.69	>.99	-11.96% (-30.75%, 11.92%)	0.30	>.99
Calories from PUFA (%)	7.99 (0.39)	7.22 (0.45)	0.77 (-0.39, 1.93)	0.19	>.99	0.71 (-0.69, 2.11)	0.32	>.99

	Results from models adjusting for age ¹					Results from models adjusting for age and physical activity ¹		
	ASD Mean (SE)	TDC Mean (SE)	ASD vs. TDC Difference (95% CI)	Nominal P-Value ²	Corrected P-Value ²	ASD vs. TDC Difference (95% CI)	Nominal P-Value ²	Corrected P-Value ²
Total Dietary Fiber (g/kg)	0.34 (0.03)	0.39 (0.03)	-13.02% (-31.17%, 9.91%)	0.24	>.99	-24.15% (-40.02%, -4.09%)	0.021	0.52
Soluble Dietary Fiber (g/kg)	0.11 (0.01)	0.12 (0.01)	-12.94% (-31.04%, 9.92%)	0.24	>.99	-22.57% (-38.51%, -2.50%)	0.030	0.62
Insoluble Dietary Fiber (g/kg)	0.23 (0.02)	0.26 (0.02)	-12.74% (-32.73%, 13.19%)	0.30	>.99	-24.88% (-43.16%, -0.71%)	0.044	0.84
Pectins (g/kg)	0.03 (0.00)	0.04 (0.01)	-17.72% (-42.82%, 18.39%)	0.29	>.99	-22.09% (-48.29%, 17.40%)	0.23	>.99
Intake from Food and Supplements								
Energy (kcal)	2050 (95.2)	2430 (120.3)	-15.67% (-26.08%, -3.79%)	0.011	0.25	-10.59% (-22.62%, 3.31%)	0.13	>.99
Total Carbohydrate (g/kg)	5.35 (0.40)	5.88 (0.38)	-9.01% (-25.33%, 10.87%)	0.35	>.99	-17.60% (-32.76%, 0.96%)	0.062	>.99
Total Protein (g/kg)	1.41 (0.09)	1.95 (0.13)	-27.77% (-39.43%, -13.87%)	< .001	0.008	-34.44% (-46.96%, -18.97%)	< .001	0.003
Total Fat (g/kg)	1.51 (0.11)	1.86 (0.14)	-18.80% (-33.20%, -1.29%)	0.037	0.66	-18.61% (-35.83%, 3.22%)	0.089	>.99
Total Saturated Fatty Acids (SFA) (g/kg)	0.47 (0.04)	0.67 (0.06)	-29.14% (-43.38%, -11.32%)	0.003	0.063	-26.15% (-43.55%, -3.39%)	0.027	0.59
Monounsaturated Fatty Acids (MUFA) (g/kg)	0.52 (0.04)	0.64 (0.05)	-18.07% (-33.56%, 1.04%)	0.062	>.99	-16.34% (-36.31%, 9.87%)	0.20	>.99
Polysaturated Fatty Acids (PUFA) (g/kg)	0.36 (0.03)	0.37 (0.03)	-4.20% (-23.65%, 20.21%)	0.71	>.99	-11.79% (-30.57%, 12.06%)	0.30	>.99
Total Dietary Fiber (g/kg)	0.35 (0.03)	0.39 (0.03)	-12.08% (-30.59%, 11.37%)	0.29	>.99	-24.15% (-40.02%, -4.09%)	0.021	0.52
Soluble Dietary Fiber (g/kg)	0.11 (0.01)	0.12 (0.01)	-10.74% (-30.10%, 14.00%)	0.36	>.99	-22.57% (-38.51%, -2.50%)	0.030	0.62
Insoluble Dietary Fiber (g/kg)	0.23 (0.02)	0.26 (0.02)	-12.74% (-32.73%, 13.19%)	0.30	>.99	-24.88% (-43.16%, -0.71%)	0.044	0.84

¹ Estimates and p-values are reported from generalized estimating equation models that accounted for covariance among siblings and included either age or age and log-transformed OPAQ physical activity levels as covariates.

² Both nominal p-values and p-values corrected for multiple comparisons using a step-down Bonferroni-adjustment are reported.

