

Sodium Intake Differences and its Relationship to the Gut Microbiome in Female Individuals
with Irritable Bowel Syndrome and Healthy Controls

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Abstract

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Irritable bowel syndrome (IBS) is a disorder of gut-brain interaction characterized by abdominal pain and changes in bowel movements. Although IBS pathophysiology is still unclear, research has suggested that IBS may be associated with diet and the gut microbiome. Sodium is a nutrient that may be associated with bloating, gut motility, and gut microbial composition. This study investigated the relationship between sodium intake, symptoms, and the gut microbiome in females with IBS and healthy controls. 113 participants provided 3-day food records as well as 28-day symptom diaries. Participants also provided a stool sample for microbiome analysis where 16S rRNA gene sequencing was used for bacterial genus identification. We compared differences in sodium intake and abundances of *Lactobacillus* and *Bifidobacterium* between 67 females with IBS and 46 healthy controls. Results showed no significant differences in sodium intake between females with IBS and healthy controls. There was also no significant correlation between sodium intake and the symptoms of interest: abdominal pain, bloating, and intestinal

gas. Sodium density (mg sodium /1000 kcal) did not significantly correlate with *Lactobacillus* and *Bifidobacterium* relative abundances, but our analysis showed significant associations in abundance of other genera that were not selected a priori. We also found significant associations between sodium, energy, and macronutrient intake. Because sodium is such an integral component in daily diet, our study indicates the need for further, more focused nutrition studies on how sodium intake is associated with gut microbial composition and IBS.

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Introduction

1.1 Irritable Bowel Syndrome

Irritable Bowel Syndrome (IBS) is a common disorder of gut brain interaction which significantly impacts quality of life in affected individuals.¹ In individuals with IBS, abdominal pain is a frequently experienced symptom and is often associated with a change in bowel habits and visceral sensitivity.²⁻⁴ The Rome criteria is a tool used in clinical practice to diagnose IBS. This criteria involves specifics on frequency of abdominal pain and its association with bowel movements and stool appearance.⁵ Clinicians also use the Bristol stool chart to classify individuals with IBS into different subtypes based on stool appearance: constipation (IBS-C), diarrhea (IBS-D), alternating diarrhea and constipation (IBS mixed or IBS-M), or unclassified (IBS-U).⁵ Other gastrointestinal symptoms may include bloating and gas.³⁻⁵ Although severity of symptoms varies across individuals, these symptoms combined can lead to interruptions in daily activities, which can decrease quality of life.³⁻⁵

The etiology of IBS is still unclear.⁶ To date, research suggests that IBS-related gastrointestinal disturbances arise from low-grade inflammation, visceral hypersensitivity, alterations in intestinal motility, and alterations in gut microbiome composition.⁶ Symptoms can start or become exacerbated following food intake without previous associations to food allergies or intolerances.⁶ As a result, IBS can affect food choice and diet quality. It is thus important to understand the pathophysiology and effects of IBS within the field of dietetics to ensure nutritional adequacy of individuals with IBS.

It is estimated that 4-11% of the global population are affected by IBS.^{6,7} Prevalence rates vary by geographic location due to different lifestyle factors such as diet as well as access to healthcare.⁶ IBS prevalence is expected to increase as IBS is becoming a more recognized

disorder and diets have shifted towards more processed foods, which can be seen in the Western diet.⁵ When compared to other countries, IBS prevalence in Western countries can be as high as 15%.⁵ IBS affects females more than males but the exact mechanisms behind this sex difference in pathophysiology are still unknown.^{5,8}

Currently, there is no cure for IBS. Individuals with IBS are usually advised to change their diet with the goal of reducing symptoms and improving quality of life. Low Fermentable, Oligosaccharides, Disaccharides, Monosaccharides, And Polyols (FODMAP), gluten free, and other elimination diets have been effective for certain individuals in decreasing symptoms such as abdominal pain and bloating.⁹ However, food group elimination diets can be highly restrictive and may not be feasible or sustainable for the general population. Adherence to restrictive diets can be linked to disordered eating, including avoidance restrictive food intake behavior (ARFID), which involves a fear of foods that cause gastrointestinal symptoms.¹⁰ Thus, more research needs to be done to understand the pathophysiology behind IBS in order to develop more sustainable treatment options.

1.2 IBS and the Microbiome

A growing area of interest in studying IBS is how gut microbiome composition is affected by diet and lifestyle.¹ The composition of the gut microbiome is important in modulating health through neural, endocrine, and immune pathways.^{6,11} In healthy individuals, the human gut microbiome is composed of a vast array of bacteria, predominantly from the phyla *Firmicutes* and *Bacteroidetes*.¹² Microbiome composition can be dependent on a variety of factors, including diet, genetics, and the environment.⁶ Healthy individuals often have a high level of microbial diversity with favorable amounts of bacteria that produce short chain fatty acids and lower amounts of endotoxin-producing bacteria.⁶ Microbiomes in dysbiosis, or out of

balance, typically result in decreased microbial diversity and less abundance of short chain fatty acid-producing bacteria.⁶

Some investigators have found dysbiosis in the gut microbiome of individuals with IBS.¹³ In several studies, individuals with IBS had lower amounts of *Lactobacillus* and *Bifidobacterium*, although abundance can differ based on the individual as well as their subtype of IBS.^{1,5,14} In fact, two studies showed increased abundance of *Lactobacillus* in individuals with IBS while other studies showed no significant difference.^{13,15} Abundance of other microbes can also differ. One study showed that abundance of methane-producing microbes was lower in individuals with IBS-D but higher in those with IBS-C.¹³ The same study found decreased levels of butyrate-producing bacteria in individuals with IBS-D, which is consistent with the main findings of a 2019 systematic review.^{13,15} IBS-D individuals may also experience malabsorption of bile acids, which may lead to increased gut motility and diarrhea.^{5,16} Long term effects of bile acid malabsorption may contribute to intestinal barrier dysfunction and alterations in the gut microbiome.¹⁶ Based on these results, the composition of the gut microbiome based on bacterial abundance and their associated metabolic functions can potentially increase IBS-associated symptoms.

1.3 The Role of Sodium in Diet and Disease

Diet and nutrition are known to affect gut microbiome composition and can be linked to both acute and chronic illnesses.¹⁷ Sodium is an essential electrolyte that plays an important role in many bodily functions.¹¹ Sodium is found naturally in many foods and can also be added to food in the form of sodium chloride, which improves palatability. Individuals consume different amounts of sodium based on taste preferences, energy intake, and the type of food that is readily available to them. Currently, the Centers for Disease Control and Prevention and US Dietary

Guidelines for Americans recommend adults to consume less than 2300 mg/day of sodium, but the average American consumes more than 3300 mg/day.¹⁸ This is partially because many foods that are top dietary contributors of sodium are also a large part of most people's diets. The INTERMAP study investigated sodium intake and dietary sources of sodium in 4 countries—United States, United Kingdom, China, and Japan.¹⁹ Most contributors of sodium were either important ingredients used in cooking or made up a significant portion of diet.¹⁹ For example, in Japan, soy sauce accounted for 20% of sodium intake in diet.¹⁹ The INTERMAP study and 2017-2018 data from the National Health and Nutrition Examination Survey (NHANES) showed that in the United States, the top contributors of sodium came from added salt as well as foods such as breads/grains/cereals, meat, sauces, and savory snacks.^{18,19} All of these foods are commonly seen in the Western diet, which is characterized as a diet high in saturated fats, sugar, and processed foods while being low in fresh fruits and vegetables.²⁰

In the recent years, processed foods have become increasingly available due to the industrialization of the food supply chain. The NOVA food classification system is a tool used to classify foods based on their level of processing. Ultra-processed foods, which NOVA defines as industrial formulations derived from food constituents, are frequently consumed within the Western diet due to convenience and availability. These include sugar-sweetened beverages, frozen meals, snack-type foods, and meat alternatives. Generally, ultra-processed foods are higher in added sugars, saturated fats, energy density, and sodium, which can potentially increase gut permeability and inflammation.^{20,21} However, it is important to note that not all ultra-processed foods have these compositions. Foods that are considered nutrient-dense or healthful can still be labeled as ultra-processed if they contain stabilizers or emulsifiers that extend their shelf life. For example, plant-based meat products and oral nutrition supplements are considered

ultra-processed foods. Even so, there are epidemiological studies that suggest excessive consumption of ultra-processed foods can be linked to chronic intestinal inflammation, which is associated with colorectal cancer and possibly IBS.^{20,22}

Similarly, populations that chronically consume higher than recommended sodium diets are also at risk for chronic diseases, including hypertension and cardiovascular disease.^{23,24} There has been a growing body of research examining if diets high in sodium may attribute to other health conditions, including disorders of gut-brain interaction such as IBS. When sodium is ingested, neural mechanisms and gut hormones work together to mediate sodium balance in the body.²⁵ The majority of sodium ingested will be absorbed through various transporters and less than 0.5% of ingested sodium will be excreted through feces.²⁶ But when sodium consumption is excessive, it can lead to decreased gut motility and increased water retention, which results in bloating and GI discomfort.²⁷ Mouse studies show that a high-sodium diet is associated with increased inflammation, excessive epithelial proliferation, and altered cellular types that can lead to gastric cancer.^{28,29} In addition to animal models, the link to increased gastric cancer has also been suggested in human studies.^{24,29,30} The suggested mechanism proposes increased sodium intake leads to higher sodium concentrations in the gut wall, which can eventually cause inflammation and damage to the mucosal layers.^{29,30} These alterations in the gut mucosal layers can create an optimal environment for bacteria such as *Helicobacter pylori*, which is a known risk factor for gastric cancer.^{29,30} It is also suggested that high sodium diets can damage the physical defense barrier in the gut and modulate the gut immune access through the T-helper 17 (Th17) pathway.^{11,21} High levels of sodium, along with a microbiome in dysbiosis, can stimulate pro-inflammatory Th17 cells to affect inflammation, autoimmunity, and hypertension.^{21,31}

Sodium intake may be associated with changes in the composition of the gut microbiome, which has been linked to altered gut function.^{27,32} High sodium diets are associated with decreased abundance of *Lactobacillus* in mouse and human studies.²⁷ *Lactobacillus* species are known to regulate intestinal barrier function, metabolic activity, and short chain fatty acid production.¹⁴ Furthermore, *Lactobacillus* and *Bifidobacteria* are commonly used in probiotic foods and supplements because they can help prevent proliferation of invasive bacteria.⁵ Thus, the composition of gut bacteria, especially *Lactobacillus* abundance, can potentially influence gut function and health.

