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Association of dietary fiber intake and gut microbiota in healthy adults

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Abstract

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Background: Increasing evidence has shown that gut microbiota may play a role in colorectal cancer. Diet, particularly fiber intake, may modify gut microbiota composition, which may consequently impact cancer risk.

Objective: We investigated the relationship between total dietary fiber intake and gut microbiota in healthy humans.

Design: Using 16S rRNA gene sequencing, we assessed gut microbiota in fecal samples from 151 healthy adults in two independent study populations: NCI, n= 75 (healthy controls from a colorectal cancer case-control study), and NYU, n=76 (polyp-free subjects from a cross-sectional colonoscopy study). We calculated energy-adjusted total dietary fiber intake of participants based on food frequency questionnaires. For each study population, we evaluated the relationship between quartiles of higher fiber intake as a continuous ordinal variable, and global gut microbiota community composition (via PERMANOVA of weighted UniFrac distance) and specific taxon abundance (via DESeq2).

Results: Total fiber intake was significantly associated with overall microbial community composition in NYU (p=0.008) but not NCI (p=0.81), after adjustment for age, sex, race, body mass index, and cigarette smoking. In a taxonomy-based meta-analysis of these two study populations, higher fiber intake was associated with higher abundance of select genera from class Clostridia: *SMB53* (fold change [FC]=1.04, p=0.04), *Lachnospira* (FC=1.03, p=0.05), and *Faecalibacterium* (FC=1.03, p=0.06), and lower abundance of genera *Actinomyces* (FC=0.95, p=0.002), *Odoribacter* (FC=0.95, p=0.03), and *Oscillospira* (FC=0.96, p=0.06). A species-level meta-analysis showed a marginal association between higher fiber intake and higher abundance of *Faecalibacterium prausnitzii* (FC=1.03, p=0.07) and lower abundance of *Eubacterium dolichum* (FC=0.96, p=0.04) and *Bacteroides uniformis* (FC=0.97, p=0.05).

Conclusions: Our results suggest that increased dietary fiber intake may impact gut microbiota composition in healthy adults, particularly in favor of putatively beneficial bacteria such as *Faecalibacterium prausnitzii*. Given the potentially modifiable nature of gut microbiota through diet, these findings warrant further study of diet-microbiota based colorectal cancer prevention strategies.

Keywords

Gut Microbiome; diet fiber intake; cross-sectional study; epidemiology

Introduction

The human gastrointestinal tract hosts an estimated 100 trillion bacteria, which play a role in key physiologic activities, including gastrointestinal immune stimulation and fermentation of nutrients into beneficial metabolites (1). Disruption of this symbiotic relationship between human host and gut microbiota has been implicated in the development of intestinal pathology, including inflammatory bowel disease and colorectal cancer (2, 3). A growing number of epidemiologic studies have provided increasing evidence that perturbation of microbial community composition in the gut exists in colorectal cancer, with alterations of microbial taxa abundance in cancer cases compared to healthy controls (4, 5).

Dietary habits have been attributed to colorectal cancer risk development, with Western-style diets—low in fiber and high in red meat and fat—associated with higher risk for colorectal cancer (6, 7). Fiber intake, in particular, has remained an appealing modifiable dietary factor, given its protective biologic effects. Fiber undergoes fermentation by microbiota to yield short-chain fatty acid end-products, such as butyrate, which is not only essential for colon energy metabolism and epithelial proliferation, but in mouse models also exhibits tumor suppressive activity through histone deacetylase inhibition (8).

Consequently, there has been growing interest to understand the impact of dietary fiber on gut microbiota composition, which may ultimately affect cancer risk. While short-term dietary intervention trials have demonstrated that different amounts of fiber intake can significantly alter microbiota composition in a span of a few weeks (9, 10), there remain fewer studies evaluating the effect of long-term dietary habits of fiber intake on gut microbiota in humans (11).

We investigated the association between long-term dietary fiber habits and gut microbiota composition in fecal samples of healthy adults from two independent study populations: healthy controls from a case-control study of colorectal cancer and gut microbiome (5), and polyp-free adults from a cross-sectional colonoscopy study (12). We sought to examine the relationship between higher dietary fiber intake and overall gut microbiota composition, as well as specific taxa abundance.

Methods

Study Population

We assessed fecal samples of healthy adults from two independent study populations: control subjects from a National Cancer Institute (NCI) case-control study, hereafter referred to as NCI (5), and polyp-free adults from a cross-sectional colonoscopy study at New York University (NYU), called the NYU Human Microbiome and Colorectal Tumor study, hereafter referred to as NYU (12).