Table 3

Daily micronutrient intake in boys with Autism Spectrum Disorder (ASD) vs. typically developing controls (TDC)

	Results from models adjusting for age ¹					Adjusted for age and physical activity ¹		
	ASD Mean (SE) or Rate (95% CI)	TDC Mean (SE) or Rate (95% CI)	ASD vs. TDC Difference (95% CI) or OR (95% CI)	Nominal P-Value ²	Corrected P-Value ²	ASD vs. TDC Difference (95% CI) or OR (95% CI)	Nominal P-Value ²	Corrected P-Value ²
Intake from Food Only								
Calcium (mg)	876.43 (98.59)	1316.44 (99.26)	-33.42% (-49.15%, -12.84%)	0.003	0.12	-30.38% (-52.46%, 1.95%)	0.063	>.99
Copper (mg)	1.10 (0.07)	1.25 (0.06)	-11.72% (-24.39%, 3.08%)	0.11	>.99	-9.69% (-24.79%, 8.45%)	0.28	>.99
Iron (mg)	14.79 (1.21)	18.32 (1.00)	-19.27% (-33.05%, -2.65%)	0.025	0.73	-20.91% (-37.95%, 0.82%)	0.058	>.99
Magnesium (mg)	268.25 (21.58)	313.43 (15.16)	-14.41% (-28.27%, 2.12%)	0.084	>.99	-16.07% (-29.67%, 0.16%)	0.052	>.99
Phosphorus (mg)	1156.66 (82.69)	1623.75 (79.95)	-28.77% (-39.95%, -15.50%)	< .001	0.004	-28.63% (-41.73%, -12.59%)	0.001	0.048
Selenium (mg)	104.17 (4.82)	132.74 (6.80)	-21.53% (-31.07%, -10.66%)	< .001	0.010	-19.28% (-32.22%, -3.87%)	0.016	0.67
Total Vitamin A Activity (Retinol Activity Equivalents) (mg)	674.03 (94.44)	1030.24(117.43)	-34.58% (-53.83%, -7.29%)	0.017	0.55	-26.77% (-51.99%, 11.69%)	0.15	>.99
Thiamin (vitamin B1) (mg)	1.73 (0.16)	2.11 (0.11)	-17.96% (-33.21%, 0.78%)	0.059	>.99	-17.13% (-33.93%, 3.96%)	0.10	>.99
Riboflavin (vitamin B2) (mg)	1.77 (0.16)	2.60 (0.20)	-31.86% (-46.03%, -13.98%)	0.001	0.050	-29.18% (-48.42%, -2.76%)	0.033	>.99
Niacin (vitamin B3) (mg)	22.04 (1.53)	27.84 (1.91)	-20.83% (-33.74%, -5.41%)	0.010	0.33	-23.19% (-40.01%, -1.64%)	0.037	>.99
Vitamin B-6 (pyridoxine, pyridoxyl, & pyridoxamine) (mg)	1.78 (0.14)	2.29 (0.17)	-22.20% (-37.25%, -3.54%)	0.022	0.66	-29.69% (-48.09%, -4.78%)	0.023	0.91
Vitamin B-12 (cobalamin) (mg)	4.37 (0.54)	6.01 (0.59)	-27.32% (-46.66%, -0.97%)	0.043	>.99	-28.34% (-48.88%, 0.45%)	0.053	>.99