1.4 Study Objectives

Currently, there is limited research on how sodium can affect gut health in the setting of IBS. There were 2 objectives of this study. The first objective was to compare sodium intake between women with IBS and healthy controls. Because our literature suggested that high sodium intake may contribute to bloating and an altered microbiome, we hypothesized that there would be a significant difference in sodium intake between females with IBS and healthy controls. We also hypothesized that females with IBS who consume higher amounts of sodium will likely experience more severe IBS symptoms. Our second objective was to explore the association between sodium intake and gut microbial composition in women with IBS and healthy controls. We hypothesized that sodium intake significantly affects gut microbiome composition at the genus level and that there would be an inverse relationship between sodium intake and abundances of *Bifidobacteria* and *Lactobacillus*.

Methods

2.1 Design

This study used a cross-sectional design to compare differences in sodium intake and gut microbiome composition between females with IBS and healthy controls. This is a post-hoc ancillary study using existing research (NIH grant R01 NR014479).¹

Approval from the Institutional Review Board was obtained prior to participant recruitment. Females with and without IBS living in the Pacific Northwest were recruited through healthcare providers or community advertisements between 2015-2018. After recruitment, potential participants were screened for eligibility. Participants met the Rome III Criteria and had to have an IBS diagnosis for at least 6 months. Participants without IBS (healthy controls) were included if they did not meet the Rome III criteria and did not have any current moderate to severe diseases or disorders. Participants were excluded from study if they had (1) a bacterial or viral gastrointestinal infection within the last 2 months; (2) any history of inflammatory bowel disease (IBD); (3) a surgical history involving a central incision; (4) a first-degree relative with colorectal cancer before the age of 60 or with IBD; (5) poorly controlled mental health disorder; (6) use of regular medications (> 4 days a week); (7) antibiotics in the past 2 months; (8) were pregnant, breastfeeding, or planning to get pregnant in the next 2 months; and (9) had a ‘red flag’ symptom such as blood in stool or unintended rapid weight loss (≥ 10 lbs).

Interested individuals who met the eligibility criteria provided their informed consent to continue with this study. Participants self-reported their demographics: age, BMI, and race. Participants were between the ages of 18 and 50 years old. Participants completed baseline questionnaires and a 4-week GI symptom diary that detailed abdominal pain, constipation,

diarrhea, and stool consistency. To control for confounding, sampling time points were standardized with consideration to menstrual cycle phase. Participants who were menstruating started their symptom diary on the first day of menstrual bleeding while participants who were using intrauterine hormone devices began symptom records within the next 2 weeks. Symptoms were rated on a scale of 0-4 with 0 indicating no symptoms present and 4 indicating severe symptoms. Participants collected their own stool samples during the early follicular phase of their menstrual cycle. Participants were instructed to store them in a home freezer for up to 2 days without any preservatives before sending them to the lab. Once in the lab, stool samples were stored in a -80°C freezer until processing could be completed. In addition to stool sampling and a symptom diary, participants also provided a 3-day food record. Food records were entered by the staff of the Nutrition Assessment Shared Resource of Fred Hutchinson. Cancer Center, Seattle, Washington. Nutrient and food intake calculations were performed using the Nutrition Data System for Research software version 2023, developed by the Nutrition Coordinating Center, University of Minnesota, Minneapolis, Minnesota.

2.2 Dietary Variables

The 3-day food records provided information on type and quantity of food consumed. Analysis of food records provided information on nutrient intake, including macronutrient and micronutrient composition, as well as serving size based on recommendations by the 2020-2025 Dietary Guidelines for Americans and US Food and Drug Administration (FDA). Variables of interest for diet were obtained from dietary analysis of the 3-day food records. We included macronutrient composition (total energy, total fat, total protein, and total carbohydrate) and fiber (total dietary fiber, soluble dietary fiber, and insoluble dietary fiber). Our primary variable of interest was daily sodium intake, which we used to see if there was a difference in consumption

between IBS females and healthy controls. We also assessed if there were correlations between sodium intake, energy, and macronutrient intakes. We also calculated sodium density (i.e. sodium intake per 1000 kcal) to examine correlations with gut microbiome composition.

In addition to these nutrient-specific variables, we examined total Healthy Eating Index (HEI) scores and HEI sodium scores, which can be found in the 2020-2025 Dietary Guidelines for Americans handbook. HEI scores assess how well an individual adheres to those dietary recommendations. Total HEI scores range from 0 to 100, with a score of 80 or higher indicating a ‘good’ diet and a score of 51 or lower indicating a ‘poor’ diet. It can be assumed that individuals with higher HEI scores consume more nutrient-dense foods such as fruits, vegetables, and whole-grains and less ultra-processed foods.³³ The total HEI score is made up of smaller score components, including a specific section for sodium consumption. Sodium HEI scores range from 0 to 10. A score of 10 indicates an individual has met the standard for sodium consumption, which is less than 1.1 g of sodium per 1000 calories. If the amount consumed does not meet these standards, points are then deducted from the maximum score of 10.

To determine what specific foods were the top contributors of sodium, we categorized foods from the 3-day food records into groups based on results of the INTERMAP study and data from NHANES.^{19,34} Groups of food included breads/grains/cereals, cold cuts/cured meats, soup/broth, savory snacks, poultry/eggs, cheese, pasta dishes, meat/meat alternatives, desserts, vegetables, and sauces/condiments.

2.3 Gut Microbiome Analysis

Stool samples were processed using 16S rRNA gene sequencing to determine composition of the microbiome.² The variable region (V4) of the bacterial 16S rRNA gene was amplified through PCR and sequenced using the MiSeq platform with the paired-end sequencing

protocol. Processing de-multiplexed raw sequencing reads was performed using the DADA2 package (version 1.8). The default parameter settings were used with some minor modifications, in which we trimmed the raw sequencing reads but still maintained any overlapping regions when merging pair-ended reads.³⁵ We also stripped sequencing primers that were retained in forward and reverse reads by its length. We used the IdTaxa function from the DECIPHER package (version 2.6.0) and its pre-built training set (LearnTaxa function) from the SILVA database (release 132) for taxonomy assignment (threshold: 0.5) of amplicon sequence variants from DADA2 output. Chimeras and amplicon sequence variants that were not classified as a bacteria domain were removed from analysis.

2.4 Statistical Analysis

Organization of data was done in Microsoft Excel (Version 16.83) and data analysis was performed through R (Version 2024.09.0+375). For each study variable, values that were missing were identified and accounted. Participants with missing values were excluded from analysis of the variables affected. Prior to analyzing our study objectives, we performed an analysis on our demographic data to see if there were any significant differences between groups. The first objective was to compare sodium intake between females with IBS and healthy controls. We first determined distribution of sodium intake within our sample and compared both the mean and median sodium intake in the IBS and control group, as well as between subtypes of IBS. We used a Mann-Whitney test to determine statistical significance. A separate analysis for sodium intake was performed using log-transformed data to account for skewness. To better understand patterns in sodium consumption, we correlated sodium intake with macronutrient consumption. Using food record data, we categorized individual food items into appropriate food groups and determined the mean intake across 3 days (See Supplemental Table 1). We determined potential

top contributors of sodium based on the results of Ahmed 2023. We used independent t-tests to determine if there was a significant difference in mean intake of sodium contributing foods between females with IBS and healthy controls. Next, we investigated if a higher intake of sodium was associated with more frequent and more severe IBS symptoms. We used linear regression to determine if sodium intake was associated with bloating, abdominal pain, and intestinal gas in the IBS group.

Our second objective was to assess the relationship between sodium density and gut microbiome composition. We specifically looked at abundances of 2 genera commonly found in the gut, *Lactobacillus* and *Bifidobacterium*. A statistician standardized mean bacterial abundance and used CLR transformation to account for zero values within the data. Then, a partial regression analysis was used to determine if there was a significant difference in the association between sodium density and relative abundances of *Lactobacillus* and *Bifidobacterium* in women with IBS compared to healthy controls. This analysis was adjusted for age and BMI, and sodium density was used to adjust for energy intake.

Results

3.1 Demographics

This study included 113 participants, with 67 individuals with IBS and 46 healthy controls. Demographic characteristics are detailed in Table 1, with information on age, BMI, education, income, and race. There were no significant differences across groups. The average age was 27.6 years for healthy controls and 29.0 years for participants with IBS. The median BMI was 23.0 kg/m² for healthy controls and 22.3 kg/m² for IBS individuals. Median education level was the same across all groups, which was a bachelor's degree. Individuals with IBS-C and IBS-D had higher incomes than other groups, but this difference was not significant. Approximately 70% of the study's population was White, with the rest comprised of Asian (12%) and Black (4%) individuals; individuals with multiple races (10%) were counted separately and individuals who identified as American Indian/Alaska Native or Native Hawaiian/Other Pacific Islander (5%) were combined into one group.

