



**Figure S1. Volcano plots of the results from ANCOM.**

Each point represents one of 709 OTUs (A), 103 genera (B), or 55 families (C) detected in this study, which were present in at least 10% of samples. The x-axis is the normalized log-fold change in relative abundance of each taxon in persons with PD versus controls. The y-axis is the  $W$ -statistics from ANCOM. Briefly, for each of the  $n$  taxa, the mean abundance in cases vs. controls is compared to the data on the other  $n-1$  taxa using a t-test and Benjamini–Hochberg procedure to control for the FDR at 0.05, and the number of null of hypotheses rejected is denoted as  $W$  (which can range from 0 to  $n-1$  in this study). The threshold for significance,  $w_0$ , is calculated empirically;  $W$ 's that were greater than  $w_0$  are denoted as significant (red points). ANCOM does not assign a P-value for this last step, but P-values and FDR control are used to arrive at  $W$ . 13 OTUs (A), 8 genera (B), and 7 families (C) achieved significance, shown in red here, and named in **Table S2** and **Table 2**.

**Table S1. Sample sizes and distribution of variables that might be potential confounders.**

		PD	Control	Total		
	Number of subjects recruited	212	136	348		
	Sample size analyzed <sup>b</sup>	197	130	327		
1 <sup>a</sup>	Albany, NY	74	61	135		
	Atlanta, GA	31	12	43		
	Seattle, WA	92	57	149		
2 <sup>a</sup>	Spouses	54	54	108		
	Non-spouses	143	76	219		
COMPARING COVARIATES IN PD VS. CONTROLS		N with data	Result	N with data	Result	P <sup>c</sup>
3 <sup>a</sup>	Sex: Female; Male (% Male)	197	65; 132 (67.0%)	130	79; 51 (39.2%)	9E-7
4 <sup>a</sup>	Age: Min, Max, Median, Mean, SD	197	44, 94, 69, 68.4, 9.2	130	36, 88, 70.5, 70.3, 8.6	0.04
5 <sup>a</sup>	Days in Transit: Min, Max, Median, Mean, SD	188	1, 10, 3, 3.2, 1.9	126	1, 8, 2, 2.6, 1.5	1E-3
6 <sup>a</sup>	Body Mass Index: Min, Max, Median, Mean, SD	190	14.6, 45.6, 25.8, 26.4, 5.3	126	17.5, 45, 26.5, 28.3, 5.7	9E-3
7	Gained ≥10 pounds in Past Year: N (%)	194	25 (12.9%)	127	10 (7.9%)	0.20
8 <sup>a</sup>	Lost ≥10 pounds in Past Year: N (%)	193	44 (22.8%)	124	15 (12.1%)	0.02
9 <sup>a</sup>	Born by cesarean section: N (%)	185	11 (5.9%)	117	0 (0%)	8E-3
10	Crohn's Disease: N (%)	191	3 (1.6%)	129	1 (0.8%)	0.65
11	Inflammatory Bowel Disease: N (%)	191	5 (2.6%)	128	2 (1.6%)	0.71
12	Irritable Bowel Syndrome: N (%)	189	14 (7.4%)	128	8 (6.2%)	0.82
13	Colitis: N (%)	190	9 (4.7%)	128	2 (1.6%)	0.21
14	Ulcers: N (%)	190	17 (8.9%)	128	9 (7.0%)	0.68
15	Any of the above GI problems (Variables 10-14): N (%)	191	37 (19.4%)	129	19 (14.7%)	0.30
16 <sup>a</sup>	Gastrointestinal discomfort on day of collection: N (%)	181	104 (57.5%)	118	26 (22.0%)	2E-9
17 <sup>a</sup>	Constipation in past 3 months: N (%)	189	82 (43.4%)	128	6 (4.7%)	6E-16
18	Diarrhea in past 3 months: N (%)	187	30 (16.0%)	125	28 (22.4%)	0.18
19	Eats yogurt at least a few times a week: N (%)	189	67 (35.4%)	126	55 (43.7%)	0.16
20	Eats grains at least once a day: N (%)	190	132 (69.5%)	127	85 (66.9%)	0.71
21	Eats meat at least once a day: N (%)	191	109 (57.1%)	129	81 (62.8%)	0.35
22 <sup>a</sup>	Eats fruit or vegetables at least once a day: N (%)	192	150 (78.1%)	129	114 (88.4%)	0.02
23	Eats nuts at least once a day: N (%)	192	42 (21.9%)	128	36 (28.1%)	0.23
24	Currently smokes: N (%)	194	14 (7.2%)	129	5 (3.9%)	0.24
25	Currently drinks caffeinated coffee: N (%)	191	136 (71.2%)	129	98 (76.0%)	0.37
26 <sup>a</sup>	Currently drinks alcohol: N (%)	192	114 (59.4%)	129	92 (71.3%)	0.03
27 <sup>a</sup>	Currently taking digestive medication: N (%)	190	58 (31.1%)	124	21 (16.9%)	5E-3
28	Currently taking anti-inflammatory drugs: N (%)	188	76 (40.4%)	126	55 (43.7%)	0.64
29	Currently taking probiotics: N (%)	182	42 (23.1%)	126	32 (25.4%)	0.68
30	Currently taking antibiotics: N (%)	191	8 (4.2%)	128	3 (2.3%)	0.54
31	Completed antibiotics in past 3 months: N (%)	188	24 (12.8%)	128	21 (16.4%)	0.41
PD MEDICATION USED AT THE TIME OF STUDY						
32 <sup>a</sup>	Carbidopa/levodopa: N (%)	185	168 (90.8%)	-	-	-
33 <sup>a</sup>	Dopamine agonist: N (%)	185	99 (53.5%)	-	-	-
34 <sup>a</sup>	COMT inhibitor: N (%)	185	37 (20.0%)	-	-	-
35 <sup>a</sup>	MAO-B inhibitor: N (%)	185	71 (38.4%)	-	-	-
36 <sup>a</sup>	Anticholinergic: N (%)	185	7 (3.8%)	-	-	-
37 <sup>a</sup>	Amantadine: N (%)	185	49 (26.5%)	-	-	-
38	Un-medicated: N (%)	185	3 (1.6%)	-	-	-
39 <sup>a</sup>	Disease duration: Min, Max, Median, Mean, SD	197	1, 35, 14, 13.7, 6.5			

