

TABLE S1 Demographic and clinical characteristics of patients included in the study

Sample code	Race/Sub-race	Country/Region	Sex	Age (years)	Proton pump inhibitor (PPI) status	<i>Helicobacter pylori</i> status	Histopathological findings
S01	Caucasian/Mediterranean	Italy/Lazio	M	46	No treatment	Negative	Mild inflammation
S02	Caucasian/Mediterranean	Italy/Lazio	F	65	No treatment	Positive	Moderate inflammation
S03	Caucasian/Mediterranean	Italy/Lazio	F	43	No treatment	Negative	Mild inflammation
S04	Caucasian/Mediterranean	Italy/Lazio	F	54	No treatment	Positive	Severe inflammation, intestinal metaplasia
S05	Caucasian/Mediterranean	Italy/Lazio	F	36	No treatment	Positive	Moderate inflammation
S06	Caucasian/Mediterranean	Italy/Lazio	M	41	No treatment	Positive	Moderate inflammation
S07	Caucasian/Mediterranean	Italy/Lazio	F	54	No treatment	Negative	Mild inflammation
S08	Caucasian/Mediterranean	Italy/Lazio	F	43	No treatment	Positive	Moderate inflammation
S09	Caucasian/Mediterranean	Italy/Lazio	M	40	No treatment	Negative	Mild inflammation
S10	Caucasian/Mediterranean	Italy/Lazio	F	44	No treatment	Negative	Mild inflammation
S11	Caucasian/Mediterranean	Italy/Lazio	M	27	No treatment	Negative	Mild inflammation
S12	Caucasian/Mediterranean	Italy/Lazio	F	43	No treatment	Negative	Moderate inflammation
PPI01	Caucasian/Mediterranean	Italy/Lazio	M	83	With treatment	Negative	Moderate inflammation
PPI02	Caucasian/Mediterranean	Italy/Lazio	F	47	With treatment	Negative	Moderate inflammation
PPI03	Caucasian/Mediterranean	Italy/Lazio	F	47	With treatment	Positive	Moderate inflammation
PPI04	Caucasian/Mediterranean	Italy/Lazio	F	54	With treatment	Negative	Moderate inflammation
PPI05	Caucasian/Mediterranean	Italy/Lazio	M	61	With treatment	Negative	Mild inflammation
PPI06	Caucasian/Mediterranean	Italy/Lazio	F	66	With treatment	Negative	Mild inflammation
PPI07	Caucasian/Mediterranean	Italy/Lazio	F	68	With treatment	Positive	Moderate inflammation, intestinal metaplasia, atrophy
PPI08	Caucasian/Mediterranean	Italy/Lazio	F	44	With treatment	Negative	Mild inflammation, gastric gland polyps
PPI09	Caucasian/Mediterranean	Italy/Lazio	F	40	With treatment	Negative	Moderate inflammation, intestinal metaplasia
PPI10	Caucasian/Mediterranean	Italy/Lazio	M	35	With treatment	Positive	Moderate inflammation
PPI11	Caucasian/Mediterranean	Italy/Lazio	F	85	With treatment	Negative	Mild inflammation, intestinal metaplasia, atrophy
PPI12	Caucasian/Mediterranean	Italy/Lazio	F	42	With treatment	Positive	Moderate inflammation

TABLE S2 Operational taxonomic units (OTUs) and coverage for the sequences obtained from gastric mucosal biopsy samples of 24 patients

Sample code	No. of OTUs		Coverage ^c
	Observed ^a	Estimated ^b	
PPI01	185	186	0.9997
PPI02	78	80	0.9987
PPI03	133	140	0.9973
PPI04	164	170	0.9976
PPI05	114	122	0.9981
PPI06	125	143	0.9958
PPI07	129	152	0.9989
PPI08	140	163	0.9967
PPI09	98	113	0.9969
PPI10	100	113	0.9898
PPI11	117	124	0.9982
PPI12	51	59	0.9849
S01	104	123	0.9938
S02	82	86	0.9988
S03	122	134	0.9931
S04	79	89	0.9960
S05	69	78	0.9968
S06	154	160	0.9996
S07	129	140	0.9914
S08	41	74	0.9979
S09	107	134	0.9882
S10	151	160	0.9966
S11	76	83	0.9898
S12	172	199	0.9969

^a Calculated with UCLUST at a default sequence similarity level of 97%.