Table 1: Demographic Characteristics of Study Population

	Healthy controls (n=46)	IBS - all subtypes (n=67)	IBS-C (n=14)	IBS-D (n=36)	IBS-M (n=17)
Age - <i>mean (SD)</i>	27.6 (6.1)	29.0 (8.2)	28.1 (8.1)	29.7 (8.4)	28.3 (8.3)
BMI – <i>median (IQR)*</i>	23.0 (21.4, 25.1)	22.3 (20.8, 25.2)	22.9 (21.6, 24.6)	22.3 (20.0, 26.6)	22.0 (20.2, 23.4)
Education ¹ – <i>median (IQR)</i>	5.0 (5.0, 6.0)	5.0 (4.0, 5.0)	5.0 (5.0, 5.8)	5.0 (4.0, 5.3)	5.0 (4.0, 5.0)
Median income ² <i>(IQR)</i>	6.0 (4.0, 7.5)	6.0 (4.0, 11.3)	8.0 (4.0, 13.0)	6.0 (4.0, 11.5)	5.0 (4.0, 7)

Race**					
Asian	8 (17.4%)	5 (7.46%)	1 (7.10%)	1 (2.80%)	3 (17.6%)
Black	0	4 (5.97%)	0	3 (8.30%)	1 (5.90%)
White	29 (63.0%)	50 (74.6%)	11 (78.6%)	27 (75.0%)	12 (70.6%)
Multiple races	5 (10.9%)	6 (0.09%)	1 (7.10%)	5 (13.9%)	0
Other***	4 (8.70%)	2 (0.03%)	1 (7.10%)	0	1 (5.90%)

*Omitted data from BMI due to NA values

**Contains omitted values

***American Indian/Alaska Native and Native Hawaiian or Other Pacific Islander

¹ Level of education is categorized as 1=less than 12th grade, 2=12th grade or GED, 3=vocational school, 4=AA degree or some college, 5=bachelors degree, 6=master's degree, 7=doctorate.

² Income is categorized in \$10,000 increments up to \$160,000 (i.e. 0=\$0-\$9,999, 1=\$10,000-\$19,999 etc)

3.2 Nutrient Intake

Dietary information of energy, macronutrients, and fiber are described in Table 2. There was no significant difference in dietary intake between healthy controls and the women in the IBS group (energy: $p = 0.8$, total fat: $p = 0.5$, total protein: $p = 0.7$, total carbohydrate: $p = 0.6$). Women in the IBS-D group consumed significantly more energy than IBS-C individuals ($p = 0.04$) but not IBS-M individuals ($p = 0.5$). Within the IBS subtypes, macronutrient consumption was fairly similar. Healthy controls and women with IBS consumed similar levels of fiber. Within the IBS group, IBS-M individuals consumed more fiber than the other subtypes, but this was not significantly different (IBS-C: $p = 0.2$, IBS-D: $p = 0.07$). In terms of total HEI score, there was no significant difference between healthy controls and IBS females ($p = 0.5$). IBS-D individuals scored significantly lower on the HEI than IBS-C ($p = 0.05$) and IBS-M ($p = 0.04$) individuals. For HEI sodium scores, there was no significant difference between healthy controls and IBS individuals ($p = 0.87$). Although IBS-D individuals had a lower sodium score, it was not significantly different from the other IBS subtypes (IBS-C: $p = 0.8$, IBS-M: $p = 0.4$).

Table 2: Mean Energy and Nutrient Intake of Healthy Controls and Females with IBS, Including Subtypes, Across 3 Days

Dietary variables <i>Mean (SD)</i>	Healthy controls (n=46)	IBS (all subtypes) (n=67)	IBS-C (n=14)	IBS-D (n=36)	IBS-M (n=17)
Macronutrient intake					
Energy intake (kcal)	1814 (486)	1843 (443)	1674 (292)	1914 (507)	1831 (376)
Total fat (g)	74 (22)	77 (24)	72 (16)	78 (23)	80 (31)
Total protein (g)	69 (19)	70 (20)	65 (18)	72 (19)	70 (25)
Total carbohydrate (g)	207 (75)	215 (69)	196 (39)	224 (79)	212 (62)
Fiber					
Total dietary fiber (g)	22.0 (9.5)	21.6 (7.0)	21.2 (6.3)	20.6 (7.5)	24.1 (5.9)
Soluble dietary fiber (g)	6.1 (3.0)	6.1 (2.3)	5.3 (1.8)	6.2 (2.5)	6.6 (1.9)
Insoluble dietary fiber (g)	15.8 (6.8)	15.4 (5)	15.6 (4.9)	14.3 (5.5)	17.5 (4.7)
Healthy Eating Index (HEI) Score					
HEI total score	59.8 (11.2)	58.3 (12.4)	62.5 (11.9)	54.7 (11.8)	62.5 (12.2)
HEI sodium score	5.0 (2.8)	5.1 (2.8)	5.2 (3.0)	4.8 (2.7)	5.5 (2.9)

3.3 Differences in Sodium Intake

The mean sodium intake was 2864 mg/day for healthy controls and 2924 mg/day for the IBS group (Table 3). Intake levels of both groups were significantly higher than the CDC recommended sodium intake level of 2300 mg ($p < 0.0001$), but still significantly lower than the national average of 3400 mg ($p < 0.0003$). Because the distribution of sodium intake was skewed, we chose to use the median when comparing differences within the study population. There was no significant difference between sodium intake between healthy controls and females with IBS ($p = 0.98$, Figure 1). When comparing across subtypes (Figure 2), individuals with IBS-D had the highest level of sodium intake; however, it was not significantly different than individuals with IBS-C ($p = 0.08$) and IBS-M ($p = 0.22$).

Table 3: Average Sodium Intake of Healthy Controls and Females with IBS, Including Subtypes, Across 3 Days

Sodium intake (mg)	Healthy controls (n=46)	IBS (all subtypes) (n=67)	IBS-C (n=14)	IBS-D (n=36)	IBS-M (n=17)
Mean (SD)	2864 (945)	2924 (1028)	2529 (757)	3095 (1020)	2887 (1189)
Median (IQR)	2849 (2195, 3308)	2657 (2163, 3386)	2384 (2006, 2754)	2883 (2498, 3562)	2530 (2141, 3253)

Fig 1: Comparison of Average Sodium Intake Between Healthy Controls and Individuals with IBS

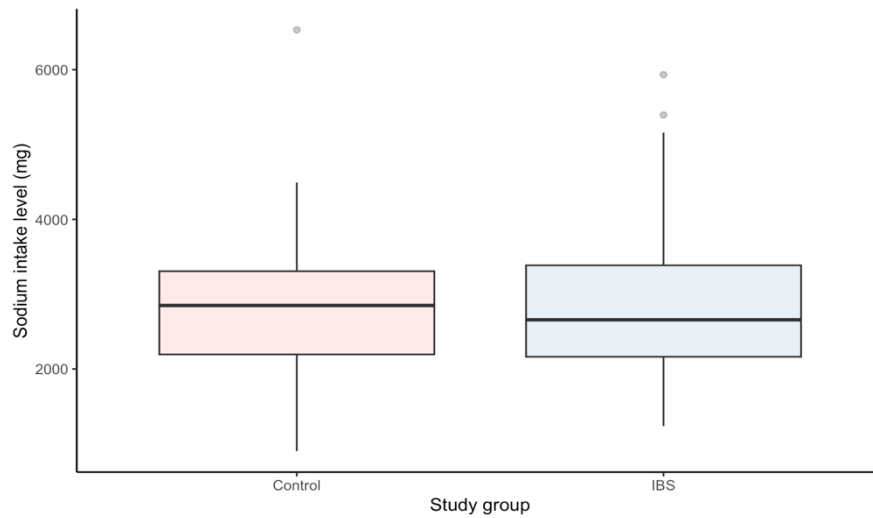
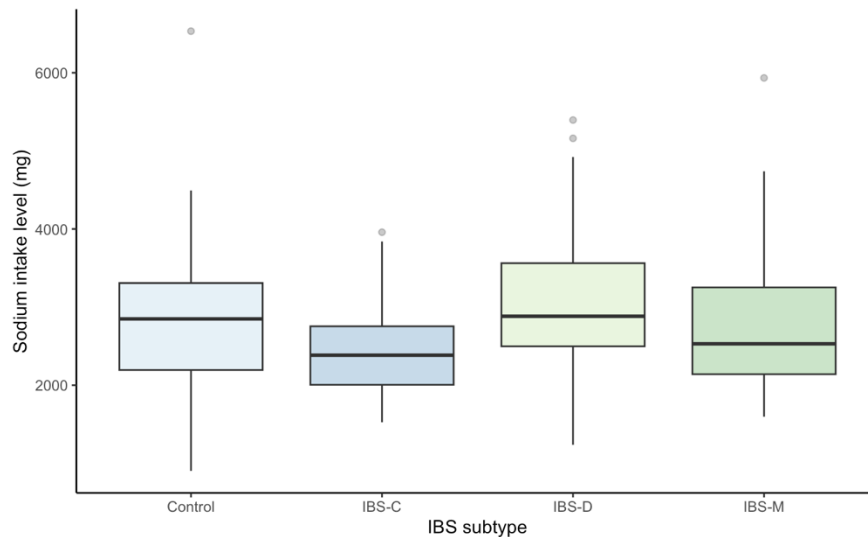


Fig 2: Comparison of Average Sodium Intake Between Healthy Controls and IBS Subtypes



3.4 Sodium, Energy, and Macronutrient Intake

In all groups, a strong relationship ($r = 0.59$; $p < 0.0001$) was found between sodium intake and caloric intake. As energy intake increased, so did sodium intake (Figure 3). Due to this significant relationship between sodium intake and caloric intake, we examined the relationship between sodium intakes and the macronutrients: carbohydrates, fats, and proteins. Log-transformed analyses showed significant associations between sodium intakes and all 3 of the macronutrients (carbohydrates: $r = 0.32$, $p = 0.0006$; fats: $r = 0.51$, $p < 0.0001$; protein: $r = 0.50$, $p < 0.0001$). When consumption of carbohydrates, fats, and protein increased, so did sodium intake (Fig 4). A separate analysis was done for fiber, where a positive trend was observed, but there was no statistically significant relationship between sodium intake and fiber intake (Fig 5, $r = 0.17$, $p = 0.06$).

