





ORIGINAL RESEARCH

Oral Microbiome Is Associated With Incident Hypertension Among Postmenopausal Women

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BACKGROUND: Oral microbiota are thought to influence blood pressure (BP) regulation. However, epidemiological data supporting this hypothesis are limited. We examined associations between oral microbiota, BP, and incident hypertension in postmenopausal women.

METHODS AND RESULTS: Baseline (1997–2001) examinations were completed on 1215 women (mean age, 63 years) during which subgingival plaque was collected, BP was measured, and medical and lifestyle histories and medication inventory were obtained. Microbiome composition of subgingival plaque was measured using 16S ribosomal RNA gene amplicon sequencing. Baseline measured BP was defined as normotensive (systolic <120 mm Hg and diastolic <80 mm Hg, no BP medication use; n=429); elevated (systolic ≥120 mm Hg or diastolic ≥80 mm Hg, no medication use; n=306); or prevalent treated hypertension (history of physician diagnosis treated with medications; n=480). Incident hypertension (375 cases among 735 without baseline treated hypertension) was defined as newly physician-diagnosed hypertension treated with medication reported on annual health surveys (mean follow-up, 10.4 years). Cross-sectional analysis identified 47 bacterial species (of 245 total) that differed significantly according to baseline BP status ($P<0.05$). Prospective analysis identified 15 baseline bacterial species significantly ($P<0.05$) associated with incident hypertension: 10 positively (age-adjusted hazard ratios [HRs], 1.10–1.16 per SD in bacterial abundance) and 5 inversely (HRs, 0.82–0.91) associated. Associations were materially unchanged after further adjustment for demographic, clinical, and lifestyle factors; were similar when analysis was restricted to the normotensive group; and were of consistent magnitudes between strata of baseline age, smoking, body mass index, and BP categories.

CONCLUSIONS: Specific oral bacteria are associated with baseline BP status and risk of hypertension development among postmenopausal women. Research to confirm these observations and elucidate mechanisms is needed.

Key Words: epidemiology ■ hypertension ■ menopause ■ microbiome ■ women's health

Hypertension is associated with substantial morbidity and health care costs among older adults.¹ When defined as systolic and diastolic blood pressure (BP) of ≥130 or ≥80 mm Hg or use of anti-hypertension medication, among US adults aged ≥65 years, hypertension prevalence exceeds 70% and is higher in women than men.² This age category is the

fastest growing and is projected to reach 95 million by the year 2060, with women outnumbering men 2 to 1.³ The societal burden of hypertension will likely increase in parallel. The US Surgeon General Call to Action to Control Hypertension⁴ indicated that despite available evidence-based strategies for hypertension primary prevention and treatment, high BP continues to be a

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CLINICAL PERSPECTIVE

What Is New?

- Greater relative abundance of certain subgingival (oral) bacteria appears to be associated with higher risk of developing hypertension treated with medication in postmenopausal women during an average follow-up of 10 years.

What Are the Clinical Implications?

- Given the extensive burden of hypertension presently among older adults and its expected growth in coming decades with population aging, if proven causal, associations between oral bacteria and blood pressure dysregulation might offer new opportunities for targeted clinical intervention aimed at preventing hypertension in later life.

Nonstandard Abbreviations and Acronyms

CARDIA	Coronary Artery Risk Development in Young Adults Study
CLR	centered log(2)-ratio
OsteoPerio	Osteoporosis and Periodontal Disease
OTU	operational taxonomic unit
WHIOS	Women's Health Initiative Observational Study

public health nemesis.⁵ Identification of causative factors contributing to hypertension in later life could enhance effectiveness of control efforts.