NCI enrolled participants from three Washington, DC area hospitals from 1985 to 1989 (13, 14). We included 75 control subjects who were awaiting elective surgery for non-oncologic, non-gastrointestinal conditions, and reported no antibiotic intake during the year prior to recruitment. Participants provided 2-day fecal samples that were freeze-dried, and samples with at least 100 mg of lyophilized fecal material available were included for analyses.

NYU enrolled participants from Kips Bay Endoscopy Center in New York City from 2012 to 2014. We included 76 polyp-free participants from this study. We excluded subjects with missing colonoscopy reports, history of inflammatory bowel disease, prior surgical anastomosis, prior history of colorectal cancer, history of familial adenomatous polyposis, and with most recent colonoscopy report >3 years prior to stool sample collection.

In both studies, participants provided written informed consent, reported no long-term antibiotic treatment, and completed diet and demographic questionnaires. We excluded subjects with less than 1000 microbial sequence reads, missing or extreme caloric intake (≤

500 or >4000 kcal/day), and with a history of other cancers, for a final sample size of 151 (n=75 in NCI, n=76 in NYU). The NYU study was approved by the institutional review board (IRB) of NYU School of Medicine, and the NCI study was approved by the IRB of NYU School of Medicine and the NCI.

Demographic information and dietary fiber assessment

Information on age, sex, height, weight, race, and cigarette smoking status was collected by questionnaire at stool collection. BMI was calculated by dividing weight in kilograms by squared height in meters, and was then categorized as underweight or normal weight (<25kg/m^2), overweight (25 ≤ BMI < 30 kg/m^2), or obese (BMI ≥ 30 kg/m^2), based on WHO definition (15). Cigarette smoking status was defined as never, current, or former smoker.

Usual dietary intake was calculated from self-administered food frequency questionnaires, which queried intake frequency and portion size of food types. Nutrient values per portion were multiplied by daily frequency of intake and summed across all relevant food items, using the US Department of Agriculture pyramid food group serving database (16). Nutrient data were standardized by total calorie intake (17). Study-specific quartiles of fiber intake were used (NCI: <11.21, 11.21-13.90, 13.91-16.50, ≥16.51 g/day; NYU: <20.07, 20.07-24.92, 24.93-30.79, ≥30.8 g/day).

Fecal samples

In NCI, fecal samples were collected by participants at home over a two day period, prior to hospitalization and treatment, and stored in a plastic container in a Styrofoam chest containing dry ice. Fecal samples were shipped to a USDA laboratory, lyophilized, and stored at a minimum of −40°C in sealed, air-tight containers. Sample aliquots were shipped to NYU for microbiome assay. In NYU, fecal samples were collected by participants onto two sections of Beckman Coulter Hemoccult II SENSA® cards (Beckman Coulter, CA) at home. Samples were shipped to NYU and stored immediately at −80°C.

Microbiota assay

In both NCI and NYU, DNA was extracted from fecal samples using the Mo Bio PowerSoil DNA Isolation Kit (Carlsbad, CA) with bead-beating, as previously reported (12). In NCI, 16S rRNA gene amplicons covering variable regions V3 to V4 were generated using the 347F-5′GG AGGCAGCAGTRRGGAAT′-3′ and 803R 5′-CTACCRGGGTATCTAATCC-3′ primer pair (5, 18). Amplicons were sequenced with the 454 Roche FLX Titanium pyrosequencing system, following the manufacturer's protocol. In NYU, 16S rRNA gene amplicons covering the V4 region were generated using the F515-5'GTGCCAGCMGCCGCGGTAA'-3' and R806-5'GGACTACHVGGGTWTCTAAT-3' primer pair (19). Amplicons were sequenced with the Illumina MiSeq platform.

Sequence data processing

Because two different sequencing platforms were used, we processed the sequence data separately. Sequences were demultiplexed, and poor-quality sequences excluded, using the default parameters of QIIME script *split_libraries.py* (for NCI) or *split_libraries_fastq.py* (for NYU) (20). Filtered sequence reads were clustered into *de novo* operational taxonomic units (OTUs) at 97% identity, and representative sequence reads for each OTU were assigned taxonomy based on fully sequenced microbial genomes (IMG/GG Greengenes) (20). Chimeric sequences were removed with ChimeraSlayer (21). Blinded quality control specimens in all sequencing batches showed good reproducibility: high intraclass correlation coefficients (ICCs) for the Shannon diversity index and abundances of bacterial phyla and genera have been previously reported (5, 12, 22).

Statistical analysis

Alpha-Diversity

We evaluated the association between quartiles of fiber intake and within-subject microbial diversity (α-diversity) indices of Shannon diversity and evenness (23). In both studies, these indices were calculated in 100 iterations of rarefied OTU tables of 1000 sequence reads per sample. We modeled the Shannon index and evenness as outcomes in linear regression, adjusting for age, sex, race, categorical BMI, and cigarette smoking status.