Fig 3: Log Transformed Association Between Energy Intake and Sodium Intake Among Healthy Controls and IBS-Subtypes

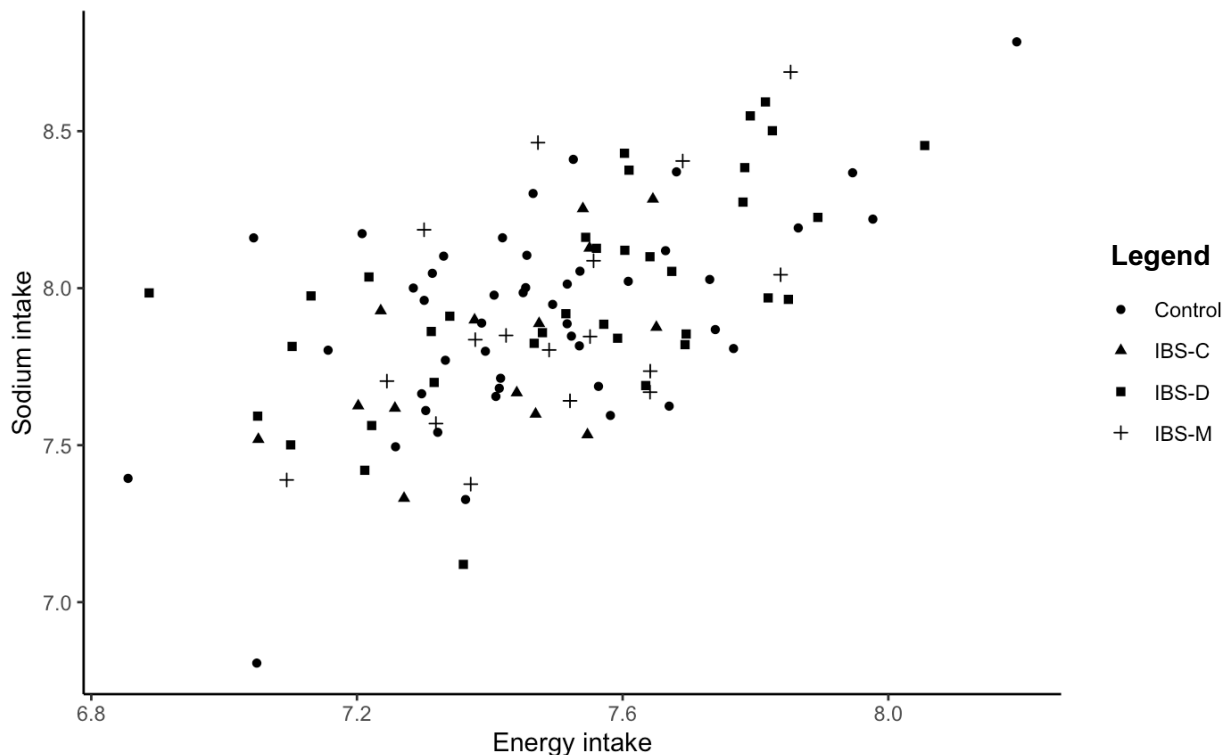


Fig 4: Log Transformed Association of Macronutrients and Sodium Intake Among Healthy Controls and IBS Subtypes (A: Carbohydrates, B: Fats, C: Protein)

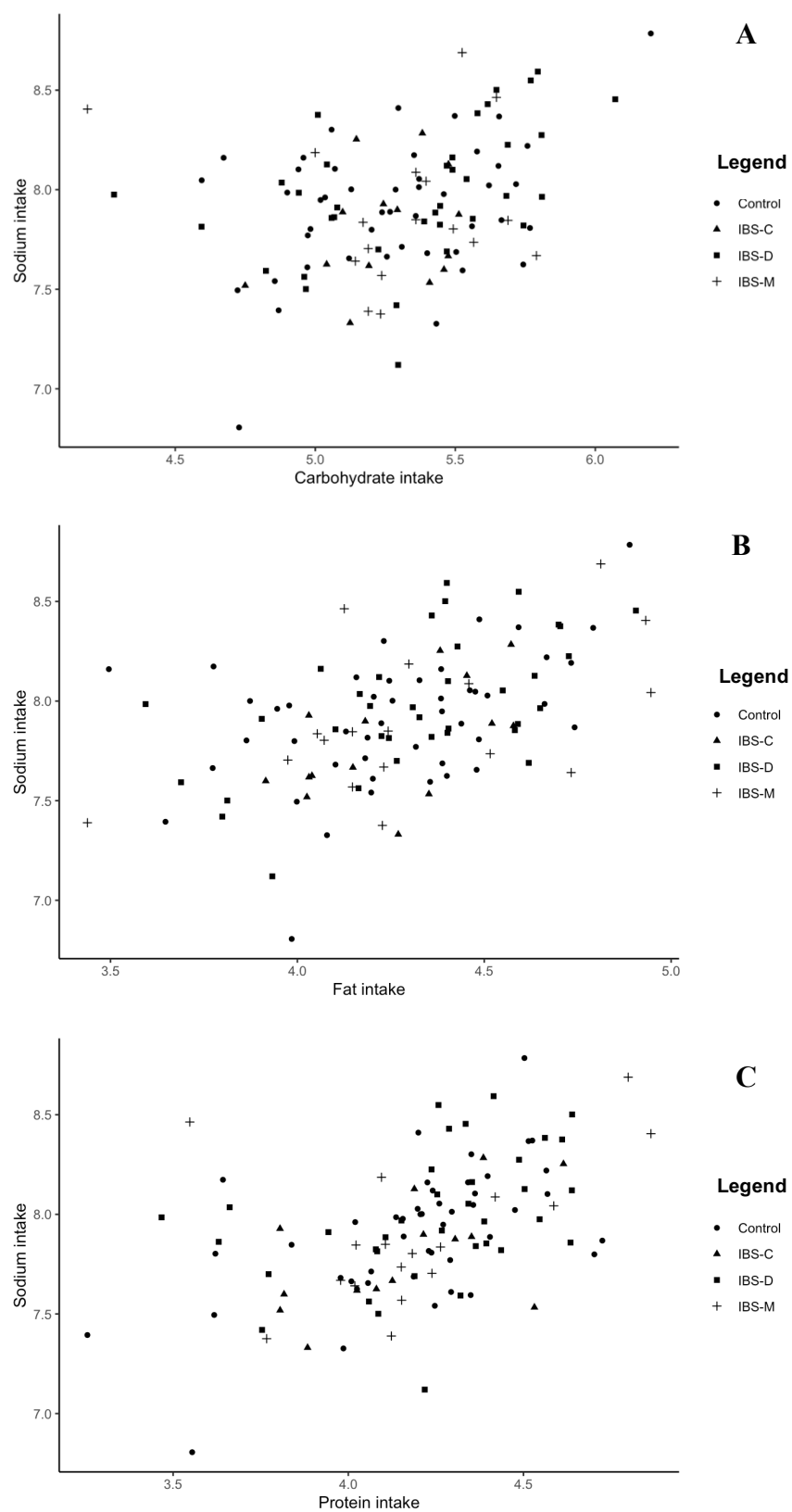
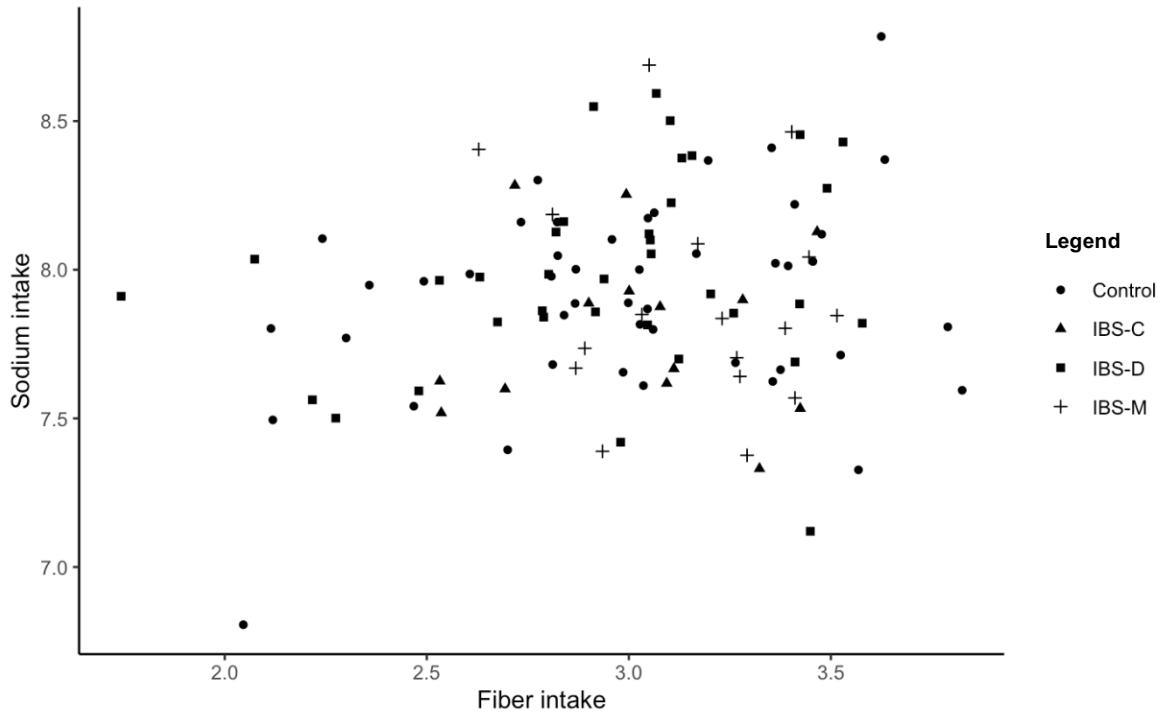