A 2017 National Heart, Lung, and Blood Institute report called for research on the microbiome's role in BP regulation.⁶ Growing evidence suggests a plausible role of gut microbiota in hypertension pathobiology.⁷ It is less clear whether the oral microbiome influences BP and hypertension risk. Certain oral bacteria, through nitrate-nitrite metabolism, provide the host with a source of bioactive NO, which is critical to arterial BP regulation.⁸ Other oral bacteria, through nonnitrate pathways, such as inflammation and atherosclerosis,⁹ might also be relevant. Previous cross-sectional studies in humans^{10,11} suggest specific oral subgingival bacteria could be associated with concurrent BP and prevalent hypertension. If proven causative, an association between oral microbiota and hypertension could lead to novel mechanism-based prevention and treatment strategies. No study, to our knowledge, has been

published on the prospective association between the oral microbiome and incident hypertension.

The primary aim of the present study was to use novel prospective data to determine the association between the oral microbiome and development of incident hypertension in older women.

METHODS

Data, analytic methods, and study materials that support the findings of this study are available from the authors on reasonable request and with permission of the US Women's Health Initiative program.

Study Participants

The present analysis includes 1215 postmenopausal women, aged 53 to 81 years at enrollment (1997–2001) into the Buffalo OsteoPerio (Osteoporosis and Periodontal Disease) study for whom complete information is available on the oral subgingival plaque microbiome, baseline information on hypertension status and measured BP, and annual follow-up for incident hypertension. The OsteoPerio study is ancillary to the WHIOS (Women's Health Initiative Observational Study), which between 1993 and 1998 enrolled 2249 ambulatory postmenopausal women, aged 50 to 79 years, from the western New York community at the University at Buffalo clinical center. Design of the WHIOS and OsteoPerio study has been published.^{12,13} Neither periodontal disease status nor BP was an inclusion criterion for either study. The University at Buffalo human subjects Institutional Review Board approved both studies for which participants provided written informed consent. Figure 1 gives the flow of participants and exclusions for the sample of 1215 women included in the present study.

Subgingival Microbiome Measurement

OsteoPerio study participants completed a baseline oral examination conducted by calibrated dental hygienists.¹⁴ Probing pocket depth and clinical attachment level are reported descriptively in the present analysis. Subgingival plaque samples for microbiome sequencing were obtained using fine paper points at sites pre-specified by a standardized protocol.¹⁵ Paper points were inserted into the gingival sulcus for 10 seconds and then placed in lactated Ringer's solution, vortexed, aliquoted into cryostraws, and placed in liquid nitrogen within 30 to 60 minutes of collection. Samples were later moved to -80°C freezers for storage. Those used in the present study had not previously been thawed.

Genomic DNA was isolated using an automated system (QIA Symphony SP; Qiagen, Valencia, CA) at the New York State Buffalo Genomics and Bioinformatics Core Laboratory following our published

