

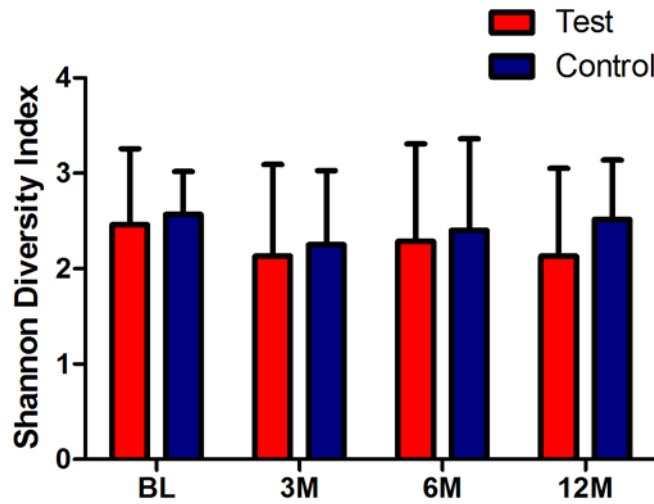
**Microbial profiles at baseline and not the use of antibiotics  
determine the clinical outcome of treatment of chronic  
periodontitis**

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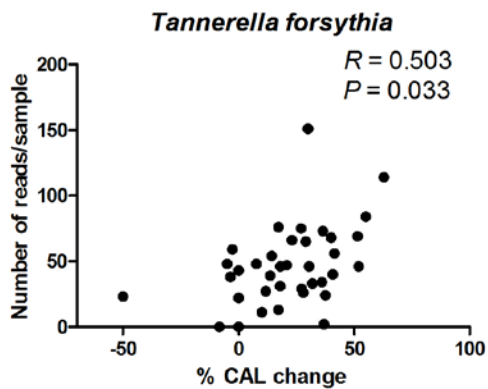
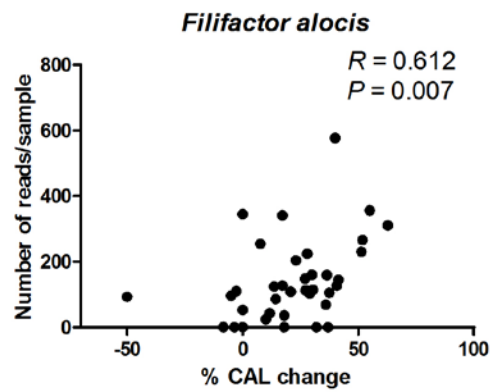
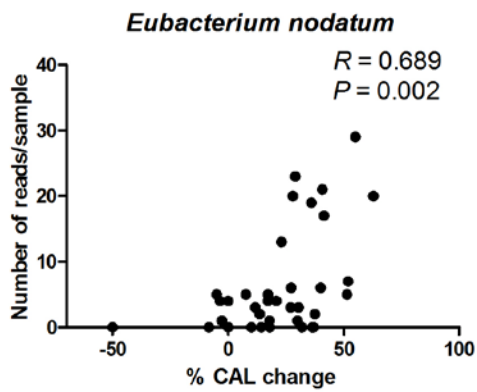
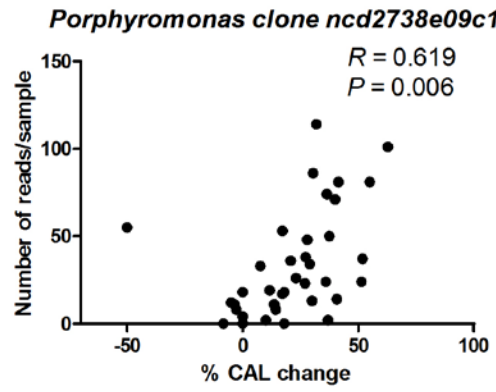
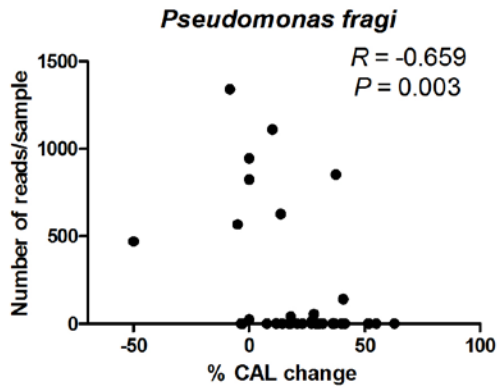
Supplementary Information