<sup>a</sup> 20 Variables considered as potential confounders.

<sup>b</sup> Excluded 2 samples with poor metadata, 6 with no called OTUs, 13 with <5000 sequences.

<sup>c</sup> To identify potential confounders, the difference between cases and controls was tested using the Mann-Whitney U test for quantitative variables (Days in transit, Age, BMI) and Fisher's Exact test for dichotomous variables. To be conservative, P values are uncorrected. Variables that differed between cases and controls at uncorrected P<0.1 were declared potential confounder.

Variable 1: Geographic site of data collection

Variable 2: Patients' spouses were asked to volunteer as controls.

Variable 3: Sex differential is due to the higher incidence of PD in men and the majority of spouse controls being women.

Variable 5: Date the laboratory received the sample minus the date stool was collected.

Variable 6: Subjects reported weight and height. BMI = Weight in pounds \* 703 / Height in inches<sup>2</sup>.

Variables 6-8: Weight change and BMI can vary by sex, and PD has a sex bias. To investigate effect of sex, we used logistic or linear regression in addition to Mann-Whitney U or Fisher's exact tests (which do not allow covariate adjustment) and included sex in the model. Results are similar whether sex is the model or not: there are significant differences between cases and controls in BMI and in loss of  $\geq 10$  pounds in past year. Variables 24 and 25: smoking and caffeine use prior to development of PD are inversely associated with the risk of developing the disease, (true in this sample as well). Here, with the effect on microbiome in mind, we asked at the time of study if they currently smoked or drank caffeinated coffee.

Sources of data: Data on variables 1-2 were collected by study staff. Data on variables 3-31 were reported by the subjects on the Gut Microbiome Questionnaire at the time of study. Data on variables 32-38 were retrieved from medical records by the neurologists and correspond to the medications that patient was prescribed for treatment of PD at the time of this study (stool collection). Data on variable 39 were collected by investigators using study records, measured as age at stool collection minus age at onset of PD.

**Table S2. Taxa with significant evidence for association with PD.** The list includes taxa that reached significance using ANCOM or Kruskal-Wallis. A) OTUs significant from ANCOM (13 OTUs) or Kruskal-Wallis (100 OTUs). B) Genera significant from ANCOM (8 genera) or Kruskal-Wallis (48 genera). C) Families significant from ANCOM (7 families) or Kruskal-Wallis (19 families). All taxa from ANCOM are represented in and are among the most significant in KW at each taxonomic level.