Fig 5: Log Transformed Association of Fiber Intake and Sodium Intake Among Healthy Controls and IBS Subtypes



3.5 Top Contributors of Sodium

Dietary analysis showed that the top 5 contributors of sodium based on serving size were: vegetables, breads/grains/cereals, sauces and condiments, savory snacks, and poultry/eggs. Average serving sizes for each contributor of sodium are listed in Table 4. Consumption patterns appeared similar across groups. There was no significant difference between IBS and healthy controls in the consumption of top contributors of sodium. For dessert consumption, the IBS-D group consumed a significantly greater amount than individuals with IBS-C ($p = 0.005$) and IBS-M ($p = 0.01$). Individuals with IBS-D also consumed a significantly higher amount of pasta than individuals with IBS-C ($p = 0.03$). Individuals with IBS-D consumed greater amounts of breads/grains/cereals than participants with IBS-C and IBS-M, but this did not reach statistical significance (IBS-C: $p = 0.08$, IBS-M: $p = 0.23$). Healthy controls appear to consume the more vegetables than the IBS group, but this was not significantly different ($p = 0.11$).

Table 4: A Comparison of Average Servings of Top Contributors of Sodium Across 3 Days For Healthy Controls, IBS Group, and IBS Subtypes

Average serving size mean (SD)										
Top contributor of sodium	Control (n=46)	IBS (n=67)	P-value	IBS-C (n=14)	IBS-D (n=36)	IBS-M (n=17)	P-value IBS-C vs IBS-D	P-value IBS-C vs IBS-M	P-value IBS-D vs IBS-M	
Breads/grains/cereals	2.0 (1.2)	2.3 (1.5)	0.23	1.7 (1.6)	2.6 (1.4)	2.0 (1.7)	0.08	0.59	0.23	
Cold cuts/cured meats	0.7 (0.9)	1.0 (1.0)	0.09	0.8 (0.9)	1.1 (0.9)	1.0 (1.2)	0.41	0.62	0.87	
Soup/broth	0.2 (0.5)	0.1 (0.2)	0.09	0.1 (0.3)	0.0 (0.1)	0.0 (0.1)	0.21	0.21	0.97	
Savory snacks	1.4 (1.4)	1.6 (1.2)	0.57	1.8 (1.0)	1.4 (1.3)	1.9 (1.1)	0.22	0.85	0.16	
Poultry/eggs	1.5 (1.5)	1.8 (1.9)	0.45	1.5 (1.9)	1.9 (1.6)	1.8 (2.3)	0.47	0.73	0.81	
Cheese	0.8 (0.8)	0.7 (0.6)	0.61	0.6 (0.5)	0.7 (0.6)	0.9 (0.8)	0.84	0.37	0.41	
Pasta dishes	0.4 (0.7)	0.6 (1.2)	0.25	0.3 (0.5)	0.9 (1.5)	0.5 (0.8)	0.03*	0.23	0.32	
Meat/meat alternatives	1.7 (1.6)	1.4 (1.7)	0.38	1.2 (1.2)	1.6 (1.7)	1.2 (2.0)	0.35	0.99	0.46	
Desserts	0.7 (0.9)	0.5 (0.7)	0.17	0.2 (0.4)	0.7 (0.8)	0.3 (0.5)	0.005*	0.73	0.01*	
Vegetables	3.3 (1.8)	2.8 (1.5)	0.11	2.9 (1.2)	2.8 (1.6)	2.7 (1.6)	0.93	0.77	0.82	
Sauces/condiments	1.7 (2.0)	1.9 (1.8)	0.46	1.9 (1.6)	2.0 (1.7)	1.7 (2.1)	0.77	0.8	0.58	

* significant association found (p<0.05)

3.6 Sodium Intake and Symptoms

During the 28-day period, females with IBS experienced moderate to very severe abdominal pain for 37% of days, bloating for 28% of days, and intestinal gas for 31% of days (Table 5). There was no correlation found between sodium intake and percent days with abdominal pain ($r = 0.09$, $p = 0.45$), bloating ($r = -.009$, $p = 0.94$), and intestinal gas ($r = 0.07$, $p = 0.56$). Symptom severity for abdominal pain, bloating, and intestinal was significantly higher in IBS females compared to healthy controls ($p < 0.0001$). However, no significant correlations were found between sodium intake and severity of abdominal pain ($r = 0.12$, $p = 0.35$), bloating ($r = 0.02$, $p = 0.89$), or intestinal gas ($r = 0.09$, $p = 0.45$) in IBS participants (See Fig 6). A separate correlation analysis was done for healthy controls and showed no relationship between sodium intake and symptoms.

Table 5: Frequency and Average Score for Severity of Symptoms: Abdominal Pain, Bloating, and Intestinal Gas in Healthy Controls and Females with IBS

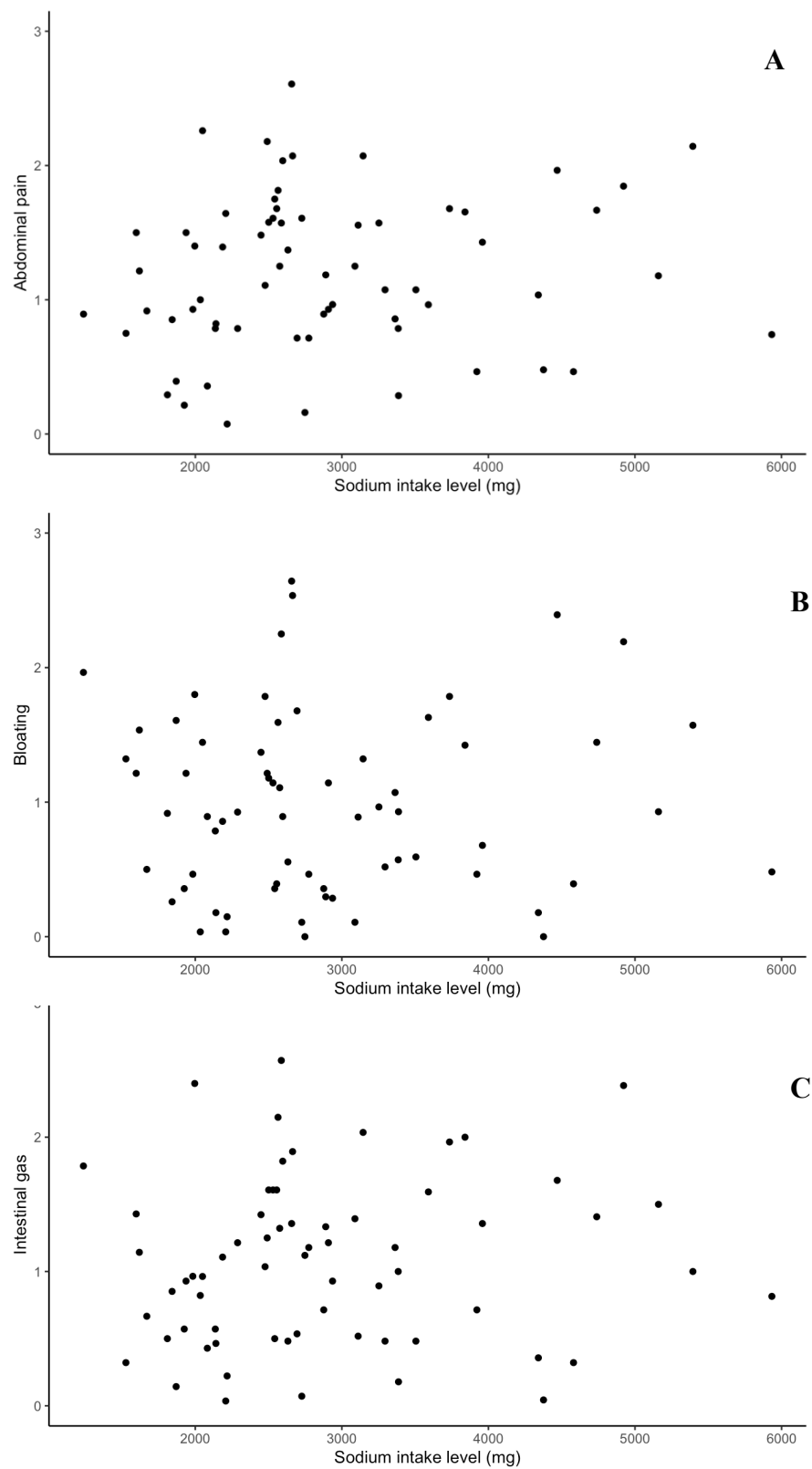
Time scale	Symptom	Healthy controls (n = 45*)			IBS (all subtypes) (n = 66*)		
		% days with moderate to very severe symptoms	% reporting ¹	Mean score (SD) ²	% days with moderate to very severe symptoms	% reporting ¹	Mean score (SD) ²
28 days	Abdominal pain	1.7%	73%	0.13 (0.16)	37%	100%	1.2 (0.58)
	Bloating	3.3%	71%	0.19 (0.27)	28%	97%	0.98 (0.67)
	Intestinal gas	1.6%	80%	0.15 (0.18)	31%	100%	1.1 (0.62)