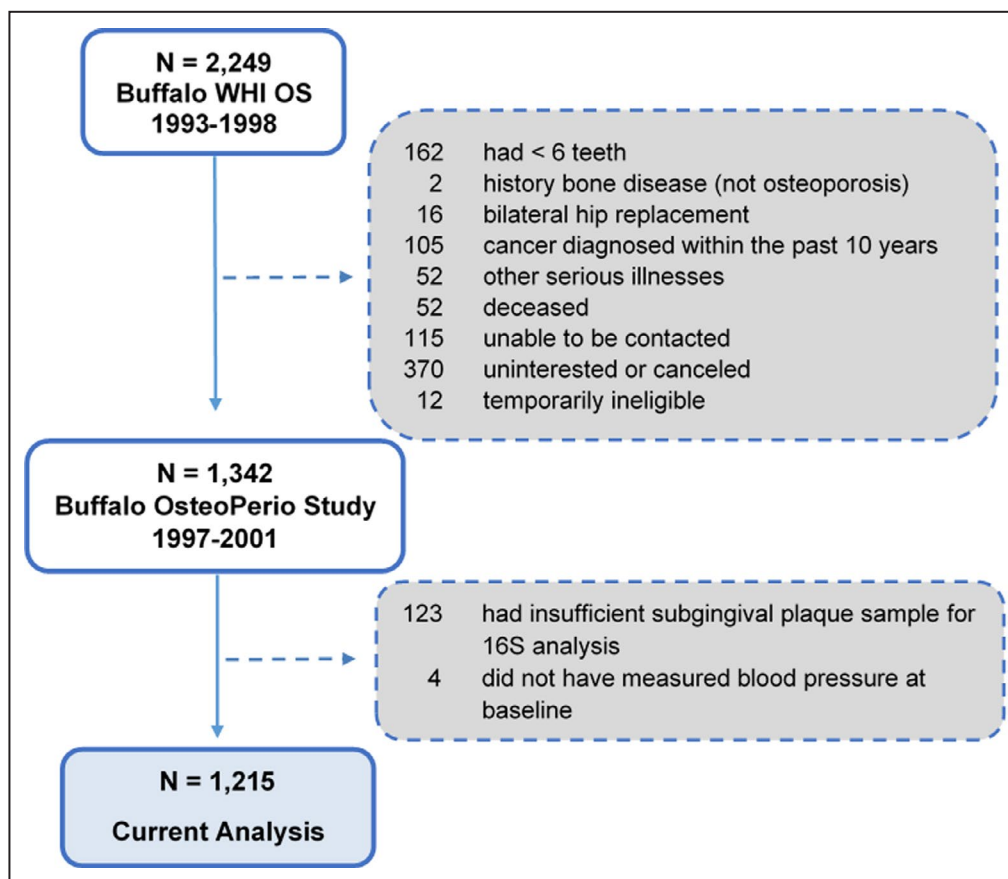


Figure 1. Flowchart of participant enrollment.

OsteoPerio indicates Osteoporosis and Periodontal Disease; and WHIOS, Women's Health Initiative Observational Study.

procedures.^{16,17} Before DNA extraction, an enzymatic pretreatment (20 mg/mL lysozyme in 20 mmol/L Tris-HCL, pH 8.0) was performed for more efficient isolation of Gram-positive bacteria; pretreatment with 2 mmol/L EDTA and 1.2% Triton X-100 was used to enhance isolation of Gram-negative bacteria.¹⁸ Extracted DNA was used for 16S ribosomal RNA gene amplification targeting the V3 to V4 hypervariable regions following the Illumina protocol with modifications published by our group.¹⁹ Polymerase chain reaction amplifications and sequencing were performed on 96 samples at a time with both positive controls (mock DNA and subgingival plaque pools) and negative controls (polymerase chain reaction–grade water and extraction buffer) on an Illumina MiSeq generating 2× 300 bp paired-end reads. Batches of 85 to 88 test samples were processed together and randomly arranged on the 96-well plate with negative and positive quality control samples, including a pooled plaque sample, to minimize batch effects.

Illumina reads were preprocessed and quality filtered, as previously described.¹⁷ Unique sequences were taxonomically annotated with Basic Local Alignment Search Tool²⁰ at a 97% similarity, for

species-level assignment approximation, against bacterial sequences from the Human Oral Microbiome Database version 14.5.²¹ Reads were given the same taxonomic label as the best hit. Reads with no hits were excluded from downstream analyses. Sequences with the same labels were clustered into one operational taxonomic unit (OTU). The raw OTU table was filtered at a frequency <0.02% of the total read count.

Baseline BP and Hypertension

Baseline BP was measured in the clinic by auscultation with a stethoscope and mercury sphygmomanometer, using an appropriately sized cuff based on measured arm circumference.²² After 5 minutes of seated rest by the participant, 2 measurements at least 2 minutes apart were recorded and averaged. Systolic and diastolic BP was defined by the first and fifth Korotkoff sounds, respectively. Antihypertensive medication use was determined from inspection of pill bottles as part of a medication inventory. Self-reported history of physician-diagnosed hypertension treated with medication was obtained by questionnaire. Using the above information, we categorized women at baseline as

follows: *normotensive* (systolic BP <120 mm Hg and diastolic BP <80 mm Hg; not using BP medication; no history of physician-diagnosed hypertension; n=429), *undiagnosed elevated BP* (systolic BP ≥120 mm Hg or diastolic BP ≥80 mm Hg; no BP medication; no history of physician-diagnosed hypertension; n=306), and *prevalent diagnosed and treated hypertension* (history of physician-diagnosed hypertension with BP medication use at WHIOS enrollment, before or at OsteoPerio study examination; n=480). These BP thresholds align with 2017 clinical guidelines.⁵