Beta-Diversity

We assessed the relationship of overall gut microbiota composition and quartiles of dietary fiber intake using weighted (quantitative) and unweighted (qualitative) phylogenetic UniFrac distance matrices (24). Permutational multivariate analysis of variance (PERMANOVA) of both weighted and unweighted UniFrac distances was used to evaluate whether fiber intake is associated with overall microbial community composition, after adjusting first for age, sex, race, categorical BMI, and cigarette smoking status (adonis function, ‘vegan’ package in R) (25). Principal coordinate analysis (PCoA) plots were generated using the first two principal coordinates (PCs), and labeled according to quartile of fiber intake.

Differential abundance testing

We assessed the relationship between higher quartiles of total fiber intake and specific taxa abundance using negative binomial generalized linear models, in the “DESeq2” package in R (22). Models were adjusted for age, sex, race, categorical BMI and cigarette smoking status. Nominal p-values and false discovery rate (FDR) adjusted q-values were calculated (26). DESeq2 default outlier replacement, independent filtering of low-count taxa, and filtering of count outliers were turned off. Taxa models with maximum Cook’s distance > 10 were removed prior to p-value adjustment for the FDR (27).

To identify similar taxa associations in both NCI and NYU, we then performed a taxonomy-based meta-analysis to evaluate for genera and species with concomitantly higher or lower abundance by fiber intake in the two study populations. In addition, we performed sub-analyses to examine associations between taxon abundance and higher intake of fiber from

specific sources, such as fruits and vegetables, grains, and beans. We calculated nominal meta-analysis p-values based on *Z*-score methods (28).

All trends were tested using the median values of each quartile of fiber intake. All analyses were performed using R, version 3.3.2.

Results

Subject characteristics.

A total of 151 healthy adult subjects were included for analysis: n = 75 in NCI, and n = 76 in NYU. Subject characteristics are reported in Table 1. Among these participants, 73.3% in NCI and 51.3% in NYU were male, and 82.7% in NCI and 85.5% in NYU were white. Median age in both study groups generally increased with higher fiber intake, though the trends were not statistically significant.

Global diversity.

PERMANOVA analyses of between-sample UniFrac distances demonstrated that fiber intake was significantly associated with overall microbial community composition in NYU (weighted UniFrac p=0.008; unweighted UniFrac p=0.01) but not NCI (weighted UniFrac p=0.81; unweighted UniFrac p=0.75) after adjusting for covariates of age, sex, race, BMI, and cigarette smoking [Figure 1C]. However, in both NCI and NYU, total fiber intake was not significantly associated with microbial community diversity as measured by the Shannon diversity index or evenness (Figure 1A).

Taxon abundance.

We found 14 genera with the same direction of association with fiber intake in NCI and NYU, out of 29 total genera observed overlapping in both studies. Higher total fiber intake was associated with lower abundance of genera *Actinomyces* (fold change [FC]=0.95, p=0.002) of class *Actinobacteria*, *Odoribacter* (FC=0.95, p=0.03) of class *Bacteroidia*, and *Oscillospira* (FC=0.96, p=0.06) of class *Clostridia*. Higher total fiber intake was associated with higher abundance of selected genera of class Clostridia: *SMB53* (FC=1.04, p=0.04), *Lachnospira* (FC=1.03, p=0.05), and *Faecalibacterium* (FC=1.03, p=0.06) [Figure 2; Table 2].

At the species level, we found 8 species with the same direction of association with fiber intake in the two study populations, out of 17 total species observed overlapping in both studies. A meta-analysis at this taxonomic level showed a marginal association between higher total fiber intake and higher abundance of *Faecalibacterium prausnitzii* (FC=1.03, p=0.07), and lower abundance of *Eubacterium dolichum* (FC=0.96, p=0.04) and *Bacteroides uniformis* (FC=0.97, p=0.05) [Figure 2; Table 2].

In a sub-analysis to identify associations between taxon abundance and fiber intake from specific dietary sources, we found that higher fiber intake from fruits and vegetables was associated with lower abundance of genera *Actinomyces* (FC=0.97, p=0.007), *Odoribacter* (FC= 0.96, p=0.04), and *Oscillospira* (FC=0.99, p=0.06). Higher abundance of genus *Faecalibacterium* was most significant specifically with higher fiber intake from beans

(FC=1.11, p=0.01). At the species level, higher fiber intake from beans was associated with higher abundance of *Faecalibacterium prausnitzii* (FC=1.11, p=0.01), and lower abundance of *Bacteroides uniformis* (FC=0.87, p=0.08) [Figure 3].