*Data from 2 participants were missing, one from each group

¹ % Reporting: percent of participants reporting symptoms at least once during the 28 days

² Mean Score (SD): overall mean and SD of symptom severity score across 28 days

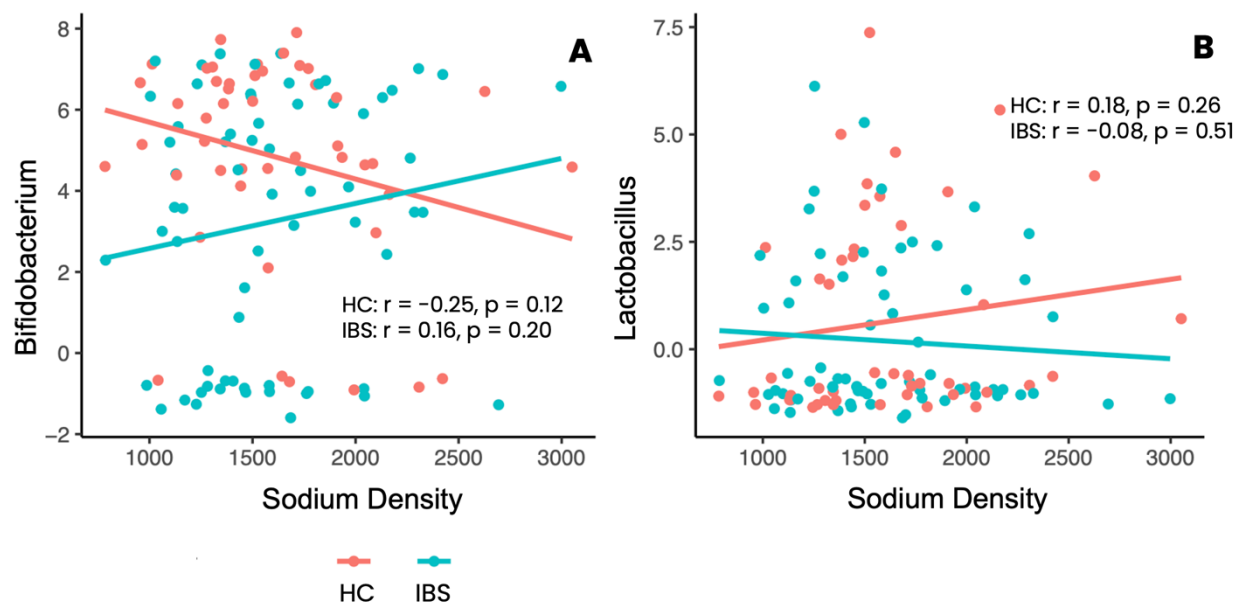
Fig 6: Correlation Between Sodium Intake Level and Symptoms in Females with IBS over a 28 Day Period (A: Abdominal Pain, B: Bloating, C: Intestinal Gas)



3.7 Sodium Density and the Microbiome

The abundances of *Bifidobacterium* and *Lactobacillus* were variable across participants, regardless of IBS status (Fig 7). Many individuals did not have detectable levels of *Bifidobacterium* (23%) or *Lactobacillus* (62%) in their stool but were still included in the analysis. We studied how relative abundances of *Bifidobacterium* and *Lactobacillus* correlated with sodium density, which measured the amount of sodium per 1000 calories. When controlled for age and BMI, there were no significant associations between sodium density and abundances of *Bifidobacterium* or *Lactobacillus*. As sodium density increased, there was a decrease in *Bifidobacterium* abundance for healthy controls ($r = -0.25$, $p = 0.12$) and an increase in abundance for the IBS group ($r = 0.16$, $p = 0.20$), but these differences were not statistically significant. There was no correlation between sodium density and *Lactobacillus* abundance in either group (Control: $r = 0.18$, $p = 0.26$; IBS: $r = -0.08$, $p = 0.51$). Some significant associations were found between sodium density and bacteria genera that were not a priori selected (Supplemental Table 2).

Fig 7: Correlation Between Sodium Density (mg/1000 kcal) and Bacteria Abundance at the Genus Level, Controlled for Age and BMI (A: *Bifidobacterium*, B: *Lactobacillus*)



Discussion

IBS is a disorder of gut-brain interaction, with many factors, including diet, affecting its pathophysiology and occurrence. This post-hoc analysis explored the relationship between sodium intake and IBS as well as the relationship to symptom severity and the gut microbiome. Our aims included comparing differences in sodium intake between females with IBS and healthy controls, as well as between IBS subtypes. We determined which foods contributed most to sodium intake based on serving size by referencing Ahmed 2023, a study that determined top sodium contributors on a national scale.³⁴ Based on average serving, we found that individuals with IBS-D consumed significantly more desserts and pasta than individuals with IBS-C. The top 5 contributors to sodium in our study were vegetables, breads/grains/cereals, sauces and condiments, savory snacks, and poultry/eggs. These food categories were taken from Ahmed 2023, which studied the top 15 contributors of sodium based on NHANES data.³⁴ The top 5 contributors to sodium in Ahmed 2023 were breads/rolls/buns, cold cuts, soups, savory snacks, and poultry, which is very similar to our findings. The only differences were sauces and condiments and vegetables made it into our top 5 list instead of cold cuts and soup. A reason why vegetables resulted as a top contributor is vegetable dishes could contain more added salt, which would contribute towards overall sodium intake. Previously, it was mentioned that ultra-processed foods may contribute to increased sodium intake.²⁰ According to NOVA classification, many of the specific foods that fall within the top 10 contributors of sodium are ultra-processed foods. For example, ready-to-eat cereals and loaf-type breads within the breads/grains/cereals category are considered ultra-processed foods due to additives and stabilizers to keep the food fresh. Even in the meat/alternative meats category, there were participants who consumed alternative meats and commercially prepared foods like fried chicken. Commercially prepared

foods found in fast food chains or restaurants may be a major contributor to sodium intake as restaurants often add more salt to foods for palatability. Because ultra-processed foods contain emulsifiers, sweeteners, and other additives, chronic consumption of ultra-processed foods may also be linked to intestinal inflammation and disorders.²⁰ Adding ultra-processed foods into consideration is important in our dietary analysis because so much food in the Western diet is composed of ultra-processed ingredients.

Individuals with IBS-D consumed the highest amount of sodium among subtypes, but this difference was not statistically significant. Average intake of top contributors of sodium did not differ between individuals with IBS and healthy controls. Similarly, there was no significant difference in total sodium intake between these two groups. We found that the study population was consuming, on average, significantly higher levels of sodium than what is recommended by the CDC.¹⁸ However, the study population was still consuming significantly less sodium than the average American. Based on our study results, it is still unclear if high sodium intake affects IBS pathophysiology. Further studies are needed to see if different levels of sodium intake have an impact on IBS or gut health. Our results did show that there was a significant association between sodium intake and energy intake. On average, study participants were consuming the lower end of the recommended ranges of calorie goals for females, which is 1600-2400 calories per day.³³ Consuming more sodium than what's recommended while still adhering to calorie goals implies that these participants could be consuming foods that are denser in sodium. We also found significant associations between sodium intake and consumption of macronutrients (carbohydrates, fat, and protein). Based on our results, on average, consumption of carbohydrates accounted for approximately 46% of total calories, which is on the lower end of the recommendations in Dietary Guidelines for Americans.³³ Protein intake for both groups was

higher than what the FDA recommends for a 2000 calorie diet.³³ Average consumption of fat was around 37% of total energy intake, which is slightly higher than the recommended levels by the Dietary Guidelines for Americans, which is 20-35% of daily calories.³³ Based on these patterns, there is an implication that higher sodium intake may be attributed to foods that are denser in sodium, including foods with more added salt. However, this study did not include added salt as a variable, so it is not possible to determine if sodium intake increased through sodium density or quantity of food consumed.

We also looked to see if there was an association between sodium intake and IBS-related symptoms, including abdominal pain, intestinal gas, and bloating. We predicted that individuals with IBS who consume more sodium will have more severe symptoms. Unadjusted and adjusted results showed no significant association between sodium and any of the IBS symptoms of interest. Based on these results, this may suggest sodium intake is not associated with symptom occurrence or severity. These results could also suggest sodium intake and IBS-related symptoms have a more complex relationship. The information we obtained on IBS symptoms was averaged on a 28-day period while dietary data was obtained from a 3-day food record, so it is difficult to say with certainty that sodium intake is not associated with symptoms. We chose to use data from the 28-day symptom log as opposed to a 3-day symptom log that corresponded to the food record days because we were operating under the assumption that dietary intake across the 28-day period should be fairly consistent. For future directions, we can see if sodium intake correlates with symptom data taken from the 3-day record.

Furthermore, there can also be many factors that lead to symptom occurrence in IBS. Some individuals are sensitive to specific foods that can trigger IBS-related symptoms.²² However, because individuals can have different triggers, dietary variables are difficult to

account for. Symptoms such as abdominal pain, intestinal gas, and bloating can also be associated with conditions that are not related to IBS. For example, these symptoms can occur due to food intolerances or constipation, which were not controlled for. We also did not focus on every IBS-related symptom that was included in the parent study. It is possible that sodium intake has a significant effect on a symptom that we did not include in this post-hoc analysis.