^b Calculated with the Chao1 estimator of species richness.

^c Calculated with the formula $[1 - (n/N)]$, where n is the number of singleton OTUs and N is the number of sequences in that sample.

TABLE S3 Percentages of bacterial phyla found in the gastric mucosal biopsies from two groups of patients with dyspepsia

	Actinobacteria	Bacteroidetes	Firmicutes	Fusobacteria	Proteobacteria	Other
PPI01	0.71	28.65	37.06	4.48	28.02	1.07
PPI02	1.11	37.81	30.58	18.30	12.00	0.20
PPI03	0.35	18.65	33.45	6.40	39.05	2.10
PPI04	5.14	24.36	38.58	4.51	23.24	4.17
PPI05	2.53	31.20	52.19	4.02	8.79	1.27
PPI06	1.49	21.95	64.92	2.81	6.71	2.12
PPI07	0.24	2.68	48.11	0.14	48.57	0.25
PPI08	0.33	34.31	15.03	12.17	37.35	0.82
PPI09	1.62	54.69	24.70	3.45	13.82	1.73
PPI10	5.33	23.88	48.39	8.65	12.21	1.54
PPI11	1.51	44.74	35.68	3.93	12.93	1.21
PPI12	0.80	41.40	39.68	2.29	14.68	1.15
Average	1.76	30.36	39.03	5.93	21.45	1.47
S01	0.44	56.85	24.88	5.80	8.83	3.19
S02	0.86	15.82	33.82	39.56	7.59	2.35
S03	3.79	60.05	25.30	6.52	3.56	0.79
S04	0.36	14.79	16.00	0.95	67.21	0.69
S05	0.34	5.89	6.23	3.16	84.20	0.18
S06	1.97	18.04	18.77	3.27	57.06	0.88
S07	0.95	20.83	41.45	2.68	27.47	6.60
S08	0.16	4.71	6.10	0.05	88.97	0.02
S09	0.39	47.61	17.62	4.79	28.45	1.14
S10	2.03	16.05	38.80	1.64	22.82	18.68
S11	1.70	40.58	16.16	0.91	26.31	14.34
S12	1.60	55.81	30.06	3.46	6.28	2.79
Average	1.22	29.75	22.93	6.07	35.73	4.30

TABLE S4 Detection of *Helicobacter* sequences by 454-pyrosequencing analysis and their relative abundances in gastric mucosal samples from the 24 patients, who did receive or not receive proton pump inhibitors for treatment

Sample code	PPI treatment	HP status by conventional testing ^a	Presence (+) or absence (-) of <i>Helicobacter</i> sequences	Abundance (%) of <i>Helicobacter</i> sequences
S01	No	Negative	+	0.03
S02	No	Positive	+	1.10
S03	No	Negative	-	0.00
S04	No	Positive	+	66.5
S05	No	Positive	+	78.8
S06	No	Positive	+	53.1
S07	No	Negative	-	0.00
S08	No	Positive	+	88.0
S09	No	Negative	-	0.00
S10	No	Negative	+	0.08
S11	No	Negative	-	0.00
S12	No	Negative	+	0.02
PPI01	Yes	Negative	+	4.55
PPI02	Yes	Negative	+	0.13
PPI03	Yes	Positive	+	25.2
PPI04	Yes	Negative	-	0.00
PPI05	Yes	Negative	-	0.00
PPI06	Yes	Negative	-	0.00
PPI07	Yes	Positive	+	47.4
PPI08	Yes	Negative	-	0.00
PPI09	Yes	Negative	-	0.00
PPI10	Yes	Positive	+	0.05
PPI11	Yes	Negative	-	0.00
PPI12	Yes	Positive	+	0.23

Abbreviations: PPI, proton pump inhibitor; HP, *Helicobacter pylori*.