A) OTU Kingdom;Phylum;Class;Order;Family;Genus;Species	Taxon ID	Mean Abundance		Abundance ratio Case/Control	ANCOM W	KW FDR_P
		Cases	Controls			
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Blautia;unclassified</i>	4465907	0.0051	0.0084	0.61	700	6E-06
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;unclassified;unclassified</i>	4457438	0.0149	0.0275	0.54	695	2E-03
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Faecalibacterium;prausnitzii</i>	4381430	0.0059	0.0125	0.47	688	4E-03
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Roseburia;unclassified</i>	4481427	0.0020	0.0044	0.45	688	2E-04
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Faecalibacterium;prausnitzii</i>	4481131	0.0155	0.0241	0.64	685	4E-03
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Roseburia;faecis</i>	4392188	0.0031	0.0060	0.53	682	8E-04
<i>Bacteria;Actinobacteria;Actinobacteria;Bifidobacteriales;Bifidobacteriaceae;Bifidobacterium;adolescentis</i>	4347159	0.0119	0.0071	1.66	672	3E-03
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;unclassified;unclassified</i>	180999	0.0005	0.0013	0.39	667	2E-04
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;unclassified;unclassified</i>	4325096	0.0008	0.0023	0.37	664	2E-03
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Coproccoccus;unclassified</i>	173969	0.0011	0.0024	0.44	656	8E-04
<i>Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Porphyromonadaceae;Parabacteroides;distasonis</i>	4365130	0.0203	0.0145	1.40	650	4E-02
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;unclassified;unclassified</i>	4439469	0.0047	0.0023	1.99	644	4E-03
<i>Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Prevotellaceae;Prevotella;unclassified</i>	1077373	0.0029	0.0004	7.29	631	5E-03
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;unclassified;unclassified</i>	4416570	0.0021	0.0037	0.57	not sig	1E-02
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;unclassified;unclassified</i>	4443172	0.0032	0.0055	0.57	not sig	1E-02
<i>Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Porphyromonadaceae;Porphyromonas;unclassified</i>	495451	0.0012	0.0002	7.43	not sig	7E-04
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Coproccoccus;unclassified</i>	4478815	0.0024	0.0034	0.68	not sig	6E-03
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;unclassified;unclassified</i>	174818	0.0005	0.0009	0.53	not sig	8E-04
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Clostridiaceae;Clostridium;unclassified</i>	3931537	0.0007	0.0012	0.60	not sig	4E-03
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;unclassified;unclassified</i>	176306	0.0010	0.0018	0.58	not sig	7E-03
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;unclassified;unclassified</i>	174840	0.0004	0.0007	0.51	not sig	3E-03
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;[Tissierellaceae];WAL_1855D;unclassified</i>	505670	0.0057	0.0017	3.43	not sig	5E-02
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;unclassified;unclassified</i>	4473509	0.0004	0.0009	0.38	not sig	9E-04
<i>Bacteria;Firmicutes;Erysipelotrichi;Erysipelotrichales;Erysipelotrichaceae;Coproccoccus;unclassified</i>	587933	0.0017	0.0001	12.55	not sig	6E-03
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;unclassified;unclassified</i>	4414476	0.0016	0.0016	1.01	not sig	7E-03
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Oscillospira;unclassified</i>	180468	0.0004	0.0008	0.57	not sig	4E-03
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;unclassified;unclassified</i>	183650	0.0008	0.0001	7.05	not sig	2E-02
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;unclassified;unclassified;unclassified</i>	4469007	0.0007	0.0018	0.39	not sig	3E-02
<i>Bacteria;Actinobacteria;Actinobacteria;Bifidobacteriales;Bifidobacteriaceae;Bifidobacterium;unclassified</i>	4335781	0.0004	0.0000	10.89	not sig	3E-03
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Blautia;unclassified</i>	4352657	0.0016	0.0025	0.61	not sig	2E-02
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;unclassified;unclassified</i>	4396297	0.0001	0.0003	0.32	not sig	4E-03
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Ruminococcus;unclassified</i>	4427459	0.0015	0.0005	3.05	not sig	4E-02
<i>Bacteria;Actinobacteria;Actinobacteria;Actinomycetales;Corynebacteriaceae;Corynebacterium;unclassified</i>	4364814	0.0018	0.0009	1.91	not sig	5E-03
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Blautia;unclassified</i>	4359797	0.0002	0.0004	0.48	not sig	4E-03
<i>Archaea;Euryarchaeota;Methanobacteria;Methanobacteriales;Methanobacteriaceae;Methanobrevibacter;unclassified</i>	849440	0.0006	0.0004	1.41	not sig	2E-02
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;unclassified;unclassified;unclassified</i>	4371061	0.0006	0.0008	0.69	not sig	1E-02
<i>Bacteria;Firmicutes;Bacilli;Lactobacillales;Lactobacillaceae;Lactobacillus;unclassified</i>	4428313	0.0004	0.0000	16.08	not sig	4E-03
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Oscillospira;unclassified</i>	4366089	0.0005	0.0000	12.52	not sig	4E-03
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;unclassified;unclassified</i>	4217963	0.0003	0.0005	0.54	not sig	5E-03
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;unclassified;unclassified</i>	195651	0.0001	0.0003	0.44	not sig	3E-03
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Ruminococcus;unclassified</i>	2979308	0.0011	0.0005	2.12	not sig	3E-02
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;unclassified;unclassified</i>	4331360	0.0002	0.0005	0.50	not sig	1E-02