Incident Hypertension Ascertainment

Among women who at baseline were without prevalent diagnosed and treated hypertension (n=735), we prospectively identified incidence of newly physician diagnosed hypertension treated with antihypertensive medication using annual health questionnaires administered nationally through Women's Health Initiative. The case finding question read: "Since the date given on the front of this form, has a doctor prescribed pills for high blood pressure or hypertension?" Strong agreement exists for hypertension based on this question and Medicare claims data in the Women's Health Initiative ($\kappa=0.84$; unpublished data, 2019 WHI Annual Investigator Report). Response reproducibility is high ($\kappa=0.86$) based on repeated question administration in a subset at study baseline.¹³

Other Assessments

Height (cm) and weight (kg) were measured using a calibrated scale and stadiometer; body mass index (BMI; kg/m²) was calculated. Self-administered questionnaires were used to obtain information on demographic factors, smoking history, recreational physical activity habits, menopausal hormone therapy, and history of diabetes treated with medication.¹³ Usual dietary intake was assessed with the Women's Health Initiative food frequency questionnaire.²³ Diet quality was summarized using the Healthy Eating Index-2015, which ranges from 0 to 100, with higher scores indicating better quality.²⁴ Neighborhood socioeconomic status was characterized using aggregate census tract information to compute a score ranging from 0 to 100, with higher scores indicating greater affluence.²⁵ Missing covariate information was relatively modest (neighborhood socioeconomic status, 1; dietary Healthy Eating Index score, 8; physical activity, 3; pocket depth, 4; clinical attachment level, 4 [calculated using pocket depth]; education, 12; smoking, 1; and general health, 5); individuals with covariate missingness were not excluded from the analysis.

Statistical Analysis

Participant characteristics were summarized according to baseline BP categories and contrasted between

groups using ANOVA (continuous variables) and χ^2 tests (categorical variables). For microbiome analysis, we first normalized individual OTU abundances using the centered log(2)-ratio (CLR) transformation, which accounts for the compositional data structure, reduces the likelihood of spurious correlations, and enhances the meaningfulness of subcomposition comparisons.²⁶ Only participants with complete information on the 16S ribosomal RNA gene amplicon sequencing were included in this analysis. Bacteria with a zero count were treated by adding 1 before the CLR transformation. The CLR OTU can be interpreted as a log(2) fold difference for the given microbiota relative to the overall compositional geometric mean, as discussed in detail elsewhere.²⁷ To describe the extent that subgingival bacteria were related with BP status at baseline, before incident hypertension was identified, we performed 2 descriptive analyses (*cross-sectional analysis*; N=1215). Linear relationships between CLR transformed bacterial abundance and continuous systolic and diastolic BP at baseline were evaluated using Pearson correlations. Mean bacterial abundance was compared according to baseline BP categories using ANOVA. We then evaluated the prospective association between baseline bacteria and incident hypertension among participants who at baseline neither had a history of physician-diagnosed hypertension nor use of antihypertensive medication (*prospective analysis*; N=735). Cox proportional hazards regression was used to estimate hazard ratios (HRs) and 95% CIs for a 1-SD unit difference in baseline bacterial abundance. The proportional hazards assumption was confirmed using the Schoenfeld residuals method.²⁸ Person-time was computed from the date of OsteoPerio study baseline assessment to the date of the annual health survey on which incident hypertension was identified, date of death or date of the health survey when last known to be without hypertension, or the end of follow-up (February 28, 2017), whichever came first. Multivariable Cox regression analyses controlled for age, race and ethnicity, education, neighborhood socioeconomic status, and self-rated general health (model 1), and additionally for history of treated diabetes (model 2), and dietary quality, physical activity, and statin use (model 3). Stratified analysis (model 1 covariates) explored whether associations between the oral microbiome and incident hypertension were consistent over categories of baseline age (above versus below median 65 years), smoking (ever versus never), BMI (<25 versus ≥25 kg/m²), and BP (normal versus elevated BP). We report 95% CIs and uncorrected *P* values for 2-tailed tests at $\alpha=0.05$. We further report significance after correction for multiple comparisons based on the Benjamini-Hochberg method.²⁹ Analyses were performed using SAS software (Cary, NC; v.9.4).