	Results from models adjusting for age ^I						Adjusted for age and physical activity ^I		
	ASD Mean (SE) or Rate (95% CI)	TDC Mean (SE) or Rate (95% CI)	ASD vs. TDC Difference (95% CI) or OR (95% CI)	Nominal P-Value ²	Corrected P-Value ²	ASD vs. TDC Difference (95% CI) or OR (95% CI)	Nominal P-Value ²	Corrected P-Value ²	
Dietary Folate Equivalents (mg)	496.21 (49.81)	697.80 (41.05)	-28.89% (-43.01%, -11.26%)	0.003	0.099	-26.73% (-44.36%, -3.52%)	0.027	>.99	
Vitamin C (ascorbic acid) (mg)	68.32 (11.03)	76.07 (14.09)	-10.19% (-43.81%, 43.56%)	0.65	>.99	-4.44% (-50.42%, 84.16%)	0.89	>.99	
Vitamin D (calciferol) (mcg)	4.62 (0.78)	6.35 (0.86)	-27.30% (-52.24%, 10.67%)	0.14	>.99	-24.51% (-54.48%, 25.22%)	0.28	>.99	
Vitamin E (Total Alpha-Tocopherol) (mg)	9.27 (1.04)	8.31 (0.75)	11.49% (-16.25%, 48.42%)	0.46	>.99	13.54% (-23.60%, 68.73%)	0.53	>.99	
Vitamin K (mg)	67.61 (9.72)	82.67 (13.19)	-18.22% (-46.01%, 23.87%)	0.34	>.99	-12.77% (-52.83%, 61.29%)	0.66	>.99	
Phytic Acid (mg)	622.00 (63.60)	719.96 (54.77)	-13.61% (-32.56%, 10.68%)	0.25	>.99	-18.49% (-37.96%, 7.10%)	0.14	>.99	
Oxalic Acid (mg)	139.47 (15.64)	154.88 (16.09)	-9.95% (-33.28%, 21.54%)	0.49	>.99	-7.11% (-37.83%, 38.78%)	0.72	>.99	
Daidzein (mg)	0.11 (0.05)	0.13 (0.05)	-15.94% (-71.14%, 144.84%)	0.75	>.99	-13.28% (-78.15%, 244.22%)	0.84	>.99	
Genistein (mg)	0.14 (0.06)	0.22 (0.07)	-38.35% (-77.50%, 68.90%)	0.35	>.99	-36.97% (-82.74%, 130.21%)	0.48	>.99	
Meeting EAR for Calcium (%)	28.0% (12.9, 50.6%)	75.0% (53.5, 88.6%)	OR=0.1 (0.0, 0.5)	0.004	0.13	OR=0.2 (0.0, 1.1)	0.061	>.99	
Meeting EAR for Vitamin D (%)	12.1% (3.0, 38.4%)	36.3% (21.8, 53.8%)	OR=0.2 (0.0, 1.3)	0.1	>.99	OR=0.2 (0.0, 1.6)	0.13	>.99	
<i>Intake from Food and Supplements</i>									
Calcium (mg)	917.54 (103.86)	1339.03 (88.97)	-31.48% (-47.22%, -11.04%)	0.005	0.16	-30.02% (-51.26%, 0.47%)	0.053	>.99	
Copper (mg)	1.13 (0.08)	1.24 (0.06)	-9.26% (-23.20%, 7.20%)	0.25	>.99	-7.12% (-23.54%, 12.82%)	0.46	>.99	
Iron (mg)	16.61 (1.51)	18.33 (1.00)	-9.39% (-26.34%, 11.47%)	0.35	>.99	-11.95% (-31.86%, 13.77%)	0.33	>.99	
Magnesium (mg)	279.08 (22.97)	314.32 (15.56)	-11.21% (-25.97%, 6.49%)	0.20	>.99	-13.00% (-27.84%, 4.89%)	0.14	>.99	