<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;unclassified;unclassified</i>	179826	0.0006	0.0008	0.79	<i>not sig</i>	6E-03
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;unclassified;unclassified</i>	4473788	0.0001	0.0005	0.30	<i>not sig</i>	4E-03
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;unclassified;unclassified</i>	4472399	0.0008	0.0012	0.68	<i>not sig</i>	2E-02
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;unclassified;unclassified;unclassified</i>	338301	0.0001	0.0003	0.26	<i>not sig</i>	6E-03
<i>Bacteria;Proteobacteria;Gammaproteobacteria;Pasteurellales;Pasteurellaceae;Haemophilus;parainfluenzae</i>	4477696	0.0003	0.0012	0.22	<i>not sig</i>	3E-02
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;unclassified;unclassified;unclassified</i>	4385326	0.0002	0.0004	0.47	<i>not sig</i>	8E-03
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;unclassified;unclassified</i>	182044	0.0004	0.0001	3.76	<i>not sig</i>	2E-02
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;unclassified;unclassified</i>	730906	0.0003	0.0005	0.68	<i>not sig</i>	4E-03
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;unclassified;unclassified</i>	4448492	0.0002	0.0005	0.45	<i>not sig</i>	3E-02
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Roseburia;unclassified</i>	2438203	0.0001	0.0003	0.46	<i>not sig</i>	6E-03
<i>Bacteria;Proteobacteria;Deltaproteobacteria;Desulfovibrionales;Desulfovibrionaceae;Bilophila;unclassified</i>	354574	0.0006	0.0001	10.01	<i>not sig</i>	5E-02
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;unclassified;unclassified</i>	195556	0.0001	0.0002	0.44	<i>not sig</i>	5E-03
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Blautia;unclassified</i>	180414	0.0002	0.0004	0.48	<i>not sig</i>	3E-02
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;unclassified;unclassified</i>	192983	0.0001	0.0002	0.47	<i>not sig</i>	4E-03
<i>Bacteria;Firmicutes;Erysipelotrichi;Erysipelotrichales;Erysipelotrichaceae;[Eubacterium];dolichum</i>	548587	0.0006	0.0003	2.26	<i>not sig</i>	1E-02
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;[Mogibacteriaceae];unclassified;unclassified</i>	3805726	0.0002	0.0001	4.34	<i>not sig</i>	4E-03
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;unclassified;unclassified</i>	4438999	0.0007	0.0000	14.49	<i>not sig</i>	4E-02
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Ruminococcus;unclassified</i>	194297	0.0003	0.0008	0.32	<i>not sig</i>	3E-02
<i>Bacteria;Firmicutes;Erysipelotrichi;Erysipelotrichales;Erysipelotrichaceae;[Eubacterium];dolichum</i>	539581	0.0010	0.0003	3.76	<i>not sig</i>	4E-02
<i>Bacteria;Actinobacteria;Actinobacteria;Bifidobacteriales;Bifidobacteriaceae;Bifidobacterium;unclassified</i>	4376828	0.0004	0.0002	2.22	<i>not sig</i>	3E-02
<i>Bacteria;Proteobacteria;Gammaproteobacteria;Pseudomonadales;Pseudomonadaceae;Pseudomonas;fragi</i>	1071450	0.0043	0.0096	0.45	<i>not sig</i>	1E-02
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;unclassified;unclassified;unclassified</i>	178712	0.0005	0.0001	5.24	<i>not sig</i>	4E-02
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;unclassified;unclassified;unclassified</i>	192015	0.0000	0.0002	0.26	<i>not sig</i>	8E-04
<i>Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Porphyromonadaceae;Porphyromonas;unclassified</i>	138179	0.0010	0.0004	2.72	<i>not sig</i>	3E-02