**Figure S1 | Average Shannon Diversity Index per treatment group and time-point.**

Error bar indicates standard deviation. No statistically significant difference between the time-points (BL – baseline, 3M – 3 months, 6M – 6 months, 12M – 12 months) ( $P>0.05$ , repeated-measures ANOVA) and the treatments was found ( $P>0.05$ , ANCOVA).



**Figure S2 | Significant correlation between bacterial OTUs at baseline and treatment outcome measured % of Clinical Attachment Level change (% CAL change). R and P values are from Spearman correlation.**



<b>Table S1   Background characteristics of the study groups at baseline.</b>				
		<b>Test</b>	<b>Controls</b>	<b>P value</b>
<i>N</i>		18	19	
Age (years)		48.1 ± 9.8	49.7 ± 6.2	NS
Gender	male	9 (50%)	13 (68%)	NS
Ethnicity	Dutch Caucasian	15 (84%)	16 (83%)	NS
Education	< high school	3 (17%)	2 (10%)	NS
	= high school	2 (11%)	3 (16%)	
	> high school	13 (72%)	14 (74%)	
Smoking	current	13 (68%)	8 (44%)	NS
	non smoker	6 (32%)	10 (56%)	
Values are means ± standard deviation or number of subjects (%). Independent T-test or $\chi^2$ <i>P</i> values indicated.				

**Table S2 | Full-mouth clinical results after therapy.**

		Test	Controls	<i>P</i> <sub>adj</sub> value*
<i>N</i>		18	19	
PPD (mm)	Baseline	3.7 ± 0.6	3.9 ± 0.6	0.305
	3 months	2.7 ± 0.5 <sup>§</sup>	3.0 ± 0.5 <sup>§</sup>	0.142
	6 months	2.6 ± 0.5 <sup>§</sup>	3.0 ± 0.5 <sup>§</sup>	0.086
	12 months	2.7 ± 0.5 <sup>§</sup>	3.0 ± 0.5 <sup>§</sup>	0.199
n° PPD ≥5 mm	Baseline	50.5 ± 22.1	51.8 ± 22.9	0.850
	3 months	12.6 ± 10.2 <sup>§</sup>	20.7 ± 16.9 <sup>§</sup>	0.071
	6 months	11.6 ± 8.9 <sup>§</sup>	20.8 ± 17.3 <sup>§</sup>	0.037
	12 months	11.9 ± 10.4 <sup>§</sup>	22.5 ± 20.7 <sup>§</sup>	0.057
n° PPD ≥6 mm	Baseline	28.0 ± 17.4	34.9 ± 20.7	0.282
	3 months	3.6 ± 3.9 <sup>§</sup>	10.5 ± 11.7 <sup>§</sup>	0.047
	6 months	3.7 ± 3.9 <sup>§</sup>	11.1 ± 12.9 <sup>§</sup>	0.054
	12 months	4.1 ± 4.7 <sup>§</sup>	11.7 ± 13.5 <sup>§</sup>	0.057
n° PPD ≥7 mm	Baseline	18.0 ± 13.2	20.0 ± 15.9	0.679
	3 months	0.8 ± 1.5 <sup>§</sup>	4.7 ± 6.2 <sup>§</sup>	0.013
	6 months	1.2 ± 2.1 <sup>§</sup>	5.3 ± 6.4 <sup>§</sup>	0.013
	12 months	0.7 ± 1.1 <sup>§</sup>	5.4 ± 7.6 <sup>§</sup>	0.016
CAL (mm)	Baseline	4.0 ± 1.1	4.4 ± 0.8	0.186
	3 months	3.3 ± 1.2 <sup>§</sup>	3.9 ± 0.8 <sup>§</sup>	0.297
	6 months	3.3 ± 1.1 <sup>§</sup>	3.9 ± 0.8 <sup>§</sup>	0.300
	12 months	3.3 ± 1.2 <sup>§</sup>	3.9 ± 0.8 <sup>§</sup>	0.438
BOP (%)	Baseline	69.5 ± 16.3	64.9 ± 13.3	0.349
	3 months	20.7 ± 11.9 <sup>§</sup>	20.1 ± 11.8 <sup>§</sup>	0.945
	6 months	20.0 ± 14.8 <sup>§</sup>	22.5 ± 14.9 <sup>§</sup>	0.512
	12 months	21.5 ± 14.7 <sup>§</sup>	22.0 ± 12.8 <sup>§</sup>	0.825
Plaque (%)	Baseline	69.1 ± 25.1	56.6 ± 27.7	0.159
	3 months	17.3 ± 14.9 <sup>§</sup>	17.6 ± 18.3 <sup>§</sup>	0.348
	6 months	17.0 ± 18.5 <sup>§</sup>	22.0 ± 21.3 <sup>§</sup>	0.169
	12 months	19.4 ± 15.1 <sup>§</sup>	19.5 ± 15.3 <sup>§</sup>	0.679