	Results from models adjusting for age ^I					Adjusted for age and physical activity ^I		
	ASD Mean (SE) or Rate (95% CI)	TDC Mean (SE) or Rate (95% CI)	ASD vs. TDC Difference (95% CI) or OR (95% CI)	Nominal P-Value ²	Corrected P-Value ²	ASD vs. TDC Difference (95% CI) or OR (95% CI)	Nominal P-Value ²	Corrected P-Value ²
Phosphorus (mg)	1158.12 (82.94)	1623.77 (79.95)	-28.68% (-39.89%, -15.37%)	<.001	0.005	-28.54% (-41.67%, -12.46%)	0.001	0.049
Selenium (mg)	107.91 (5.90)	132.74 (6.80)	-18.71% (-29.54%, -6.21%)	0.005	0.16	-16.28% (-30.51%, 0.87%)	0.062	>.99
Thiamin (mg)	1.86 (0.18)	2.11 (0.11)	-11.76% (-29.26%, 10.08%)	0.27	>.99	-11.25% (-30.08%, 12.65%)	0.33	>.99
Riboflavin (vitamin B2) (mg)	1.96 (0.18)	2.60 (0.20)	-24.62% (-40.69%, -4.19%)	0.021	0.65	-22.32% (-43.63%, 7.04%)	0.12	>.99
Niacin (vitamin B3) (mg)	24.28 (1.84)	27.85 (1.91)	-12.83% (-28.12%, 5.71%)	0.16	>.99	-16.07% (-34.61%, 7.73%)	0.17	>.99
Vitamin B-6 (pyridoxine, pyridoxyl, & pyridoxamine) (mg)	2.05 (0.19)	2.32 (0.18)	-11.88% (-31.02%, 12.57%)	0.31	>.99	-18.40% (-41.26%, 13.36%)	0.23	>.99
Vitamin B-12 (cobalamin) (mg)	5.25 (0.68)	6.10 (0.63)	-13.96% (-37.93%, 19.27%)	0.37	>.99	-10.54% (-37.31%, 27.66%)	0.54	>.99
Vitamin C (ascorbic acid) (mg)	85.96 (17.59)	76.57 (14.25)	12.27% (-33.98%, 90.91%)	0.67	>.99	22.37% (-40.23%, 150.57%)	0.58	>.99
Vitamin D (calciferol) (mcg)	6.94 (1.14)	6.86 (0.99)	1.11% (-34.54%, 56.19%)	0.96	>.99	16.10% (-28.48%, 88.47%)	0.55	>.99
Vitamin E (Total Alpha-Tocopherol) (mg)	9.27 (1.04)	8.31 (0.75)	11.49% (-16.25%, 48.42%)	0.46	>.99	13.54% (-23.60%, 68.73%)	0.53	>.99
Vitamin K (mg)	68.99 (10.07)	82.66 (13.19)	-16.54% (-45.07%, 26.80%)	0.40	>.99	-11.06% (-52.07%, 65.02%)	0.71	>.99
Phytic Acid (mg)	622.00 (63.60)	719.96 (54.77)	-13.61% (-32.56%, 10.68%)	0.25	>.99	-18.49% (-37.96%, 7.10%)	0.14	>.99
Daidzein (mg)	0.11 (0.05)	0.13 (0.05)	-15.94% (-71.14%, 144.84%)	0.75	>.99	-13.28% (-78.15%, 244.22%)	0.84	>.99
Genistein (mg)	0.14 (0.06)	0.22 (0.07)	-38.35% (-77.50%, 68.90%)	0.35	>.99	-36.97% (-82.74%, 130.21%)	0.48	>.99

	Results from models adjusting for age ¹					Adjusted for age and physical activity ¹		
	ASD Mean (SE) or Rate (95% CI)	TDC Mean (SE) or Rate (95% CI)	ASD vs. TDC Difference (95% CI) or OR (95% CI)	Nominal P–Value ²	Corrected P–Value ²	ASD vs. TDC Difference (95% CI) or OR (95% CI)	Nominal P–Value ²	Corrected P–Value ²
Meeting EAR for Calcium (%)	32.7% (16.3, 54.9%)	74.6% (54.6, 87.7%)	OR=0.2 (0.0, 0.6)	0.006	0.22	OR=0.2 (0.0, 1.1)	0.061	>.99
Meeting EAR for Vitamin D (%)	36.1% (18.9, 57.7%)	41.6% (26.4, 58.5%)	OR=0.8 (0.3, 2.4)	0.68	>.99	OR=0.9 (0.2, 3.6)	0.88	>.99

¹ Estimates and p-values are reported from generalized estimating equation models that accounted for covariance among siblings and included either age or age and log-transformed OPAQ physical activity levels as covariates.

² Both nominal p-values and p-values corrected for multiple comparisons using a step-down Bonferroni-adjustment are reported.