^aPatients were categorized as HP-positive or HP-negative according to both conventional (non-sequencing) methods such as histology and rapid urease test.

TABLE S5 Adonis comparison of gastric bacterial community composition for patient groups included in the study

Comparisons		Adonis Statistics	
Group A	Group B	R ²	P value
HP+ / PPI-treated	HP+ / untreated	0.2959	0.088
HP+ / PPI-treated	HP- / PPI-treated	0.1835	0.082
HP+ / PPI-treated	HP- / untreated	0.3054	0.018
HP+ / untreated	HP- / PPI-treated	0.5693	0.001
HP- / PPI-treated	HP- / untreated	0.1183	0.159
HP- / untreated	HP+ / untreated	0.5905	0.001

Bold denotes statistically significant ($P < 0.05$) differences among pairwise comparisons.

FIG S1 Rarefaction curves of the 24 gastric biopsy samples studied. Biopsies were named as PPI01 to PPI12 or as S01 to S12, depending on whether the patients were ('PPI') or not ('S') treated with a proton pump inhibitor (PPI) drug at the time of sampling. Each curve plots the number of OTUs (observed species) as a function of the number of reads, and was calculated using 1000-fold resampling without replacement. All curves were cut off at 10,000 reads as indicated.

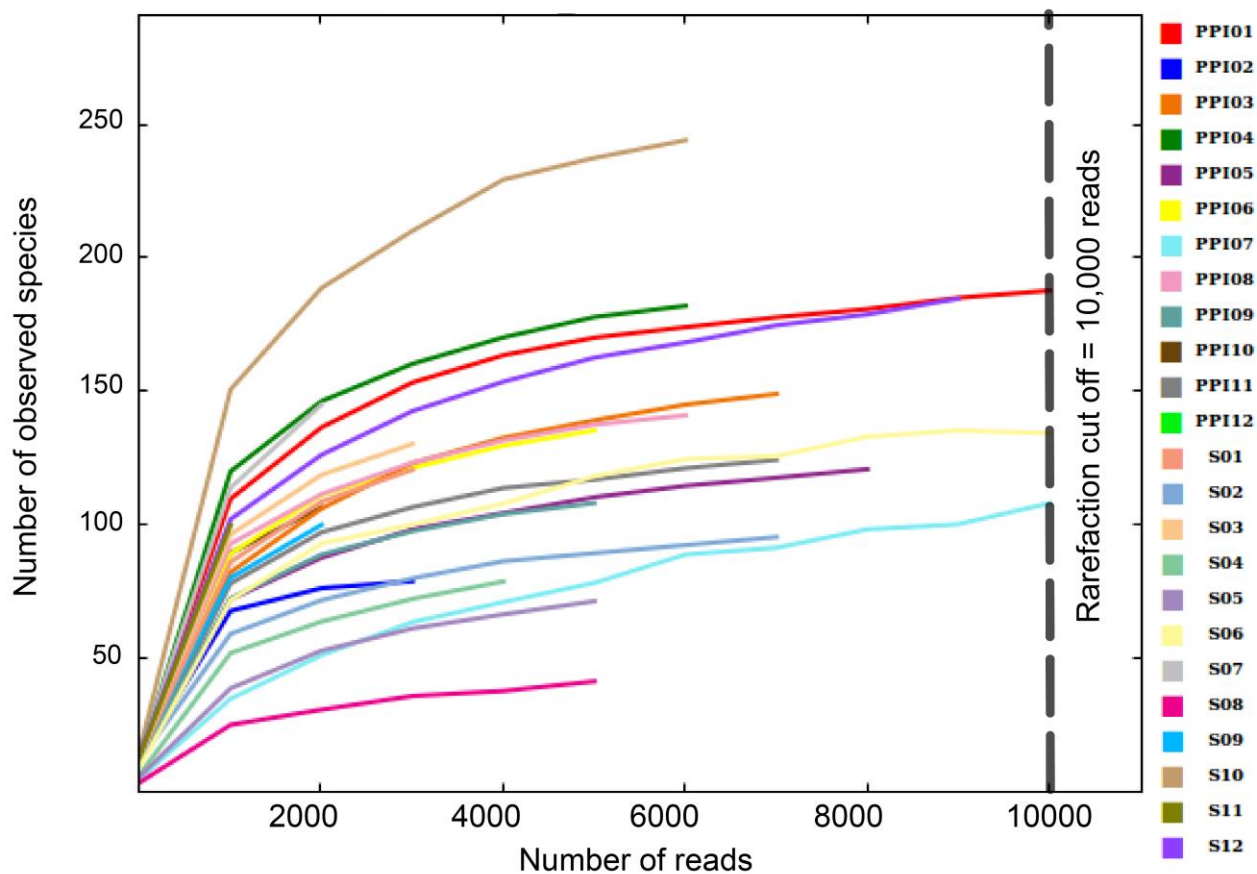


FIG S2 Results of the analyses as shown in Fig. 4 that were obtained after *Helicobacter* sequences were left out of the analysis