RESULTS

Participant characteristics at baseline are given in Table 1. Women with elevated BP or prevalent diagnosed hypertension were, on average, older, had higher BMI and systolic and diastolic BP, and had lower physical activity compared with normotensive women ($P<0.001$, each). Diet quality, neighborhood socioeconomic status, and periodontal pocket depth and clinical attachment level did not differ between

groups. History of treated diabetes, use of statin medication, and fair/poor self-rated health were more frequent ($P<0.001$) in women with prevalent hypertension than normotensive and elevated BP. Current menopausal hormone therapy use was lower ($P=0.02$) in women with prevalent hypertension and elevated BP compared with normotensive. Table S1 gives baseline characteristics according to incident hypertension status among the 735 women who were without prevalent diagnosed hypertension at baseline. Women who

Table 1. Baseline Characteristics by Baseline BP and Hypertension Status (N=1215)

Characteristic	Normal BP (N=429)*	Undiagnosed elevated BP (N=306)*	Prevalent hypertension (N=480)*	P value†
Age, y	64.5 (6.4)	67.5 (6.8)	68.1 (7.1)	<0.001
nSES	76.5 (6.6)	76.0 (7.1)	76.0 (7.0)	0.44
BMI, kg/m ²	25.1 (4.3)	26.2 (4.3)	28.2 (5.9)	<0.001
Systolic BP, mm Hg	106 (8.1)	133 (12.6)	129 (17.8)	<0.001
Diastolic BP, mm Hg	66.3 (6.3)	74.8 (8.3)	72.5 (9.5)	<0.001
Dietary HEI score	67.7 (10.3)	68.1 (10.3)	67.2 (10.1)	0.46
Physical activity, MET h/wk	15.9 (14.4)	14.9 (13.9)	12.1 (13.3)	<0.001
Whole mouth CAL, mm	2.4 (0.6)	2.4 (0.8)	2.4 (0.7)	0.26
Whole mouth PPD, mm	2.2 (0.4)	2.2 (0.4)	2.2 (0.4)	0.56
Race				0.09
White	421 (98.1)	299 (97.7)	464 (96.7)	
Black	3 (0.7)	2 (0.7)	12 (2.5)	
Other§	5 (1.2)	5 (1.6)	4 (0.8)	
Education				0.34
High school or less	78 (18.4)	65 (21.7)	110 (23.2)	
At least some college	187 (44.1)	130 (43.5)	213 (44.8)	
Postgraduate	159 (37.5)	104 (34.8)	152 (32.0)	
Smoking status				0.59
Never	225 (52.4)	166 (54.2)	253 (52.8)	
Former	188 (43.8)	135 (44.1)	211 (44.1)	
Current	16 (3.7)	5 (1.6)	15 (3.1)	
Treated diabetes	9 (2.1)	7 (2.3)	42 (8.8)	<0.001
Statin use	31 (7.2)	39 (12.8)	124 (26.0)	<0.001
HT use				0.02
Never	132 (30.8)	110 (35.9)	147 (30.6)	
Former	70 (16.3)	69 (22.5)	106 (22.1)	
Current	227 (52.9)	127 (41.5)	227 (47.3)	
Self-rated general health				<0.001
Excellent	110 (25.6)	51 (16.7)	50 (10.4)	
Very good	202 (47.1)	173 (56.5)	195 (40.6)	
Good	103 (24.0)	72 (23.5)	177 (36.9)	
Fair or poor	10 (2.3)	9 (2.9)	54 (11.3)	

Data are mean (SD) or number (percentage) for continuous and categorical variables, respectively. Missing data: nSES (1), HEI (8), physical activity (3), PPD (4), CAL (4), education (12), smoking (1), and general health (5). BMI indicates body mass index; BP, blood pressure; CAL, clinical attachment level; HEI, Healthy Eating Index; HT, menopausal hormone therapy; MET, metabolic equivalent task; nSES, neighborhood socioeconomic status; and PPD, probing pocket depth.