<i>Bacteria;Firmicutes;Bacilli;Lactobacillales;Streptococcaceae;Streptococcus;unclassified</i>	4315958	0.0001	0.0000	8.80	<i>not sig</i>	4E-03
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;unclassified;unclassified;unclassified</i>	179785	0.0000	0.0002	0.25	<i>not sig</i>	4E-03
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;unclassified;unclassified</i>	193863	0.0001	0.0002	0.59	<i>not sig</i>	4E-03
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;unclassified;unclassified;unclassified</i>	360890	0.0006	0.0003	1.85	<i>not sig</i>	2E-02
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Coproccoccus;unclassified</i>	178686	0.0003	0.0004	0.67	<i>not sig</i>	2E-02
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;unclassified;unclassified</i>	190226	0.0003	0.0001	2.70	<i>not sig</i>	2E-02
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;[Tissierellaceae];Anaerococcus;unclassified</i>	4476950	0.0005	0.0001	3.97	<i>not sig</i>	4E-02
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;unclassified;unclassified;unclassified</i>	182073	0.0001	0.0004	0.39	<i>not sig</i>	4E-02
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;[Tissierellaceae];Peptoniphilus;unclassified</i>	4429335	0.0010	0.0002	4.98	<i>not sig</i>	4E-02
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;unclassified;unclassified</i>	48084	0.0035	0.0039	0.88	<i>not sig</i>	4E-02
<i>Bacteria;Firmicutes;Erysipelotrichi;Erysipelotrichales;Erysipelotrichaceae;Coproccoccus;unclassified</i>	151870	0.0002	0.0001	2.69	<i>not sig</i>	3E-02
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Faecalibacterium;prausnitzii</i>	181422	0.0001	0.0003	0.41	<i>not sig</i>	3E-02
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;unclassified;unclassified</i>	193709	0.0003	0.0004	0.77	<i>not sig</i>	3E-02
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;[Tissierellaceae];Peptoniphilus;unclassified</i>	1100471	0.0003	0.0001	5.77	<i>not sig</i>	5E-02
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;unclassified;unclassified</i>	175145	0.0001	0.0002	0.56	<i>not sig</i>	5E-02
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;EtOH8;unclassified;unclassified</i>	4311620	0.0001	0.0000	4.87	<i>not sig</i>	8E-03
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;unclassified;unclassified</i>	183698	0.0001	0.0002	0.61	<i>not sig</i>	2E-02
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;unclassified;unclassified;unclassified</i>	188127	0.0000	0.0001	0.45	<i>not sig</i>	4E-03
<i>Bacteria;Actinobacteria;Actinobacteria;Actinomycetales;Actinomycetaceae;Mobiluncus;unclassified</i>	104135	0.0001	0.0000	6.90	<i>not sig</i>	3E-02
<i>Bacteria;Actinobacteria;Actinobacteria;Bifidobacteriales;Bifidobacteriaceae;Bifidobacterium;adolescentis</i>	584375	0.0001	0.0000	2.64	<i>not sig</i>	4E-02
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Roseburia;unclassified</i>	162623	0.0001	0.0001	0.44	<i>not sig</i>	4E-02
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;unclassified;unclassified</i>	4094259	0.0001	0.0001	0.52	<i>not sig</i>	2E-02
<i>Bacteria;Proteobacteria;Gammaproteobacteria;Enterobacteriales;Enterobacteriaceae;Proteus;unclassified</i>	4385479	0.0054	0.0042	1.30	<i>not sig</i>	5E-03
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;unclassified;unclassified</i>	177581	0.0001	0.0001	0.50	<i>not sig</i>	5E-02
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;unclassified;unclassified;unclassified</i>	359762	0.0001	0.0002	0.49	<i>not sig</i>	2E-02