Although we observed similar associations with taxon abundance and fiber intake in both the NCI and NYU studies, we also noted some inconsistent associations [Supplementary Table 1]. For example, at the phylum level, higher total fiber intake was associated with higher abundance of *Proteobacteria* in NCI (p=0.03, q=0.10) but not in NYU (p=0.53, q=0.62). Higher total fiber intake was also marginally associated with higher abundance of phylum *Bacteroidetes* in NYU (p=0.07, q=0.26), but not in NCI (p=0.47, q=0.89). At the order level, higher total fiber intake was associated with lower abundance of *Coriobacteriales* (of phylum *Actinobacteria)* in NYU (p=0.008, q=0.10), but not in NCI (p=0.82, q=0.99).

Discussion

In this study, we examined the association of usual dietary fiber intakes with gut microbiota composition in healthy adults from two independent study populations. In a taxonomy-based meta-analysis, we found that higher total fiber intake is associated with specific taxon abundances, including higher abundance of select genera of Clostridia class. Some of these fiber and taxon abundance associations were consistent with specific fiber food sources, such as fruits and vegetables, grains, and beans.

The usual dietary intake of participants measured in our study provides additional insight into the potential effect of longer-term dietary patterns on gut microbiota composition, compared with controlled dietary intervention studies. Although Wu et al demonstrated that certain dietary modifications altered microbiome composition, they did not affect overall enterotype, possibly because this may be better correlated with long-term diet (11). Moreover, our study associations are more likely to represent microbial composition in an uncontrolled, real-world setting.

We found that higher fiber intake was associated with higher abundance of select genera of *Clostridia* class. This finding is notable given the particular role of *Clostridium* spp in colonocyte metabolism through production of short chain fatty acids (SCFAs) via fermentation. Butyrate, one of these SCFAs, serves as the preferred energy source for colonocytes (29, 30). Mouse models have shown that butyrate inhibits histone deacetylases and consequently affects gene expression and causes tumor suppression (8, 31), carrying implications for colorectal cancer treatment.

Within the *Clostridia* class, we noted a marginal association between higher fiber intake and higher abundance of species *Faecalibacterium prausnitzii*. The fiber and *F. prausnitzii* relationship has also been observed in a cross-sectional cohort of middle-age and older adults in Spain, in which greater adherence to a Mediterranean diet, rich in higher fiber content foods such as fruits, vegetables, and whole grains, correlated with higher levels of *F. prausnitzii* as well as *Clostridium* cluster XVIa (32). *F. prausnitzii*, one of the most abundant species found in the gut and a key producer of butyrate, has been associated with anti-inflammatory activity (33-35). Sokol and colleagues suggested that it

exerts its anti-inflammatory effects on cellular and colitis mouse models, in part due to associated metabolites blocking NF-kB and IL-8 production (35). Moreover, a reduction in *F. prausnitzii* was associated with higher risk of recurrence of Crohn's disease in patients post-resection. In addition to inflammatory bowel disease, Lopez-Siles et al. reported that lower levels of *F. prausnitzii* were also found in patients with colorectal cancer compared to healthy controls (36). Thus, these results suggest a potential therapeutic and preventive role of *F. prausnitzii* in countering microbial dysbiosis in human disease. Our finding of higher abundance of *F. prausnitzii* particularly with higher fiber intake from beans lends support to future investigation of specific diet modifications that could impact disease states.

We also observed that higher fiber intake was associated with lower abundance of genera *Odoribacter*, *Actinomyces*, and *Oscillospira*, and higher abundance of genus *Lachnospira*. In mouse models, Zackular et al. reported significant microbial shifts found within stool samples of mice with colon tumors, specifically with enrichment of OTUs affiliated with members of *Odoribacter* (37). Along similar lines, Thomas and colleagues examined human tissue samples collected during colonoscopy from rectal cancer cases and non-cancer controls, and noted higher abundance of *Odoribacter* in the case tissues (38). Kasai et al noted higher proportions of several genera, including *Actinomyces*, in fecal samples from human subjects with colorectal carcinoma (39). Furthermore, higher abundance of *Actinomyces* has been reported in both colorectal adenoma and carcinoma cases (12, 39). Whether or not enrichment or depletion of these specific microbiota reflects cause or consequence of colon tumor development remains uncertain. Nonetheless, their opposite relationship with higher fiber intake in our healthy adult population is notable, and merits further examination of diet, microbiota, and disease associations.