*Normal BP (systolic BP <120 mm Hg and diastolic BP <80 mm Hg; no history of physician-diagnosed hypertension; not using BP medication); undiagnosed elevated BP (systolic BP ≥120 mm Hg or diastolic BP ≥80 mm Hg; no history of physician-diagnosed hypertension; not using BP medication); prevalent hypertension (history of physician-diagnosed hypertension treated with medication).

†P values from ANOVA F-test and Pearson χ^2 test for continuous and categorical variables, respectively.

§Other was a response option on the question pertaining to race and ethnicity within the Demographics Questionnaire.

developed hypertension had higher baseline mean BMI and systolic and diastolic BP compared with women without incident hypertension ($P<0.001$). Those developing hypertension also were more likely ($P<0.05$) to have been former or current smokers and have treated diabetes. Incident hypertension cases also were older, had poorer diet quality, and had lower physical activity compared with women without incident hypertension, although differences did not achieve statistical significance. Statin use was not different according to incident hypertension status.

Cross-Sectional Analysis

A total of 245 bacterial species were identified in the subgingival plaque samples.¹⁶ Pearson correlations between subgingival microbiota and systolic and diastolic BP at baseline were relatively small and are given in Table S2. For systolic BP, there were 117 positive and 128 negative correlations, and for diastolic BP, there were 115 and 130, respectively. Three bacteria positively correlated with systolic BP (*Prevotella sp. oral taxon 292*, $r=0.15$; *Treponema scoranskii*, $r=0.13$; and *Anaeroblobus geminatus*, $r=0.12$) remained significant after correction for multiple comparison; scatterplots of these relationships are in Figure 2. Remaining correlations with systolic BP and all correlations with diastolic BP were $|r|<0.10$ and not significant after correction for multiple comparisons. Microbial α diversity indexes (Observed OTUs, Chao1 Index, and Shannon Index) did not differ according to BP categories at baseline ($P>0.05$, all; Figure S1). Comparison of bacteria relative abundances according to BP categories at baseline are given in Table 2 and Table S3. Significant differences (uncorrected $P<0.05$) were observed for 47 (of 245 total) species-level OTUs across baseline BP categories (Table 2). Of these, 25 were enriched in elevated BP and prevalent hypertension, and 22 were enriched in normal BP. The greatest mean differences in bacteria were between normal BP and prevalent hypertension. For those enriched in prevalent hypertension, the 5 largest mean differences were for *Treponema socranskii* (CLR mean difference [d]=0.79; $P<0.001$), *Oribacterium oral taxon 078* (d=0.76; $P<0.001$), *Veillonellaceae G1 sp. oral taxon 155* (d=0.74; $P=0.001$), *Prevotella oralis* (d=0.69; $P=0.003$), and *Veillonellaceae G1 sp. oral taxon 150* (d=0.66; $P=0.01$). For those enriched in normal BP, the 5 largest mean differences were for *TM7 G1 sp. oral taxon 869* (d=0.77; $P<0.001$), *Leptotrichia sp. oral taxon 212* (d=0.76; $P=0.001$), *Rothia aeria* (d=0.73; $P=0.001$), *Leptotrichia sp. oral taxon 225* (d=0.67; $P=0.01$), and *Streptococcus sanguinis* (d=0.64; $P<0.001$). Following correction for multiple comparisons, 12 (of 47) bacteria remained statistically significant (corrected $P<0.05$). Results for all 245 species-level OTUs included in the analysis are given Table S3.