PPD, probing pocket depth; CAL, clinical attachment level; BOP, bleeding on probing. Values are means ± standard deviations. \*Difference between Test and Control (ANCOVA, adjusted for the corresponding variable at baseline). <sup>§</sup>*P* < 0.05 in comparison with baseline (repeated-measures ANOVA)

**Table S3 | Classification of reads at genus level or higher taxon.**

<b>Genus</b>	<b>Test</b>	<b>Control</b>
<i>Fusobacterium</i>	24.00 ± 18.11	22.11 ± 13.77
<i>Uncl. Pseudomonodaceae</i>	13.24 ± 30.46	13.86 ± 23.01
<i>Filifactor</i>	8.88 ± 8.03	11.33 ± 9.96
<i>Treponema</i>	5.67 ± 7.18	6.60 ± 6.49
<i>Paludibacter</i>	4.98 ± 5.66	7.18 ± 8.55
<i>Porphyromonas</i>	4.40 ± 5.60	4.45 ± 3.94
<i>Tannerella</i>	3.01 ± 1.87	3.69 ± 3.69
<i>Clostridiales Fam.xiii IS</i>	3.10 ± 2.27	2.86 ± 2.17
<i>Prevotella</i>	3.52 ± 4.38	4.28 ± 4.21
<i>Acinetobacter</i>	2.73 ± 7.54	0.12 ± 0.25
<i>Parvimonas</i>	2.86 ± 2.33	2.57 ± 2.71
<i>Synergistaceae</i>	2.17 ± 1.51	2.79 ± 1.70
<i>Actinomyces</i>	1.63 ± 2.12	1.41 ± 1.28
<i>Streptococcus</i>	0.68 ± 0.66	0.76 ± 1.34
<i>Neisseria</i>	0.96 ± 1.05	1.11 ± 2.91
<i>Campylobacter</i>	0.73 ± 0.54	1.17 ± 1.21
<i>Rothia</i>	0.65 ± 1.02	0.59 ± 1.16
<i>Capnocytophaga</i>	0.60 ± 0.95	0.13 ± 0.19
<i>Veillonella</i>	0.38 ± 0.49	0.80 ± 1.35
<i>Haemophilus</i>	0.24 ± 0.37	0.38 ± 1.06
<i>Micrococcales</i>	0.07 ± 0.17	0.12 ± 0.46
<i>Gemella</i>	0.40 ± 0.61	0.26 ± 0.32
<i>Corynebacterium</i>	0.35 ± 0.48	0.23 ± 0.49
<i>Selenomonas</i>	0.69 ± 0.70	0.84 ± 0.98
<i>Peptostreptococcus Fam. IS</i>	0.33 ± 0.31	0.72 ± 1.11
<i>Wchb1-69</i>	0.52 ± 0.71	1.04 ± 2.09
<i>Leptotrichia</i>	0.35 ± 0.48	0.13 ± 0.22
<i>Johnsonella</i>	0.48 ± 0.55	0.82 ± 1.11
<i>Derxia</i>	0.10 ± 0.14	0.08 ± 0.35
<i>Aggregatibacter</i>	0.85 ± 2.40	0.03 ± 0.09