Table 4

Associations between nutrition parameters and bone mineral density (BMD) in boys with Autism Spectrum Disorder (ASD) and typically developing controls (TDC)

Dependent Variable						
	Femoral Neck BMD Z-Score		Lumbar Spine BMD Z-Score		Total Hip BMD Z-Score	
	Effect of 10% incr.		Effect of 10% incr.		Effect of 10% incr.	
Independent Variable	ASD	TDC	ASD	TDC	ASD	TDC
Intake from Food Only						
Calories from Carbohydrate (%)	−0.02 (−0.09, 0.06) (p=0.65)	−0.01 (−0.08, 0.05) (p=0.68)	−0.04 (−0.11, 0.04) (p=0.36)	0.00 (−0.04,0.04) (p=0.87)	−0.01 (−0.08, 0.07) (p=0.88)	−0.02 (−0.08,0.05) (p=0.57)
Calories from Fat (%)	0.00 (−0.08,0.09) (p=0.96)	0.02 (−0.05, 0.09) (p=0.63)	0.01 (−0.07,0.10) (p=0.76)	0.02 (−0.04,0.08) (p=0.55)	−0.03 (−0.12, 0.06) (p=0.57)	0.03 (−0.05,0.11) (p=0.43)
Calories from SFA (%)	0.06 (−0.15,0.27) (p=0.57)	0.03 (−0.11, 0.17) (p=0.69)	0.09 (−0.11,0.29) (p=0.39)	0.07 (−0.05,0.19) (p=0.25)	0.02 (−0.19, 0.23) (p=0.86)	0.11 (−0.04,0.27) (p=0.14)
Calories from MUFA(%)	−0.02 (−0.13, 0.10) (p=0.77)	0.03 (−0.15, 0.22) (p=0.73)	0.01 (−0.11, 0.14) (p=0.82)	0.03 (−0.13,0.18) (p=0.73)	−0.06 (−0.19, 0.08) (p=0.39)	0.07 (−0.13,0.27) (p=0.51)
Calories from PUFA(%)	−0.07 (−0.21, 0.06) (p=0.28)	0.01 (−0.08, 0.11) (p=0.77)	−0.12 (−0.30,0.07) (p=0.23)	−0.01 (−0.13, 0.11) (p=0.83)	−0.15 (−0.32, 0.03) (p=0.097)	−0.03 (−0.18, 0.11) (p=0.64)
Calories from Protein(%)	0.16 (0.00,0.31) (p=0.046)	0.01 (−0.08, 0.09) (p=0.89)	0.24 (0.08,0.41) (p=0.004)	−0.04 (−0.11, 0.02) (p=0.21)	0.27 (0.06, 0.47) (p=0.011)	−0.01 (−0.10, 0.08) (p=0.90)
Animal Protein (g)	0.08 (0.01,0.15) (p=0.027)	0.05 (−0.02, 0.12) (p=0.18)	0.10 (0.03,0.18) (p=0.008)	−0.03 (−0.10, 0.05) (p=0.50)	0.15 (0.05, 0.25) (p=0.004)	0.04 (−0.05,0.12) (p=0.40)
Vegetable Protein (g)	−0.02 (−0.13,0.09) (p=0.71)	0.09 (0.00, 0.18) (p=0.040)	0.03 (−0.11,0.17) (p=0.70)	0.06 (−0.03,0.15) (p=0.16)	−0.02 (−0.12, 0.09) (p=0.77)	0.07 (−0.04, 0.19) (p=0.20)
Pectins (g)	−0.01 (−0.06, 0.04) (p=0.68)	0.07 (0.02, 0.11) (p=0.003)	0.01 (−0.05,0.06) (p=0.82)	0.01 (−0.03,0.04) (p=0.74)	0.01 (−0.05, 0.08) (p=0.66)	0.05 (−0.00,0.11) (p=0.062)
Oxalic Acid (mg)	−0.00 (−0.05,0.05) (p=0.95)	0.03 (−0.02, 0.08) (p=0.19)	0.03 (−0.04,0.09) (p=0.43)	0.00 (−0.05,0.06) (p=0.95)	0.01 (−0.05, 0.07) (p=0.75)	0.00 (−0.06,0.06) (p=0.97)
Intake from Food and Supplements						
Energy (kcal)	0.08 (−0.01, 0.17) (p=0.086)	0.09 (−0.02, 0.20) (p=0.092)	0.13 (−0.01,0.27) (p=0.077)	0.02 (−0.13,0.17) (p=0.78)	0.16 (0.02, 0.29) (p=0.021)	0.08 (−0.08,0.23) (p=0.32)
Total Carbohydrate (g)	0.05 (−0.10,0.21) (p=0.51)	0.08 (−0.05, 0.21) (p=0.21)	0.07 (−0.13,0.27) (p=0.49)	0.03 (−0.08,0.14) (p=0.59)	0.16 (−0.03, 0.34) (p=0.096)	0.07 (−0.08,0.21) (p=0.37)
Total Protein (g)	0.09 (0.01,0.17) (p=0.027)	0.07 (−0.02, 0.17) (p=0.14)	0.16 (0.06, 0.25) (p=0.001)	−0.02 (−0.13, 0.10) (p=0.79)	0.18 (0.05, 0.31) (p=0.008)	0.05 (−0.06,0.17) (p=0.38)
Total Fat (g)	0.04 (−0.06,0.13) (p=0.46)	0.07 (0.00, 0.13) (p=0.039)	0.07 (−0.03, 0.17) (p=0.18)	0.02 (−0.08, 0.13) (p=0.66)	0.05 (−0.07, 0.16) (p=0.42)	0.07 (−0.04,0.17) (p=0.21)