Similarly, we previously reported an association between lower abundance of *Clostridia* and both colorectal carcinoma and adenoma (5, 12). In a case-control study of colorectal cancer cases and controls, stool samples from colorectal cancer cases were characterized by depletion of phylum *Firmicutes*, predominantly of class *Clostridia*, relative to controls (5). In addition, we noted a depleted abundance of members of *Clostridia* class in stool samples of colorectal adenoma cases, compared with controls (12). These findings suggest a potential relationship between this shift in Clostridia composition and both pre-cancerous and cancerous events. Thus, our finding that higher dietary fiber intake is associated with a higher abundance of select genera of *Clostridia* class carries implications for protective strategies against colorectal cancer risk.

Several potential limitations need to be considered. Measurement error is an inherent limitation in self-reported dietary assessment. Subjects in both study cohorts were mostly white, and thus our findings may not be generalizable to more racially diverse populations. The cross-sectional design of both studies limits assessment of the temporality of the diet-microbiota relationship. Nonetheless, strengths of this study include the relatively large sample size, excellent quality control of microbiome assays in both studies, and adjustment for potential confounders. Furthermore, our study hypothesis was tested in two independent study populations, and our meta-analysis findings confirmed similar taxon abundance associations across both populations.

In summary, we demonstrate that fiber intake may impact gut microbiota composition in healthy humans. Given the mounting evidence that microbial dysbiosis may impact human health and contribute to development of colorectal cancer, it is imperative to better elucidate the association of diet-microbiota relationships and their potential impact on colorectal cancer risk. This understanding may lay the groundwork needed for diet-microbiota based colorectal cancer prevention strategies.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations List:

NCI	National Cancer Institute
NYU	New York Unviversity
FC	fold change
BMI	body mass index

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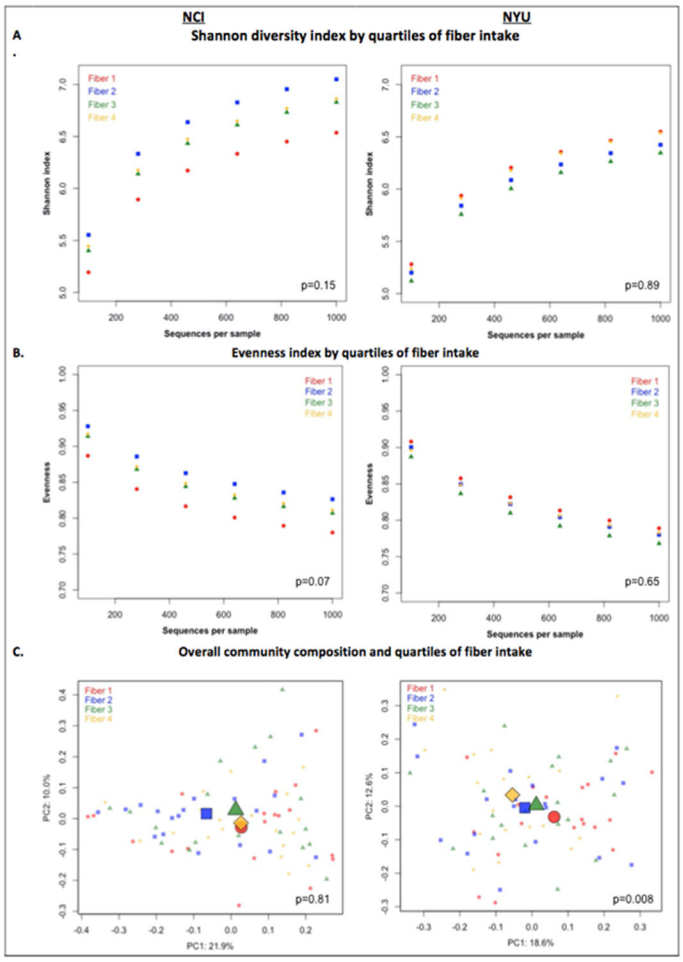

Figure 1. Alpha and beta diversity in relation to quartiles of fiber intake

A) Shannon diversity index and **B)** Evenness index by quartiles of fiber intake are shown in N=151 healthy adult subjects from two independent study populations (NCI=75, NYU=76). These indices were calculated in 100 iterations of rarefied OTU tables of 1000 sequence reads per sample. Fiber 1, Fiber 2, Fiber 3, and Fiber 4 represent increasing quartiles of fiber intake. Shannon index and evenness were modeled as outcomes in linear regression, adjusting for age, sex, race, categorical BMI, and cigarette smoking status. P-values of fiber variable in regression analysis are reported in the figure. **C)** Principal Coordinate Analysis (PCoA) plots, based on weighted Unifrac phylogenetic distances, showed a difference between lowest and highest fiber intake in NYU. This relationship was not observed in NCI. PCoA plots were generated using the first two principal coordinates. P-values reported in the figure are based on PERMANOVA of weighted UniFrac distances evaluating the association between fiber intake and overall microbial community composition, after adjusting for age, sex, race, categorical BMI, and cigarette smoking status.