Reads account for 90% of all OTUs at baseline for Test and Control. Values indicate relative abundance (mean ± standard deviation).

**Table S4 | Full mouth clinical parameters at baseline and after treatment according to the response to therapy.**

		<b>BMR</b>	<b>AMR</b>	<b><i>P</i><sub>adj</sub> value*</b>
<i>N</i>		19	18	
CAL (mm)	Baseline	4.4 ± 1.0	3.9 ± 0.9	0.139
	3 months	4.0 ± 1.1 <sup>§</sup>	3.1 ± 0.8 <sup>§</sup>	0.003
	6 months	4.0 ± 1.1 <sup>§</sup>	3.1 ± 0.9 <sup>§</sup>	0.002
	12 months	4.1 ± 1.1	3.0 ± 0.8 <sup>§</sup>	<0.001
PPD (mm)	Baseline	3.9 ± 0.6	3.8 ± 0.6	0.785
	3 months	3.1 ± 0.6 <sup>§</sup>	2.6 ± 0.3 <sup>§</sup>	0.001
	6 months	3.1 ± 0.6 <sup>§</sup>	2.6 ± 0.3 <sup>§</sup>	<0.001
	12 months	3.1 ± 0.6 <sup>§</sup>	2.5 ± 0.3 <sup>§</sup>	<0.001
BOP (%)	Baseline	66.7 ± 16.8	67.6 ± 12.8	0.869
	3 months	23.2 ± 12.5 <sup>§</sup>	17.4 ± 10.3 <sup>§</sup>	0.115
	6 months	26.7 ± 17.2 <sup>§</sup>	15.5 ± 8.7 <sup>§</sup>	0.017
	12 months	25.2 ± 16.9 <sup>§</sup>	21.3 ± 14.7 <sup>§</sup>	0.143
Plaque (%)	Baseline	62.1 ± 23.4	63.2 ± 30.8	0.899
	3 months	15.7 ± 15.4 <sup>§</sup>	19.2 ± 17.8 <sup>§</sup>	0.511
	6 months	23.9 ± 23.1 <sup>§</sup>	15.0 ± 15.2 <sup>§</sup>	0.137
	12 months	22.5 ± 16.2 <sup>§</sup>	16.2 ± 13.5 <sup>§</sup>	0.187

BMR, below median responders; AMR, above median responders. Values are means ± standard deviations.

\*Difference between groups (ANCOVA). *P* values are adjusted for the corresponding baseline variable. <sup>§</sup>*P* <0.05 in comparison with baseline (repeated-measures ANOVA).

<b>Table S5   Association between presence of taxa with treatment outcome per treatment group at the different time visits.</b>				
	<b>Test</b>		<b>Control</b>	
<b>time visit</b>	<b>BMR</b>	<b>AMR</b>	<b>BMR</b>	<b>AMR</b>
Baseline		<i>Porphyromonas</i>	-	-
3 months		<i>Actinomyces</i> <i>Haemophilus</i>		<i>Haemophilus</i> <i>Rothia</i> <i>Streptococcus</i>
6 months			<i>Paludibacter</i> <i>Tannerella</i> <i>Clostridiales fam</i> <i>xiii is</i> <i>Treponema</i> <i>Unc. Synergistaceae</i> <i>Filifactor</i>	
12 months		<i>Capnocytophaga</i>	<i>Paludibacter</i> <i>Tannerella</i> <i>Unc. Synergistaceae</i>	<i>Rothia</i>
BMR= below median responders. AMR= above median responders. Taxa, which show significant higher abundance between BMR and AMR, are represented.				