Prospective Analysis of Incident Hypertension

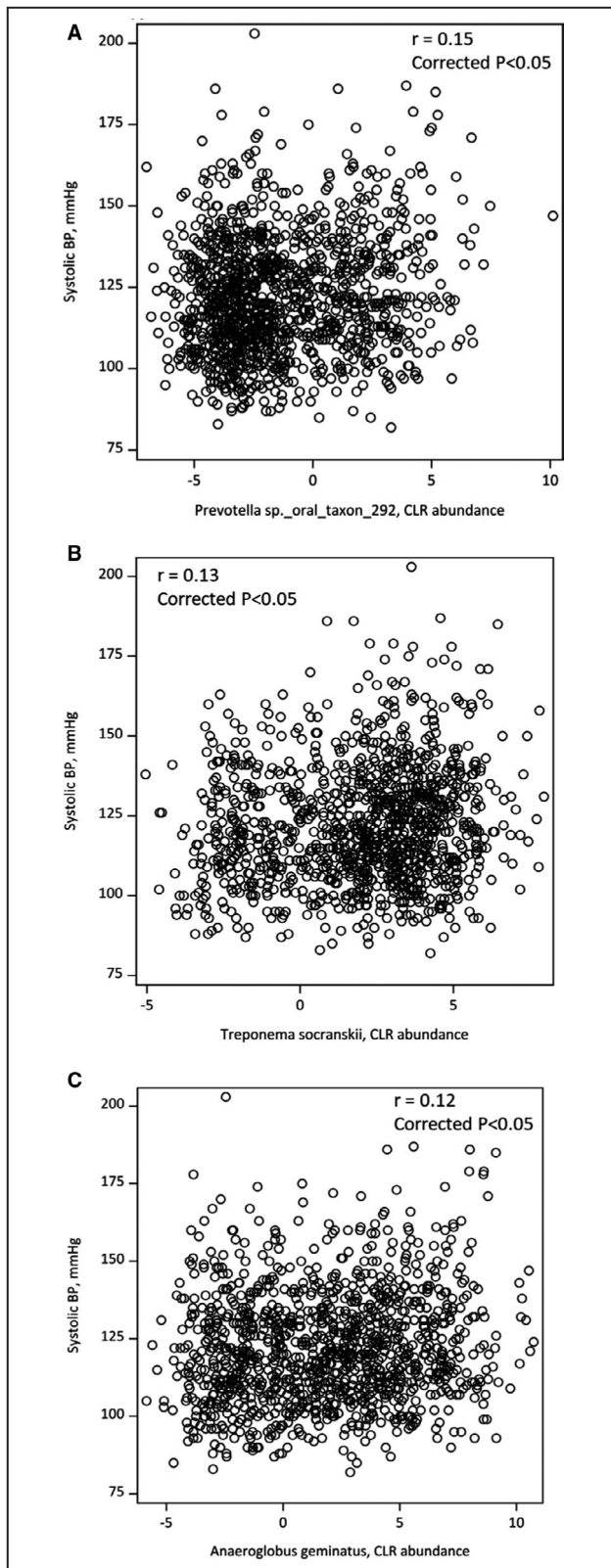
During a mean follow-up of 10.4 years (SD=5.9 years; range, 0.4–19.2 years) among 735 women without baseline prevalent diagnosed hypertension, there were 387 (52.7%) cases of incident physician-diagnosed hypertension treated with medication. Prospective analysis identified 15 baseline bacterial species that were significantly associated with risk of incident hypertension (Table 3). Of these, 10 were associated with greater hypertension risk with age-adjusted HRs of 1.10 to 1.16 (*Streptococcus anginosus*, *Streptococcus salivarius*, *Fretibacterium sp. oral taxon 362*, *Selenomonas infelix*, *Prevotella sp. oral taxon 526*, *Prevotella sp. oral taxon 292*, *Megasphaera sp. oral taxon 123*, *Capnocytophaga sp. oral taxon 903*, *Prevotella sp. oral taxon 376*, and *Streptococcus lactarius*); and 5 were associated with lower risk with age-adjusted HRs of 0.82 to 0.91 (*Neisseria subflava*, *Bergeyella sp. oral taxon 907*, *Gemella morbillorum*, *Leptotrichia sp. oral taxon 212*, and *Aggregatibacter segnis*). Associations remained materially unchanged in the fully adjusted analysis (Table 3, model 3) with only 2 species (*Prevotella sp. oral taxon 292* and *Streptococcus lactarius*) no longer achieving significance. After correcting for multiple comparisons, none of the associations achieved significance. Results for all 245 species-level OTUs are given in Table S4.