Dependent Variable										
	Femoral Neck BMD Z-Score		Lumbar Spine BMD Z-Score		Total Hip BMD Z-Score		Whole body less head z-scores			
	Effect of 10% incr.		Effect of 10% incr.		Effect of 10% incr.		Effect of 10% incr.			
Independent Variable	ASD	TDC	ASD	TDC	ASD	TDC	ASD	TDC		
Total Saturated Fatty Acids (SEA) (g)	0.05 (−0.05,0.14) (p=0.36)	0.06 (−0.02, 0.13) (p=0.14)	0.07 (−0.03,0.17) (p=0.16)	0.03 (−0.08,0.14) (p=0.64)	0.06 (−0.04, 0.16) (p=0.25)	0.07 (−0.04,0.18) (p=0.20)	0.04 (−0.05,0.13) (p=0.38)		0.03 (−0.05,0.11) (p=0.43)	
Monounsaturated Fatty Acids (MUFA) (g)	0.02 (−0.07,0.11) (p=0.65)	0.06 (0.01, 0.12) (p=0.029)	0.05 (−0.04,0.15) (p=0.28)	0.02 (−0.08,0.12) (p=0.71)	0.03 (−0.08, 0.15) (p=0.55)	0.07 (−0.03,0.16) (p=0.18)	−0.01 (−0.10, 0.08) (p=0.80)		0.02 (−0.04,0.09) (p=0.49)	
Polynsaturated Fatty Acids (PUFA) (g)	0.02 (−0.06,0.10) (p=0.63)	0.03 (−0.02, 0.08) (p=0.23)	0.04 (−0.07,0.14) (p=0.49)	0.01 (−0.07,0.08) (p=0.86)	0.03 (−0.06, 0.12) (p=0.50)	0.01 (−0.07,0.10) (p=0.75)	0.02 (−0.07,0.10) (p=0.69)		0.03 (−0.02,0.09) (p=0.25)	
Total Dietary Fiber (g)	0.01 (−0.08,0.10) (p=0.87)	0.08 (−0.01, 0.16) (p=0.069)	0.06 (−0.05,0.17) (p=0.28)	0.01 (−0.06,0.07) (p=0.79)	0.05 (−0.05, 0.15) (p=0.30)	0.03 (−0.08, 0.13) (p=0.60)	0.04 (−0.07,0.15) (p=0.53)		0.08 (0.02, 0.14) (p=0.010)	
Soluble Dietary Fiber(g)	0.02 (−0.07,0.11) (p=0.68)	0.06 (−0.02, 0.14) (p=0.13)	0.06 (−0.03,0.16) (p=0.19)	−0.00 (−0.09, 0.08) (p=0.96)	0.04 (−0.05, 0.14) (p=0.36)	0.03 (−0.08,0.15) (p=0.56)	0.06 (−0.04,0.15) (p=0.24)		0.06 (−0.02,0.13) (p=0.14)	
Insoluble Dietary Fiber(g)	−0.00 (−0.08,0.07) (p=0.95)	0.07 (−0.00, 0.14) (p=0.062)	0.05 (−0.05,0.15) (p=0.35)	0.01 (−0.04,0.07) (p=0.64)	0.04 (−0.05, 0.13) (p=0.35)	0.02 (−0.07,0.10) (p=0.66)	0.02 (−0.08,0.12) (p=0.74)		0.07 (0.02,0.12) (p=0.003)	
Calcium (mg)	0.06 (0.01,0.11) (p=0.025)	0.04 (−0.05, 0.13) (p=0.38)	0.08 (0.01,0.15) (p=0.019)	0.01 (−0.08,0.09) (p=0.91)	0.11 (0.03, 0.18) (p=0.004)	0.04 (−0.05,0.13) (p=0.41)	0.08 (0.03, 0.13) (p=0.002)		−0.00 (−0.08, 0.08) (p=0.99)	