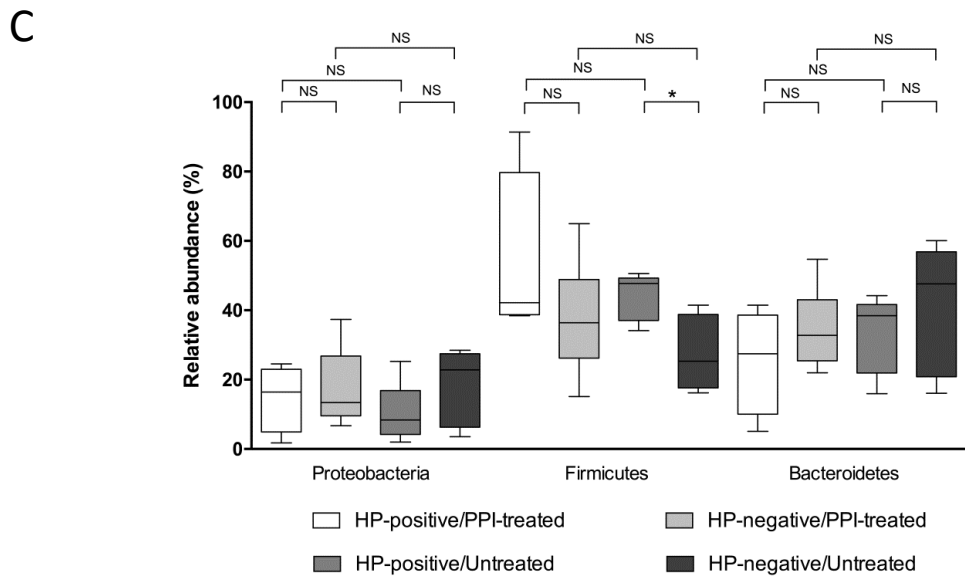
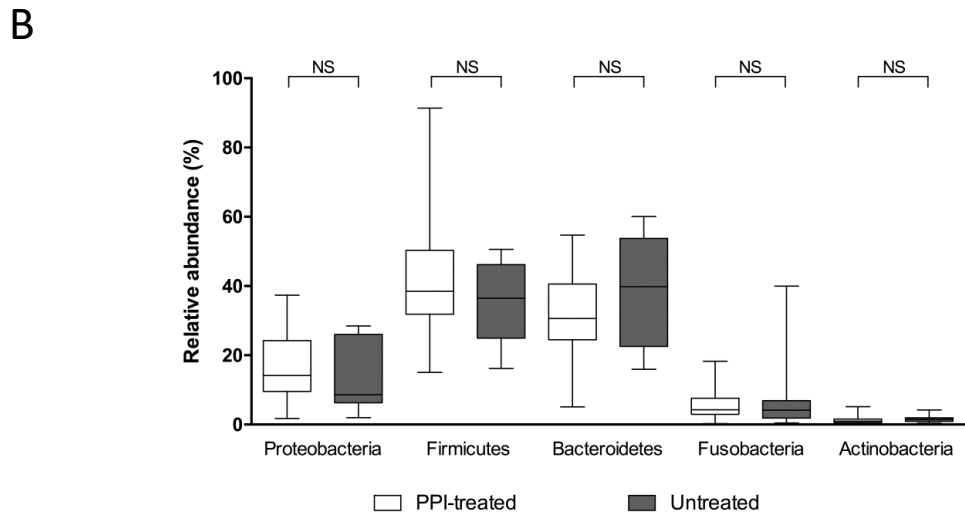
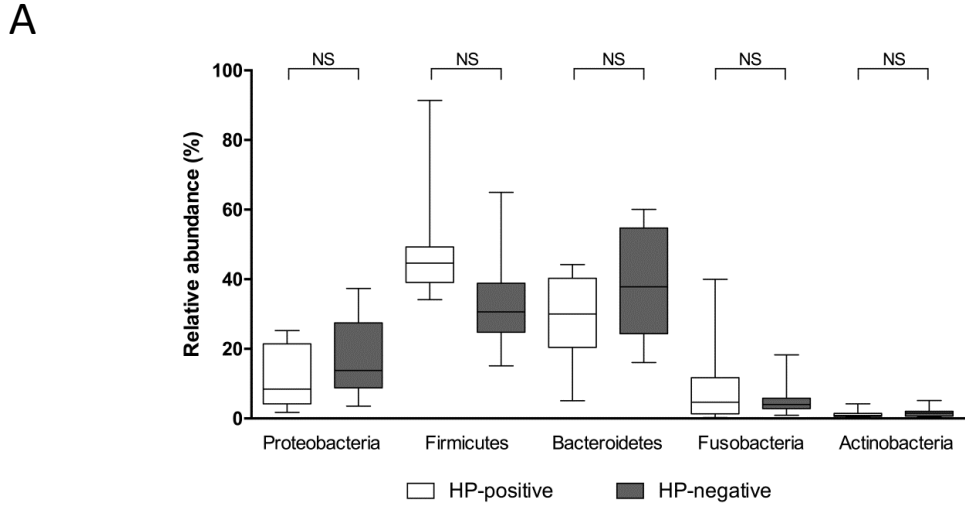
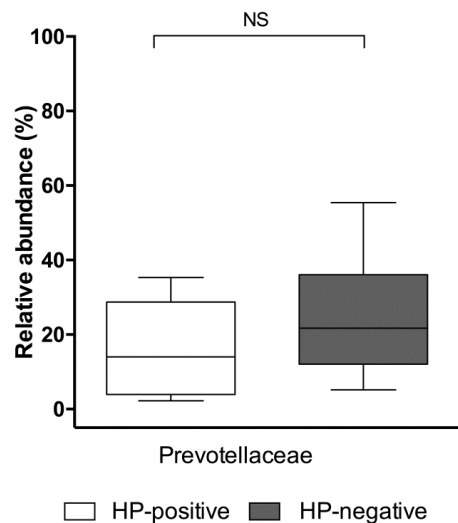
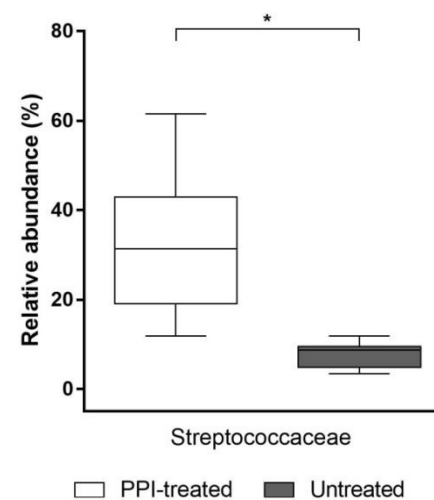


FIG S3 Results of the analyses as shown in Fig. 5 that were obtained after *Helicobacter* sequences were left out of the analysis

A



B



C