Because our study population is on average consuming significantly less sodium than the average American, another interpretation could be that a higher level of sodium intake is needed for noticeable symptoms to occur. Peng et al performed a post-hoc analysis on the DASH-Sodium Trial where they studied sodium intake and bloating in healthy adults. Sodium intake was split into 3 categories: low (1150 mg), intermediate (2300 mg), and high (3500 mg).²⁷ Our study population, on average, consumed 2894 mg of sodium, which is closer to the intermediate level. Peng et al found individuals who had high sodium intake experienced more severe bloating.²⁷ The same study found that a high fiber diet also increased bloating severity but bloating severity decreased as sodium intake decreased, implying that high fiber and high sodium together may synergistically contribute to bloating.²⁷ Peng et al further suggested gut microbiome composition may also modulate the effect of sodium on bloating symptoms.²⁷ This elucidates the complex interactions between dietary factors and the gut brain axis. In relation to our study, we did not find these patterns for sodium intake and bloating. Unlike Peng et al, we did not stratify sodium intake levels due to our small sample size. More research is needed to determine if there is a relationship between sodium intake and symptoms such as bloating.

The second aim of the study was to explore the relationship between sodium intake and the gut microbiome in our study population at the genus level. We had hypothesized that increased sodium intake would be associated with decreased abundances of *Bifidobacterium* and

Lactobacillus. However, we found no significant association between sodium intake and bacteria abundance. Abundances of *Lactobacillus* and *Bifidobacterium* were variable amongst our study population. A sizeable portion of participants did not have detectable levels of these genera in their stool samples. This may be because *Lactobacillus* does not have a dominant presence in stool, making it hard to analyze with 16S rRNA gene sequencing.³¹ It is also possible that some participants were consuming more foods that naturally contain *Lactobacillus*, such as yogurt or pickled vegetables, which could have contributed to *Lactobacillus* being detected in their stool samples.³⁶ Many environmental and genetic factors can influence gut microbiome composition, so it can be hard to determine if there are specific elements that influence the microbiome independently or these factors combined will alter composition. Our study findings were not consistent with Wilck et al, who found a significant loss of *Lactobacillus* in healthy individuals after a high salt diet.³¹ However, the high salt diet consisted of 6 g of sodium chloride slow release tablets every day in addition to the participants' regular diet. The investigators estimated study participants consumed on average 13.8 g of salt every day for a total of 14 days, which is approximately 4 times the amount of sodium our participants consumed.³¹ This is an extremely high amount of sodium, and is most likely not what most populations typically consume regularly. Furthermore, Wilck et al studied healthy individuals, so their study's results may not be applicable to the IBS population. Although we did not find significant associations between sodium intake and *Lactobacillus* or *Bifidobacterium*, we did find significant associations with some bacteria genera that were not listed in our aims (Supplemental Table 2). More research focused on the gut microbiome and sodium intake can be helpful in illustrating which specific genera have significant associations with sodium intake.

To date, this post-hoc analysis is one of the few that compares differences in sodium intake between IBS females and healthy controls as well as investigates the relationship of sodium and the gut microbiome. A major strength of this study was that we accounted for the menstrual cycle as a confounding variable in order to control for variations in symptoms and dietary intake. At the same time, we were also able to control for hormone fluctuations associated with the menstrual cycle in relation to gut microbiome composition. Because this was a cross-sectional study, another strength of this study is that we were able to look at multiple variables to gain more understanding of IBS. We were also able to study the participants in their usual routine, without making any significant changes that would affect diet, lifestyle, or IBS-related symptoms. However, due to the cross-sectional nature, we were unable to assess trends of variables of interest over time. For example, we only collected one stool sample for 16S microbiome analysis, so we could not see changes in the microbiome over the course of the study. Future studies that take multiple stool samples may help with stronger understanding of the relationship between sodium intake and gut microbiome composition. Other limitations of this study include a limited sample size, which was composed of females with and without IBS from the Pacific Northwest. Thus, this may not be the most representative sample of the general population. In addition, food records only reflected 3 days of consumption, which may not be totally representative of what people normally eat. On the other hand, symptom occurrence and severity were recorded for 28 days. Food record data and symptom data only overlapped for the 3 days that the food record was taken. Because of this, it is possible that we could have missed a pattern involving a specific food or food group that was correlated to IBS-related symptoms. For people with IBS, it can be common practice to change diets or only eat specific foods based on severity of symptoms. It's possible that within the IBS group, participants have already identified

their trigger foods, which may include certain foods high in sodium, and have therefore already excluded those high sodium foods from their diet prior to the study. For people in general, diets can also change depending on lifestyle and food availability. In the future, a question asking if food records are representative of usual intake could be helpful to overcome this limitation. Additionally, because sodium was not the primary focus of the parent study, it was hard to quantify sodium as a variable in this post-hoc analysis. Although we studied average sodium intake across 3 days, we did not have data on added salt for this study. Because most foods naturally contain sodium, studying additional amounts of salt added to food can be an important measure. As a result, it is unclear which specific foods were denser in sodium due to additional seasoning. Having added salt as another measure could have helped to further understand dietary patterns regarding sodium intake. There are also limitations in relying on the NHANES database or NOVA classification system in this study. Although the NHANES data we used assessed sodium intake on a national scale, it is possible that the results are not representative of our small study population in the Pacific Northwest. For the NOVA classification system, because we did not have enough details on specific brands of foods from the food records, it was hard to classify if foods were actually ultra-processed foods or in another classification. There is also the misconception that all ultra-processed foods are unhealthy or ‘junk’ foods. Ultra-processed foods can be nutrient-dense, but because of the presence of additives to keep the food more shelf stable, it is labeled as ultra-processed. Because of this, we should not rely on the NOVA classification system to determine health of food products. There needs to be more large-scale studies that focus on sodium as the primary variable of interest when studying the relationships between diet and IBS. To better assess amount of sodium consumed, it may be valuable to measure urinary sodium levels in subjects because dietary sodium is mostly secreted through the

urine. Our results showed that the study participants were consuming significantly higher amounts of sodium than recommended but sodium intake was still significantly lower than the national average. Because sodium and salt are such prevalent components in our diet, it is worth conducting more research on how it can impact our health. Our study did not find significant relationships between sodium intake and IBS-related symptoms. We also did not find significant correlations between sodium density and the relative abundances of *Lactobacillus* and *Bifidobacteria* in the gut microbiome. These results were inconsistent with other studies in our literature review.^{27,31} Thus, more research is needed to determine these associations in order to deeper understand the complexities of IBS pathophysiology.

In conclusion, sodium intake levels in IBS females were not significantly different than healthy controls. There were also no significant differences in sodium intake within the IBS-subtypes. Energy and macronutrient intake was significantly correlated with increased sodium intake. There was no significant relationship between sodium intake and IBS-related symptoms such as bloating, abdominal pain, and intestinal gas. Lastly, we did not find significant associations between sodium density and *Lactobacillus* or *Bifidobacteria* but found significant associations for other genera listed in Supplemental Table 2. This study contributed more knowledge towards understanding the relationship between diet, IBS, and the gut microbiome. Furthermore, it elucidates the gaps in knowledge on how sodium consumption can be associated with IBS and gut health.

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Supplementary Material:**Supplemental Table 1:** Categorization of Food Items with Assigned Code Obtained from Food Record into Top Contributors of Sodium

Breads/grains/cereals	
GRW0200	Loaf-type Bread and Plain Rolls - Whole Grain
GRS0200	Loaf-type Bread and Plain Rolls - Some Whole Grain
GRR0200	Loaf-type Bread and Plain Rolls - Refined Grain
GRW0300	Other Breads (quick breads, corn muffins, tortillas) - Whole Grain
GRS0300	Other Breads (quick breads, corn muffins, tortillas) - Some Whole Grain
GRR0300	Other Breads (quick breads, corn muffins, tortillas) - Refined Grain
GRW0600	Ready-to-eat Cereal (not presweetened) - Whole Grain
GRS0600	Ready-to-eat Cereal (not presweetened) - Some Whole Grain
GRR0600	Ready-to-eat Cereal (not presweetened) - Refined Grain
GRW0700	Ready-to-eat Cereal (presweetened) - Whole Grain
GRS0700	Ready-to-eat Cereal (presweetened) - Some Whole Grain
GRR0700	Ready-to-eat Cereal (presweetened) - Refined Grain
Cold cuts/cured meats	
MCF0200	Cured Pork
MCL0200	Lean Cured Pork
MFF0100	Fish - Fresh and Smoked
MFL0100	Lean Fish - Fresh and Smoked
MCF0100	Cold Cuts and Sausage
MCL0100	Lean Cold Cuts and Sausage
Soup/broth	
MSC0800	Soup Broth
Savory snacks	
FRU0700	Fruit-based Savory Snack
FMC0100	Vegetable-based Savory Snack
GRW0400	Crackers - Whole Grain
GRS0400	Crackers - Some Whole Grain
GRR0400	Crackers - Refined Grain
GRW1000	Snack Bars - Whole Grain
GRS1000	Snack Bars - Some Whole Grain
GRR1000	Snack Bars - Refined Grain
GRW0900	Snack Chips - Whole Grain
GRS0900	Snack Chips - Some Whole Grain
GRR0900	Snack Chips - Refined Grain
GRW1200	Flavored Popcorn
FMC0200	Meat-based Savory Snack
MOF0500	Nuts and Seeds
Poultry/eggs	
MPF0100	Poultry
MPL0100	Lean Poultry
MOF0400	Egg Substitute