<b>Table S6   Inclusion/exclusion criteria</b>	
Inclusion	<p>2 teeth per quadrant with pocket <math>\geq 5</math> mm with clinical evidence of attachment loss</p> <p>&gt;50% bleeding on probing</p> <p><math>\geq 20</math> teeth present</p>
Exclusion	<p>Any systemic disease</p> <p>Chronic use of medications</p> <p>Use of systemic antibiotics in the last 6 months</p> <p>Previous periodontal treatment in the last 2 years</p> <p>Pregnancy/lactation</p> <p>Presence of implants or orthodontic appliances</p>

<b>Table S7   Dataset of relative abundances of reads used for microbial co-occurrence or mutual exclusion.</b>				
<b>Genus or higher taxon</b>	<b>BMR</b>		<b>AMR</b>	
	<b>Test</b>	<b>Control</b>	<b>Test</b>	<b>Control</b>
<i>Fusobacterium</i>	0.2534 ± 0.2091	0.2357 ± 0.1387	0.2265 ± 0.1599	0.2049 ± 0.1430
<i>Pseudomonadaceae</i>	0.2633 ± 0.3983	0.1882 ± 0.2541	0.0017 ± 0.0042	0.0834 ± 0.2000
<i>Prevotella</i>	0.0252 ± 0.0327	0.0378 ± 0.0358	0.0451 ± 0.0528	0.0484 ± 0.0499
<i>Paludibacter</i>	0.0715 ± 0,0728	0.0911± 0,1081	0.0280 ± 0,0213	0.0502 ± 0.0484
<i>Acinetobacter</i>	0.0247 ± 0.0719	0.0016 ± 0.0032	0.0299 ± 0.0831	0.0008 ± 0.0013
<i>Neisseria</i>	0.0121 ± 0.0128	0.0052 ± 0.0060	0.0071 ± 0.0076	0.0176 ± 0.0422
<i>Filifactor</i>	0.0669 ± 0.0805	0.0859 ± 0.0765	0.1108 ± 0.0783	0.1437 ± 0.1172
<i>Actinomyces</i>	0.0219 ± 0.0286	0.0143 ± 0.0132	0.0106 ± 0.0082	0.0139 ± 0.0132
<i>Rothia</i>	0.0097 ± 0.0123	0.0061 ± 0.0132	0.0033 ± 0.0072	0.0057 ± 0.0104
<i>Treponema</i>	0.0296 ± 0.0322	0.0454 ± 0.0490	0.0838 ± 0.0910	0.0889 ± 0.0754
<i>Parvimonas</i>	0.0286 ± 0.0226	0.0300 ± 0.0295	0.0287 ± 0.0254	0.0209 ± 0.0249
<i>Porphyromonas</i>	0.0142 ± 0.0139	0.0402 ± 0.0502	0.0737 ± 0.0670	0.0493 ± 0.0248
<i>Streptococcus</i>	0.0071 ± 0.0068	0.0086 ± 0.0146	0.0065 ± 0.0069	0.0063 ± 0.0128
<i>Veillonella</i>	0.0036 ± 0.0055	0.0110 ± 0.0169	0.0040 ± 0.0046	0.0048 ± 0.0080
<i>Clostridiales Fam xiii IS</i>	0.0273 ± 0.0233	0.0284 ± 0.0188	0.0517 ± 0.0267	0.0441 ± 0.0307
<i>Tannerella</i>	0.0260 ± 0.0201	0.0269 ± 0.0113	0.0342 ± 0.0174	0.0481 ± 0.0308
<i>Capnocytophaga</i>	0.0066 ± 0.0118	0.0016 ± 0.0023	0.053 ± 0.0072	0.0010 ± 0.0015
<i>Unc Synergistaceae</i>	0.0194 ± 0.0152	0.0245 ± 0.0201	0.0240 ± 0.0155	0.0316 ± 0.0131