<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Christensenellaceae;unclassified;unclassified</i>	231952	0.0000	0.0000	2.59	<i>not sig</i>	4E-02
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;unclassified;unclassified;unclassified</i>	190864	0.0000	0.0001	0.34	<i>not sig</i>	3E-02
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;unclassified;unclassified</i>	2835813	0.0002	0.0001	1.27	<i>not sig</i>	5E-02
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Faecalibacterium;prausnitzii</i>	4476527	0.0000	0.0001	0.33	<i>not sig</i>	2E-02
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Blautia;unclassified</i>	184561	0.0000	0.0001	0.48	<i>not sig</i>	2E-02
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Blautia;unclassified</i>	181756	0.0001	0.0001	0.58	<i>not sig</i>	3E-02
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;unclassified;unclassified</i>	564320	0.0001	0.0000	1.91	<i>not sig</i>	4E-02
<i>Bacteria;Proteobacteria;Gammaproteobacteria;Enterobacteriales;Enterobacteriaceae;Serratia;unclassified</i>	4328189	0.0022	0.0002	10.63	<i>not sig</i>	5E-02
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;unclassified;unclassified;unclassified</i>	182196	0.0000	0.0001	0.27	<i>not sig</i>	3E-02

B) Genus Kingdom;Phylum;Class;Order;Family;Genus	Mean Abundance		Abundance ratio	ANCOM	KW
	Cases	Controls	Case/Control	W	FDR_P
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Roseburia</i>	0.0065	0.0125	0.52	101	8E-07
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Faecalibacterium</i>	0.0317	0.0480	0.66	91	9E-04
<i>Bacteria;Actinobacteria;Actinobacteria;Bifidobacteriales;Bifidobacteriaceae;Bifidobacterium</i>	0.0140	0.0076	1.85	90	6E-05
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;unclassified</i>	0.0487	0.0725	0.67	90	1E-04
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Blautia</i>	0.0140	0.0194	0.72	90	6E-04
<i>Bacteria;Firmicutes;Bacilli;Lactobacillales;Lactobacillaceae;Lactobacillus</i>	0.0026	0.0004	7.27	89	5E-06
<i>Bacteria;Verrucomicrobia;Verrucomicrobiae;Verrucomicrobiales;Verrucomicrobiaceae;Akkermansia</i>	0.0485	0.0185	2.63	86	1E-03
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Christensenellaceae;unclassified</i>	0.0073	0.0020	3.63	84	6E-04
<i>Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Porphyromonadaceae;Porphyromonas</i>	0.0033	0.0008	4.33	<i>not sig</i>	5E-04
<i>Bacteria;Firmicutes;Erysipelotrichi;Erysipelotrichales;Erysipelotrichaceae;unclassified</i>	0.0025	0.0040	0.63	<i>not sig</i>	5E-03
<i>Bacteria;Firmicutes;Erysipelotrichi;Erysipelotrichales;Erysipelotrichaceae;[Eubacterium]</i>	0.0043	0.0020	2.21	<i>not sig</i>	6E-04
<i>Bacteria;Proteobacteria;Gammaproteobacteria;Pasteurellales;Pasteurellaceae;Haemophilus</i>	0.0003	0.0012	0.21	<i>not sig</i>	3E-03
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Peptococcaceae;rc4-4</i>	0.0001	0.0003	0.34	<i>not sig</i>	2E-03
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Anaerostipes</i>	0.0008	0.0014	0.60	<i>not sig</i>	1E-02
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Lachnospira</i>	0.0044	0.0052	0.84	<i>not sig</i>	2E-02
<i>Bacteria;Actinobacteria;Actinobacteria;Actinomycetales;Corynebacteriaceae;Corynebacterium</i>	0.0027	0.0012	2.34	<i>not sig</i>	2E-03
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Coprococcus</i>	0.0124	0.0144	0.86	<i>not sig</i>	1E-02
<i>Bacteria;Firmicutes;Erysipelotrichi;Erysipelotrichales;Erysipelotrichaceae;Coproccillus</i>	0.0020	0.0005	4.48	<i>not sig</i>	1E-03
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Veillonellaceae;Megasphaera</i>	0.0046	0.0012	3.74	<i>not sig</i>	1E-03
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;[Tissierellaceae];WAL_1855D</i>	0.0053	0.0015	3.47	<i>not sig</i>	5E-03
<i>Bacteria;Proteobacteria;Deltaproteobacteria;Desulfovibrionales;Desulfovibrionaceae;Bilophila</i>	0.0038	0.0025	1.49	<i>not sig</i>	6E-03
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;[Tissierellaceae];Anaerococcus</i>	0.0015	0.0004	3.79	<i>not sig</i>	2E-03
<i>Archaea;Euryarchaeota;Methanobacteria;Methanobacteriales;Methanobacteriaceae;Methanobrevibacter</i>	0.0005	0.0004	1.32	<i>not sig</i>	2E-03
<i>Bacteria;Actinobacteria;Coriobacteriia;Coriobacteriales;Coriobacteriaceae;unclassified</i>	0.0006	0.0003	1.94	<i>not sig</i>	1E-03
<i>Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Bacteroidaceae;Bacteroides</i>	0.2467	0.2810	0.88	<i>not sig</i>	8E-03
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Clostridiaceae;Sarcina</i>	0.0001	0.0001	0.85	<i>not sig</i>	2E-02
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Anaerotruncus</i>	0.0007	0.0003	2.65	<i>not sig</i>	1E-02
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Veillonellaceae;Phascolarctobacterium</i>	0.0047	0.0068	0.69	<i>not sig</i>	4E-02
<i>Bacteria;Proteobacteria;Deltaproteobacteria;Desulfovibrionales;Desulfovibrionaceae;Desulfovibrio</i>	0.0013	0.0012	1.11	<i>not sig</i>	6E-03
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;[Mogibacteriaceae];unclassified</i>	0.0010	0.0006	1.71	<i>not sig</i>	8E-03
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;[Tissierellaceae];Peptoniphilus</i>	0.0024	0.0009	2.86	<i>not sig</i>	5E-03
<i>Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Porphyromonadaceae;Parabacteroides</i>	0.0407	0.0300	1.36	<i>not sig</i>	8E-03
<i>Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Rikenellaceae;Alistipes</i>	0.0013	0.0005	2.74	<i>not sig</i>	7E-03
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;[Tissierellaceae];1-68</i>	0.0016	0.0007	2.36	<i>not sig</i>	1E-02
<i>Bacteria;Synergistetes;Synergistia;Synergistales;Synergistaceae;Cloacibacillus</i>	0.0006	0.0000	15.89	<i>not sig</i>	1E-02
<i>Bacteria;Actinobacteria;Coriobacteriia;Coriobacteriales;Coriobacteriaceae;Adlercreutzia</i>	0.0001	0.0001	1.98	<i>not sig</i>	4E-02
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;[Tissierellaceae];ph2</i>	0.0003	0.0001	3.81	<i>not sig</i>	3E-03