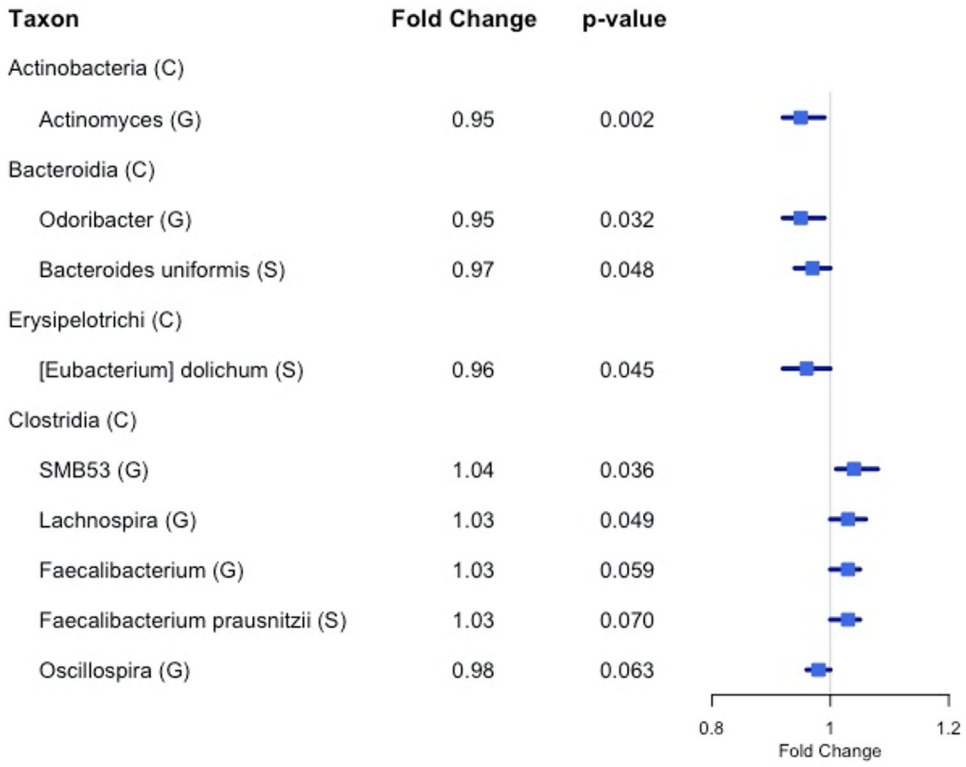

Figure 2. Forest plot of fold change of select genera (G) and species (S) in both NYU and NCI with significant or marginally significant association with higher fiber intake, based on meta-anlysis of the two study populations.

Nominal meta-analysis p-values were calculated based on *Z*-score methods. (C) denotes class.