Magnesium (mg)	0.00 (−0.06,0.07) (p=0.89)	0.11 (−0.02, 0.23) (p=0.092)	0.08 (−0.00,0.16) (p=0.052)	0.00 (−0.14,0.14) (p=0.99)	0.11 (−0.00, 0.23) (p=0.058)	0.04 (−0.12,0.20) (p=0.63)	0.08 (−0.03,0.20) (p=0.16)		0.06 (−0.07,0.19) (p=0.34)	
Phosphorus (mg)	0.08 (0.00,0.16) (p=0.037)	0.08 (−0.03, 0.19) (p=0.13)	0.13 (0.04,0.22) (p=0.004)	−0.00 (0.13, 0.13) (p=0.96)	0.13 (−0.04, 0.22) (p=0.005)	0.05 (−0.09,0.19) (p=0.48)	0.11 (0.02,0.20) (p=0.016)		0.01 (−0.10,0.12) (p=0.80)	
Vitamin D (calciferol) (mg)	−0.01 (−0.05,0.03) (p=0.54)	0.01 (−0.03, 0.04) (p=0.61)	0.03 (−0.01,0.07) (p=0.16)	−0.00 (−0.03, 0.03) (p=0.98)	0.00 (−0.05, 0.06) (p=0.89)	0.01 (−0.03,0.05) (p=0.74)	−0.02 (−0.08,0.03) (p=0.38)		−0.01 (−0.05, 0.02) (p=0.49)	
Phytic Acid (mg)	0.03 (−0.03,0.08) (p=0.36)	0.04 (−0.02, 0.09) (p=0.17)	0.08 (0.01, 0.14) (p=0.022)	0.02 (−0.03,0.07) (p=0.43)	0.07 (−0.01, 0.15) (p=0.069)	0.00 (−0.07,0.07) (p=0.94)	0.06 (−0.02, 0.13) (p=0.12)		0.03 (−0.03,0.09) (p=0.28)	
Daidzein (mg)	0.00 (−0.02,0.02) (p=0.99)	−0.01 (−0.03, 0.01) (p=0.21)	0.01 (−0.01,0.03) (p=0.47)	0.00 (−0.02,0.02) (p=0.95)	0.01 (−0.02, 0.03) (p=0.57)	−0.00 (−0.02, 0.01) (p=0.68)	−0.00 (−0.02, 0.02) (p=0.71)		−0.00 (−0.02, 0.01) (p=0.90)	
Genistein (mg)	0.01 (−0.01,0.02) (p=0.37)	−0.01 (−0.03, 0.02) (p=0.61)	0.02 (−0.00,0.04) (p=0.073)	−0.00 (−0.03, 0.02) (p=0.85)	0.01 (−0.01, 0.04) (p=0.26)	−0.00 (−0.03,0.03) (p=0.87)	0.00 (−0.02,0.03) (p=0.75)		−0.00 (−0.02, 0.02) (p=0.85)	

Estimates and nominal p-values are reported from a generalized estimating equation model that accounted for covariance among siblings and included age and log-transformed OPAQ physical activity levels as covariates. The measure of associated reported is the estimated magnitude of difference in each BMD z-score for a 10% increase in the intake of a given nutrient.