<i>Bacteria;Firmicutes;Clostridia;Clostridiales;EtOH8;unclassified</i>	0.0001	0.0000	4.56	<i>not sig</i>	1E-03
<i>Bacteria;Actinobacteria;Actinobacteria;Actinomycetales;Actinomycetaceae;Mobiluncus</i>	0.0001	0.0000	6.75	<i>not sig</i>	4E-03
<i>Bacteria;Actinobacteria;Actinobacteria;Actinomycetales;Actinomycetaceae;Varibaculum</i>	0.0005	0.0001	4.00	<i>not sig</i>	3E-02
<i>Bacteria;Firmicutes;Bacilli;Bacillales;Staphylococcaceae;Staphylococcus</i>	0.0001	0.0000	2.53	<i>not sig</i>	2E-02
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;[Mogibacteriaceae];Mogibacterium</i>	0.0001	0.0000	6.49	<i>not sig</i>	7E-03
<i>Bacteria;Proteobacteria;Epsilonproteobacteria;Campylobacteriales;Campylobacteraceae;Campylobacter</i>	0.0007	0.0002	3.55	<i>not sig</i>	4E-02
<i>Bacteria;Lentisphaerae;[Lentisphaeria];Victivallales;Victivallaceae;unclassified</i>	0.0004	0.0002	2.36	<i>not sig</i>	4E-02
<i>Bacteria;Proteobacteria;Gammaproteobacteria;Enterobacteriales;Enterobacteriaceae;Proteus</i>	0.0049	0.0041	1.21	<i>not sig</i>	9E-04
<i>Bacteria;Proteobacteria;Gammaproteobacteria;Pseudomonadales;Pseudomonadaceae;Pseudomonas</i>	0.0105	0.0119	0.88	<i>not sig</i>	3E-02
<i>Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;[Odoribacteraceae];Butyricimonas</i>	0.0020	0.0015	1.32	<i>not sig</i>	4E-02
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Veillonellaceae;Acidaminococcus</i>	0.0037	0.0020	1.85	<i>not sig</i>	4E-02

<b>C) Family</b>	<b>Mean Abundance</b>		<b>Abundance ratio</b>	<b>ANCOM</b>	<b>KW</b>
<b>Kingdom;Phylum;Class;Order;Family</b>	<b>Cases</b>	<b>Controls</b>	<b>Case/Control</b>	<b>W</b>	<b>FDR_P</b>
<i>Bacteria;Actinobacteria;Actinobacteria;Bifidobacteriales;Bifidobacteriaceae</i>	0.0140	0.0076	1.85	46	5E-05
<i>Bacteria;Firmicutes;Bacilli;Lactobacillales;Lactobacillaceae</i>	0.0029	0.0004	7.24	46	5E-05
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Christensenellaceae</i>	0.0073	0.0020	3.62	46	1E-03
<i>Bacteria;Verrucomicrobia;Verrucomicrobiae;Verrucomicrobiales;Verrucomicrobiaceae</i>	0.0481	0.0184	2.61	46	3E-03
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae</i>	0.1099	0.1447	0.76	39	2E-03
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;[Tissierellaceae]</i>	0.0122	0.0040	3.08	38	8E-03
<i>Bacteria;Proteobacteria;Gammaproteobacteria;Pasteurellales;Pasteurellaceae</i>	0.0003	0.0012	0.21	37	8E-03
<i>Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Porphyromonadaceae</i>	0.0437	0.0305	1.44	<i>not sig</i>	2E-03
<i>Bacteria;Proteobacteria;Deltaproteobacteria;Desulfovibrionales;Desulfovibrionaceae</i>	0.0052	0.0038	1.38	<i>not sig</i>	3E-03
<i>Bacteria;Actinobacteria;Actinobacteria;Actinomycetales;Corynebacteriaceae</i>	0.0027	0.0012	2.30	<i>not sig</i>	3E-03
<i>Bacteria;Synergistetes;Synergistia;Synergistales;Synergistaceae</i>	0.0008	0.0001	10.31	<i>not sig</i>	3E-03
<i>Archaea;Euryarchaeota;Methanobacteria;Methanobacteriales;Methanobacteriaceae</i>	0.0006	0.0004	1.36	<i>not sig</i>	4E-03
<i>Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Bacteroidaceae</i>	0.2441	0.2789	0.88	<i>not sig</i>	2E-02
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;[Mogibacteriaceae]</i>	0.0011	0.0006	1.89	<i>not sig</i>	2E-02
<i>Bacteria;Actinobacteria;Coriobacteriia;Coriobacteriales;Coriobacteriaceae</i>	0.0019	0.0013	1.43	<i>not sig</i>	1E-02
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;EtOH8</i>	0.0001	0.0000	4.62	<i>not sig</i>	3E-03
<i>Bacteria;Firmicutes;Bacilli;Bacillales;Staphylococcaceae</i>	0.0001	0.0000	2.77	<i>not sig</i>	4E-02
<i>Bacteria;Firmicutes;Clostridia;Clostridiales;Eubacteriaceae</i>	0.0001	0.0000	3.51	<i>not sig</i>	4E-02
<i>Bacteria;Lentisphaerae;[Lentisphaeria];Victivallales;Victivallaceae</i>	0.0004	0.0002	2.56	<i>not sig</i>	4E-02

Table S3. Replication of statistically significant findings of prior studies.