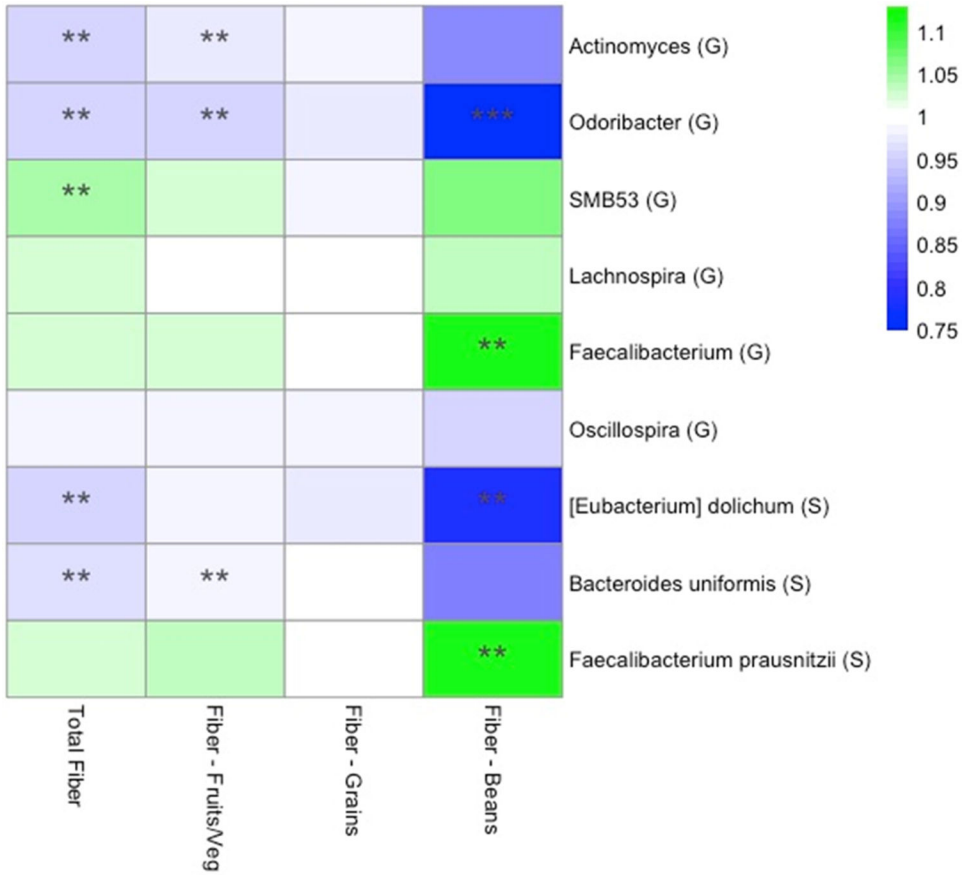

Figure 3.

Heat map representing color-coded fold changes of select genera (G) and species (S), by total fiber and fiber from specific sources. ** denotes $p<0.05$

Table 1.

Participant demographic characteristics

	NCI (n=75)					NYU (n=76)				
	Q1[a]	**Q2[a]**	**Q3[a]**	**Q4[a]**	**p-value**	**Q1[b]**	**Q2[b]**	**Q3[b]**	**Q4[b]**	**p-value**
N	19	19	18	19		19	19	19	19	
Age (median)	50	55	61.5	62	0.11	56	57	62	61	0.34
Sex, %					0.08					0.16
Female	31.6	21.1	50.0	57.9		36.8	36.8	52.6	68.4	
Male	68.4	78.9	50.0	42.1		63.2	63.2	47.4	31.6	
Race, %					0.46					0.10
White	89.5	89.5	77.8	73.7		94.7	89.5	89.5	68.4	
Non-White	10.5	10.5	22.2	26.3		5.3	10.5	10.5	31.6	
BMI (kg/m^2), %										
<25	57.9	68.4	33.3	68.4	0.19	36.8	63.2	57.9	63.2	0.29
25-30	36.8	15.8	38.9	21.1		42.1	31.6	26.3	36.8	
≥30	5.3	15.8	27.8	10.5		21.1	5.3	15.8	-	
Smoking History, %					0.10					0.13
Never	26.3	36.8	61.1	57.9		63.2	84.2	47.4	63.2	
Former/Current	73.7	63.2	38.9	42.1		36.8	15.8	52.6	36.8	

[a] NCI quartiles of fiber intake: Q1: < 11.25 g; Q2: 11.25-14.34 g; Q3: 14.35-16.68 g; Q4: ≥ 16.69 g

[b] NYU quartiles of fiber intake: Q1: < 19.82 g; Q2: 19.82-23.82 g; Q3: 23.83-31.63 g; Q4: ≥ 31.64 g

Table 2.

Meta-analysis of the association between total fiber intake and genera and species with concomitantly increasing or decreasing abundance in NCI and NYU study populations