MOF0300	Eggs
Cheese	
DCF0100	Cheese - Full Fat
DCR0100	Cheese - Reduced Fat
DCL0100	Cheese - Low Fat and Fat Free
DCN0100	Cheese - Nondairy
Pasta dishes	
GRW0500	Pasta - Whole Grain
GRS0500	Pasta - Some Whole Grain
GRR0500	Pasta - Refined Grain
Meat/meat alternatives	
MRF0100	Beef
MRL0100	Lean Beef
MRF0200	Veal
MRL0200	Lean Veal
MRF0300	Lamb
MRL0300	Lean Lamb
MRF0400	Fresh Pork
MRL0400	Lean Fresh Pork
MRF0500	Game
MPF0200	Fried Chicken - Commercial Entree and Fast Food
MFF0200	Fried Fish - Commercial Entree and Fast Food
MSL0100	Shellfish
MSF0100	Fried Shellfish - Commercial Entree and Fast Food
MOF0100	Organ Meats
MOF0700	Meat Alternatives
Desserts	
GRW0800	Cakes, Cookies, Pies, Pastries, Danish, Doughnuts and Cobblers - Whole Grain
GRS0800	Cakes, Cookies, Pies, Pastries, Danish, Doughnuts and Cobblers - Some Whole Grain
GRR0800	Cakes, Cookies, Pies, Pastries, Danish, Doughnuts and Cobblers - Refined Grain
DOT0300	Pudding and Other Dairy Dessert
DOT0400	Artificially Sweetened Pudding and Other Dairy Dessert
MSC0600	Miscellaneous Dessert
DOT0100	Frozen Dairy Dessert
DOT0200	Frozen Nondairy Dessert
Vegetables	
VEG0900	Fried Vegetables
VEG0100	Dark-green Vegetables
VEG0200	Deep-yellow Vegetables
VEG0300	Tomato
VEG0800	Fried Potatoes
VEG0450	Other Starchy Vegetables
VEG0700	Legumes (cooked dried beans)

VEG0600	Other Vegetables
Sauces/condiments	
FDF0100	Salad Dressing - Regular
FDR0100	Salad Dressing - Reduced Fat/Reduced Calorie/Fat Free
MSC0100	Gravy - Regular
MSC0200	Gravy - Reduced Fat/Fat Free
MSC0300	Sauces and Condiments - Regular
MSC0400	Sauces and Condiments - Reduced Fat
MSC0500	Pickled Foods
MOF0600	Nut and Seed Butters

Supplemental Table 2: Partial Regression Associations Between Sodium Intake and Bacteria Genera Found in Stool Sample for Healthy Controls and IBS Individuals

Genus	IBS (all subtypes)				Healthy controls			
	Partial R	95% CI		p-value	Partial R	95% CI		p-value
Intestinimonas	-0.27	-0.51	-0.03	0.03*	-0.37	-0.67	-0.07	0.02*
Lachnospiraceae UCG004	0.04	-0.20	0.28	0.75	-0.33	-0.62	-0.03	0.03*
Eubacterium xylanophilum	-0.08	-0.32	0.17	0.53	0.29	-0.02	0.60	0.07
Lachnoclostridium	-0.13	-0.38	0.13	0.33	-0.27	-0.58	0.04	0.09
Ruminococcaceae UCG004	0.02	-0.23	0.28	0.86	0.26	-0.04	0.57	0.09
Parasutterella	-0.09	-0.33	0.17	0.50	-0.24	-0.52	0.05	0.11
Ruminococcaceae UCG013	-0.18	-0.43	0.07	0.15	-0.26	-0.58	0.06	0.11
Bifidobacterium	0.16	-0.09	0.41	0.20	-0.25	-0.56	0.07	0.12
Lachnospira	-0.34	-0.58	-0.10	0.01*	-0.25	-0.56	0.07	0.12
Turicibacter	0.07	-0.18	0.32	0.59	-0.23	-0.54	0.08	0.14
Dialister	0.24	0.01	0.47	0.04*	-0.22	-0.52	0.08	0.15
Lachnospiraceae ND3007	0.05	-0.20	0.31	0.68	-0.23	-0.55	0.09	0.15
Ruminococcus gauvreauii	-0.14	-0.39	0.10	0.25	0.22	-0.09	0.53	0.16
Coprococcus 2	0.21	-0.04	0.46	0.10	0.21	-0.1	0.53	0.18
Akkermansia	0.13	-0.12	0.38	0.30	-0.21	-0.52	0.10	0.19
Gordonibacter	0.22	-0.02	0.47	0.07	0.18	-0.11	0.48	0.21
Phascolarctobacterium	-0.16	-0.41	0.09	0.20	-0.18	-0.49	0.13	0.24
Lactobacillus	-0.08	-0.34	0.17	0.51	0.18	-0.14	0.50	0.26
Ruminococcaceae UCG011	-0.09	-0.33	0.15	0.47	0.16	-0.16	0.48	0.31
Streptococcus	-0.00	-0.25	0.25	0.98	-0.15	-0.46	0.16	0.34
Ruminococcaceae UCG002	0.21	-0.03	0.45	0.09	-0.14	-0.45	0.17	0.37
Ruminococcaceae UCG005	-0.17	-0.42	0.08	0.17	0.14	-0.17	0.46	0.37
Ruminococcus 2	0.03	-0.22	0.28	0.80	0.13	-0.18	0.44	0.40
Christensenellaceae R7	0.18	-0.07	0.43	0.15	-0.12	-0.43	0.20	0.46
Actinomyces	0.10	-0.15	0.34	0.44	0.11	-0.21	0.43	0.49

Eisenbergiella	-0.02	-0.27	0.23	0.89	0.11	-0.21	0.44	0.49
Erysipelotrichaceae.UCG.003	-0.08	-0.31	0.15	0.47	-0.11	-0.42	0.21	0.49
Eubacterium coprostanoligenes	-0.03	-0.28	0.22	0.82	0.11	-0.21	0.42	0.50
Parabacteroides	0.09	-0.17	0.34	0.50	0.11	-0.21	0.43	0.51
DTU089	0.29	0.05	0.53	0.02*	-0.09	-0.41	0.22	0.56
Lachnospiraceae FCS020	0.01	-0.24	0.26	0.95	-0.09	-0.41	0.23	0.56
Marvinbryantia	-0.10	-0.34	0.15	0.43	-0.08	-0.38	0.22	0.58
Ruminococcaceae UCG014	-0.01	-0.26	0.25	0.97	0.09	-0.23	0.41	0.58
Ruminiclostridium	-0.03	-0.29	0.22	0.79	0.08	-0.23	0.41	0.59
Eubacterium hallii	0.08	-0.17	0.33	0.51	0.08	-0.21	0.36	0.60
Collinsella	0.14	-0.11	0.39	0.26	-0.08	-0.38	0.22	0.61
Oscillibacter	-0.20	-0.45	0.05	0.11	-0.07	-0.36	0.22	0.61
Flavonifractor	-0.12	-0.37	0.13	0.36	0.08	-0.25	0.40	0.62
Desulfovibrio	0.13	-0.12	0.37	0.31	0.07	-0.24	0.38	0.65
Faecalibacterium	0.14	-0.11	0.39	0.27	-0.07	-0.39	0.25	0.66
Eubacterium eligens	0.05	-0.20	0.29	0.72	0.07	-0.25	0.39	0.66
Ruminococcaceae UCG003	-0.09	-0.34	0.16	0.48	-0.07	-0.39	0.25	0.67
Shuttleworthia	-0.01	-0.25	0.24	0.96	-0.07	-0.39	0.26	0.68
Ruminococcaceae NK4A214	0.05	-0.20	0.30	0.71	0.06	-0.26	0.39	0.69
Moryella	0.07	-0.18	0.32	0.56	-0.06	-0.37	0.25	0.71
Gemella	0.03	-0.22	0.28	0.82	0.06	-0.25	0.36	0.71
Ruminococcus 1	0.03	-0.23	0.28	0.82	0.06	-0.26	0.38	0.72
Eubacterium fissicatena	0.14	-0.11	0.39	0.26	-0.06	-0.38	0.27	0.72
Butyricicoccus	-0.09	-0.35	0.16	0.46	-0.05	-0.38	0.27	0.74
Ruminiclostridium 6	-0.14	-0.39	0.11	0.27	0.04	-0.29	0.36	0.82
Sutterella	0.02	-0.24	0.27	0.88	-0.03	-0.36	0.29	0.83
Bacteroides	-0.11	-0.36	0.14	0.39	-0.03	-0.35	0.29	0.85
Lachnospiraceae NC2004	-0.09	-0.33	0.16	0.48	0.03	-0.3	0.36	0.85
Lachnospiraceae UCG001	-0.00	-0.26	0.25	0.99	-0.03	-0.34	0.28	0.85
Alistipes	-0.03	-0.29	0.22	0.79	-0.03	-0.35	0.29	0.86
UBA1819	0.01	-0.24	0.27	0.92	-0.02	-0.34	0.30	0.90
Prevotella 9	0.14	-0.10	0.38	0.25	0.02	-0.29	0.33	0.91
Eubacterium ventriosum	-0.03	-0.29	0.22	0.80	-0.01	-0.31	0.29	0.93
Ruminiclostridium 5	0.07	-0.18	0.32	0.58	-0.01	-0.34	0.31	0.93
Bilophila	-0.06	-0.31	0.19	0.62	0.01	-0.31	0.32	0.98
GCA 900066575	-0.05	-0.31	0.20	0.68	-0.00	-0.33	0.32	0.98

*significant associations found