Phylum	Class	Order	Family	Genus	Species	Other grouping	A	B	C	D	E
							Scheperjans et al. (2014)	Keshavarzian et al. (2015)	Hasegawa et al. (2015)	Unger et al. (2016)	Present study
							N=72, 72 Finland	N=38, 34 U.S.	N=45, 35 Japan	N=34, 34 Germany	N=197, 130 U.S.
<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Prevotellaceae</i>				Decreased	NS	NR	NS	NS
<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Lachnospiraceae</i>	<i>Blautia</i>			NR	Decreased	NR	NR	Decreased P=0.01 P=0.52 <sup>a</sup>
<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Lachnospiraceae</i>	<i>Coprococcus</i>			NR	Decreased	NR	NR	IC
<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Lachnospiraceae</i>	<i>Dorea</i>			NR	Decreased	NR	NR	NS
<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Lachnospiraceae</i>	<i>Roseburia</i>			NR	Decreased	NR	NR	Decreased P=5E-4
<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Lachnospiraceae</i>				NR	Decreased	NR	NR	Decreased P=3E-3
<i>Firmicutes</i>	<i>Erysipelotrichi</i>	<i>Erysipelotrichales</i>	[ <i>Coprobacillaceae</i> ]				NR	Decreased	NR	NR	NC
<i>Firmicutes</i>							NR	Decreased	NR	NS	NS
<i>Bacteroidetes</i>							NR	Increased	NR	Decreased	NS
<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Bacteroidaceae</i>	<i>Bacteroides</i>			NR	Increased	NR	NR	NS
<i>Bacteroidetes</i>	<i>Bacteroidia</i>	<i>Bacteroidales</i>	<i>Bacteroidaceae</i>				NR	Increased	NR	NR	NS
<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Clostridiaceae</i>				NR	Increased	NR	NR	NS
<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Ruminococcaceae</i>	<i>Oscillospira</i>			NR	Increased	NR	NR	NS
<i>Proteobacteria</i>							NR	Increased	NR	NR	NS
<i>Verrucomicrobia</i>	<i>Verrucomicrobiae</i>	<i>Verrucomicrobiales</i>	<i>Verrucomicrobiaceae</i>	<i>Akkermansia</i>			NR	Increased	NR	NR	Increased P=1E-4
						<i>C. coccoides</i> group	NR	NR	Decreased	NR	NC
						<i>C. leptum</i> group	NR	NR	Decreased	NR	NC
						<i>B. fragilis</i> group	NR	NR	Decreased	NR	NC
<i>Firmicutes</i>	<i>Bacilli</i>	<i>Lactobacillales</i>	<i>Lactobacillaceae</i>	<i>Lactobacillus</i>			NR	NR	Increased	NR	Increased P=4E-8
<i>Firmicutes</i>	<i>Clostridia</i>	<i>Clostridiales</i>	<i>Ruminococcaceae</i>	<i>Faecalibacterium prausnitzii</i>			NR	NR	NR	Decreased	Decreased P=6E-3 P=0.05 <sup>a</sup>
						<i>Lactobacillaceae</i> + <i>Enterococcaceae</i>	NR	NR	NR	Decreased	NS
<i>Actinobacteria</i>	<i>Actinobacteria</i>	<i>Bifidobacteriales</i>	<i>Bifidobacteriaceae</i>	<i>Bifidobacterium</i>			NR	NS	NS	Increased	Increased P=3E-6
<i>Proteobacteria</i>	<i>Gammaproteobacteria</i>	<i>Enterobacteriales</i>	<i>Enterobacteriaceae</i>				NR	NS	NS	Increased	NS

Only findings that achieved statistical significance in the original papers were included here. We did not include non-significant trends and descriptive associations (even if they were highlighted in the article Abstracts as a major finding) because they were selectively reported by only some authors and were not based on a set criterion that we could apply across studies.

Decreased or Increased: statistically significant decreased or increased abundance in PD vs. control samples.

N=number of cases and controls analyzed

NR: Not reported.

NS: Not significant. For prior reports, we deferred to their definition of statistical significance. For present study, NS represents not significant by Kruskal-Wallis and by ANCOM.

NC: Not called

IC: Inconclusive. An OTU belonging to genus *Coprococcus* was significantly decreased in PD (abundance=0.001 in cases, 0.002 in controls, see **Table 2**); when collapsed to the genus level per prior study, the reduced abundance in patients (0.012 in cases, 0.014 in controls) was significant by Kruskal-Wallis (P=0.01), but not by ANCOM or GLM.

<sup>a</sup> The second P value reflects the drug effect, testing 141 cases not on COMT inhibitor or anticholinergic drugs vs. 130 controls.