Phylum; Class; Order; Family; Genus; Species	NCI				NYU				Meta FC	Meta 95% CI	Meta p
	Base Mean	FC	p-value	p-adj	Base Mean	FC	p-value	p-adj			
Genus Level											
Actinobacteria; Actinobacteria; Actinomycetales; Actinomycetaceae; Actinomyces	2.16	0.884	0.003	0.110	0.75	0.969	0.130	0.454	0.951	(0.917-0.986)	0.0015
Bacteroidetes; Bacteroidia; Bacteroidales; [Odoribacteraceae]; Odoribacter	0.68	0.995	0.916	0.967	10.88	0.946	0.004	0.176	0.953	(0.921-0.987)	0.0318
Firmicutes; Clostridia; Clostridiales; Clostridiaceae; SMB53	0.62	1.035	0.443	0.913	0.88	1.045	0.029	0.391	1.044	(1.007-1.082)	0.0360
Firmicutes; Clostridia; Clostridiales; Lachnospiraceae; Lachnospira	31.63	1.042	0.279	0.875	163.91	1.026	0.091	0.406	1.028	(1.000-1.057)	0.0497
Firmicutes; Clostridia; Clostridiales; Ruminococcaceae; Faecalibacterium	230.42	1.030	0.367	0.913	549.73	1.025	0.078	0.391	1.025	(1.000-1.051)	0.0589
Firmicutes; Clostridia; Clostridiales; Ruminococcaceae; Oscillospira	22.58	0.973	0.386	0.913	85.60	0.983	0.079	0.391	0.982	(0.965-1.000)	0.0630
Firmicutes; Bacilli; Lactobacillales; Streptococcaceae; Streptococcus	55.61	0.957	0.299	0.875	57.84	0.985	0.443	0.797	0.980	(0.947-1.015)	0.2023
Firmicutes; Clostridia; Clostridiales; Lachnospiraceae; Anaerostipes	5.92	1.007	0.859	0.967	10.66	1.018	0.287	0.641	1.016	(0.986-1.048)	0.3772
Firmicutes; Clostridia; Clostridiales; Lachnospiraceae; Dorea	104.47	1.022	0.418	0.913	65.24	1.004	0.666	0.797	1.006	(0.988-1.025)	0.3815
Firmicutes; Clostridia; Clostridiales; Veillonellaceae; Phascolarctobacterium	18.58	1.009	0.832	0.967	34.43	1.012	0.558	0.797	1.012	(0.975-1.049)	0.5709
Firmicutes; Clostridia; Clostridiales; Veillonellaceae; Dialister	16.99	0.984	0.713	0.967	25.15	0.994	0.780	0.869	0.992	(0.955-1.031)	0.6476
Proteobacteria; Betaproteobacteria; Burkholderiales; Alcaligenaceae; Sutterella	4.32	1.009	0.849	0.967	85.39	1.008	0.653	0.797	1.008	(0.976-1.040)	0.6502
Actinobacteria; Actinobacteria; Bifidobacteriales; Bifidobacteriaceae; Bifidobacterium	84.01	1.001	0.973	0.973	90.68	1.004	0.850	0.925	1.003	(0.967-1.041)	0.8745
Actinobacteria; Coriobacteriia; Coriobacteriales; Coriobacteriaceae; Eggerthella	6.18	0.985	NA	NA	2.09	0.990	0.631	0.797	0.989	(0.951-1.028)	NA
Species Level											
Firmicutes; Erysipelotrichi; Erysipelotrichales; Erysipelotrichaceae; [Eubacterium]; dolichum	7.70	0.933	0.198	0.770	3.34	0.963	0.122	0.540	0.958	(0.917-1.000)	0.045
Bacteroidetes; Bacteroidia; Bacteroidales; Bacteroidaceae; Bacteroides; uniformis	32.05	0.948	0.202	0.770	305.56	0.972	0.128	0.540	0.968	(0.936-1.001)	0.048
Firmicutes; Clostridia; Clostridiales; Ruminococcaceae; Faecalibacterium; prausnitzii	230.05	1.032	0.354	0.884	540.38	1.024	0.103	0.540	1.026	(0.999-1.053)	0.070
Firmicutes; Clostridia; Clostridiales; Ruminococcaceae; Ruminococcus; bromii	24.12	0.966	0.489	0.951	1.65	0.969	0.161	0.578	0.968	(0.930-1.008)	0.138
Firmicutes; Clostridia; Clostridiales; Lachnospiraceae; Dorea; formicigenerans	1.92	1.033	0.447	0.915	20.11	1.018	0.323	0.730	1.020	(0.988-1.054)	0.216
Bacteroidetes; Bacteroidia; Bacteroidales; Bacteroidaceae; Bacteroides; ovatus	5.59	0.987	0.790	0.951	12.37	0.982	0.309	0.730	0.982	(0.950-1.016)	0.363
Actinobacteria; Actinobacteria; Bifidobacteriales; Bifidobacteriaceae; Bifidobacterium; adolescentis	38.42	1.007	0.898	0.951	75.56	1.002	0.932	0.964	1.003	(0.959-1.049)	0.880

Phylum; Class; Order; Family; Genus; Species	NCI				NYU				Meta FC	Meta 95% CI	Meta p
	Base Mean	FC	p-value	p-adj	Base Mean	FC	p-value	p-adj			
Actinobacteria; Coriobacteriia; Coriobacteriales; Coriobacteriaceae; Eggerthella; lenta	6.14	0.984	NA	NA	1.99	0.986	0.613	0.839	0.986	(0.939-1.035)	NA

Relationship between higher quartiles of fiber intake and differential taxon abundance was evaluated using negative binomial generalized linear models in the DESeq2 package in R. Models were adjusted for age, sex, race, categorical BMI and cigarette smoking status. This table reports results from a taxonomy-based meta-analysis to evaluate for genera and species with concomitantly higher or lower abundance by fiber intake (as determined by fold change [FC]) in both study populations.