<i>Haemophilus</i>	0.0016 ± 0.0030	0.0025 ± 0.0062	0.0032 ± 0.0043	0.0052 ± 0.0144
<i>Campylobacter</i>	0.0058 ± 0.0049	0.0125 ± 0.0147	0.0089 ± 0.0056	0.0108 ± 0.0094
<i>Micrococcales</i>	0.0008 ± 0.0019	0.0003 ± 0.0006	0.0006 ± 0.0017	0.0023 ± 0.0066
<i>Gemella</i>	0.0032 ± 0.0072	0.0033 ± 0.0037	0.0049 ± 0.0054	0.0017 ± 0.0025
<i>Corynebacterium</i>	0.0037 ± 0.0064	0.0030 ± 0.0064	0.0034 ± 0.0029	0.0016 ± 0.0026
<i>Selenomonas</i>	0.0048 ± 0.0054	0.0086 ± 0.0108	0.0092 ± 0.0082	0.0083 ± 0.0092
<i>Peptostreptococcaceae IS</i>	0.0036 ± 0.0035	0.0071 ± 0.0140	0.0031 ± 0.0029	0.0075 ± 0.0094
<i>Sphingobacteriales Wchb1-69</i>	0.0028 ± 0.0059	0.0028 ± 0.0036	0.0076 ± 0.0077	0.0190 ± 0.0286
<i>Johnsonella</i>	0.0037 ± 0.0056	0.0065 ± 0.0119	0.0059 ± 0.0055	0.0102 ± 0.0105
<i>Leptotrichia</i>	0.0022 ± 0.0036	0.0016 ± 0.0026	0.0048 ± 0.0056	0.0011 ± 0.0018
<i>Derxia</i>	0.0012 ± 0.0017	0.0001 ± 0.0002	0.0010 ± 0.0013	0.0017 ± 0.0052
<i>Aggregatibacter</i>	0.0062 ± 0.0165	0.0001 ± 0.0003	0.0108 ± 0.0300	0.0006 ± 0.0013
<i>Dialister</i>	0.0017 ± 0.0023	0.0062 ± 0.0116	0.0030 ± 0.0033	0.0013 ± 0.0015
<i>Pasteurellaceae</i>	0.0021 ± 0.0035	0.0014 ± 0.0022	0.0045 ± 0.0072	0.0036 ± 0.0039
<i>Burkholderia</i>	0.0015 ± 0.0045	0.0036 ± 0.0113	0.0486 ± 0.1204	0.0007 ± 0.0021
<i>Candidate division tm7</i>	0.0038 ± 0.0052	0.0055 ± 0.0072	0.0036 ± 0.0041	0.0034 ± 0.0050
<i>Veillonellaceae</i>	0.0024 ± 0.0035	0.0030 ± 0.0057	0.0052 ± 0.0067	0.0028 ± 0.0029
<i>Anaeroglobus</i>	0.0021 ± 0.0038	0.0025 ± 0.0041	0.0010 ± 0.0024	0.0015 ± 0.0026
<i>Bacteria</i>	0.0019 ± 0.0033	0.0025 ± 0.0031	0.0054 ± 0.0100	0.0047 ± 0.0027
<i>Mycoplasma</i>	0.0017 ± 0.0029	0.0034 ± 0.0075	0.0024 ± 0.0032	0.0034 ± 0.0048
<i>Desulfobulbus</i>	0.0055 ± 0.0060	0.0037 ± 0.0026	0.0057 ± 0.0048	0.0053 ± 0.0026
<i>Firmicutes</i>	0.0050 ± 0.0058	0.0031 ± 0.0038	0.0057 ± 0.0063	0.0046 ± 0.0036

<i>Bulleidia</i>	0.0013 ± 0.0015	0.0044 ± 0.0064	0.0005 ± 0.0010	0.0028 ± 0.0039
<i>Leptotrichiaceae</i>	0.0003 ± 0.0006	0.0020 ± 0.0058	0.0047 ± 0.0093	0.0011 ± 0.0033
<i>Propionibacteriaceae</i>	0.0006 ± 0.0012	0	0.0005 ± 0.0009	0.0002 ± 0.0007
<i>Brevundimonas</i>	0.0006 ± 0.0017	0.0003 ± 0.0009	0.0010 ± 0.0029	0
<i>Mogibacterium</i>	0.0040 ± 0.0079	0.0031 ± 0.0030	0.0029 ± 0.0029	0.0028 ± 0.0026
<i>Prevotellaceae</i>	0.0006 ± 0.0008	0.0009 ± 0.0011	0.0013 ± 0.0016	0.0038 ± 0.0055
<i>Peptococcus</i>	0.0006 ± 0.0006	0.0004 ± 0.0008	0.0037 ± 0.0045	0.0011 ± 0.0013
<i>Rikenellaceae Rc9 gut group</i>	0.0010 ± 0.0016	0.0016 ± 0.0018	0.0011 ± 0.0019	0.0052 ± 0.056
<i>Catonella</i>	0.0005 ± 0.0012	0.0016 ± 0.0029	0.0025 ± 0.0024	0.0026 ± 0.0052
<i>Actinobaculum</i>	0.0006 ± 0.0017	0	0.0021 ± 0.0028	0.0004 ± 0.0005
<i>Cardiobacterium</i>	0.0006 ± 0.0008	0.0002 ± 0.0003	0.0013 ± 0.0023	0.0003 ± 0.010
<i>Abiotrophia</i>	0.0001 ± 0.0002	0	0.0002 ± 0.0005	0
<i>Micrococcus</i>	0.0002 ± 0.0007	0	0.0007 ± 0.0014	0
<i>Oribacterium</i>	0.0011 ± 0.0023	0.0021 ± 0.0031	0.0003 ± 0.0007	0.0020 ± 0.0054
<i>Xylanibacter</i>	0.0001 ± 0.0002	0.0009 ± 0.0018	0.0090 ± 0.0215	0.0018 ± 0.0028
<i>Bergeyella</i>	0.0002 ± 0.0005	0.0001 ± 0.0002	0.0007 ± 0.0019	0.0006 ± 0.0011
<i>Desulfohalobiaceae</i>	0	0.0003 ± 0.0009	0.0130 ± 0.0390	0
<i>Peptostreptococcus</i>	0.0005 ± 0.0012	0.0010 ± 0.0029	0.0014 ± 0.0021	0.0015 ± 0.0045
<i>Atopobium</i>	0.0006 ± 0.0009	0.0008 ± 0.0012	0.0004 ± 0.0007	0
<i>Phocaeicola</i>	0.0006 ± 0.0014	0.0009 ± 0.0013	0.0010 ± 0.0018	0.0032 ± 0.0053
<i>Solobacterium</i>	0.0004 ± 0.0010	0.0007 ± 0.0018	0	0.0002 ± 0.0003
<i>Odoribacter</i>	0	0.0061 ± 0.0192	0.0025 ± 0.0052	0

<i>Brachy bacterium</i>	0.0001 ± 0.0002	0	0.0017 ± 0.0050	0
<i>Clostridiales Fam xi IS</i>	0.0006 ± 0.0019	0.0023 ± 0.0050	0.0037 ± 0.0067	0.0002 ± 0.0005
<i>Rhizobiales</i>	0.0001 ± 0.0002	0.0001 ± 0.0002	0.0029 ± 0.0088	0.0000 ± 0.0000
<i>Enhydro bacter</i>	0.0001 ± 0.0002	0.0001 ± 0.0002	0	0.0002 ± 0.0003
<i>Neisseriaceae</i>	0.0002 ± 0.0004	0.0001 ± 0.0002	0.0003 ± 0.0005	0.0001 ± 0.0002
Others	0.0062 ± 0.0049	0.0043 ± 0.0050	0.0171 ± 0.0152	0.0050 ± 0.0056
BMR, below median responders; AMR, above median responders. Values are means ± standard deviations.				