To determine whether associations for the 15 species significantly associated with incident hypertension were consistent within cohort subgroups, we next explored associations stratified on baseline categories of age, smoking status, BP, and BMI (Table 4). Stratified associations were broadly consistent with primary results in Table 3, although some positive associations were slightly stronger and some inverse associations were slightly attenuated among women whose BMI was ≥ 25 kg/m².

Last, to explore the robustness of the results in our primary prospective analysis (Table 3), we conducted a sensitivity analysis restricting the hazard model to only women who at baseline had normal measured BP, were not using antihypertensive medication, and did not have a history of physician-diagnosed hypertension (N=429; 151 incident hypertension cases). Results were similar to the primary results with respect to the pattern and magnitudes of association (Table S5); however, with the smaller sample size, statistical precision was limited compared with the larger primary analysis.

DISCUSSION

The present study provides both cross-sectional and longitudinal evidence of an association for specific oral



bacteria with BP and hypertension in a community cohort of postmenopausal women. On the basis of untargeted 16S sequencing of subgingival plaque in 1215 women aged 53 to 81 years, mean CLR abundances

Figure 2. Scatterplots of systolic blood pressure (BP; mm Hg) with centered log(2)-ratio (CLR) transformed abundances of *Prevotella sp._oral_taxon_292* (A), *Treponema socranskii* (B), and *Anaeroglobus geminatus* (C).

Correlations were statistically significant ($P < 0.05$) following correction for multiple comparisons using the Benjamin-Hochberg method.

for 47 bacterial species (12 when correcting for multiple comparisons) were significantly different according to baseline measured BP categories. In prospective analysis, 10 bacterial species were significantly associated with higher risk of developing incident hypertension and 5 were significantly associated with lower risk of incident hypertension. Of these, 13 associations remained significant in multivariable adjusted analysis. Similar patterns of association were seen when analysis was restricted to those who were normotensive and not using BP medication at baseline. After correcting for multiple comparisons, the prospective associations were no longer significant. With these collective results, we add to a limited amount of published data on the human oral microbiome and BP, and, to our knowledge, we report the first prospective epidemiological results on the subgingival microbiome and hypertension incidence in aging women.

A recent epidemiologic analysis in the CARDIA (Coronary Artery Risk Development in Young Adults Study) cohort examined cross-sectional relationships between the gut microbiome and BP using untargeted sequencing of the 16S ribosomal RNA gene amplicon in fecal samples from 529 adults aged 48 to 60 years.³⁰ Analyses were conducted at the genus level for 149 fecal microbiota and indicated that both systolic BP and prevalent hypertension were significantly inversely related to gut microbiome α diversity. Several specific fecal taxa appeared to be related with systolic BP and prevalent hypertension; however, relationships tended to not achieve significance after correction for multiple testing. We conducted our analysis on 245 oral bacteria at the species level in 1215 older women and did not see clear variation in α diversity according to baseline BP categories. Differences in fecal and oral plaque microbial composition and diversity could be one explanation.³¹ As in CARDIA, we also identified specific microbial taxa that were related with measured BP and prevalent hypertension, but most of these relationships were likewise not robust to correction for multiple testing. There is general consistency in the cross-sectional epidemiologic results in CARDIA and our present study on a potential relationship between the microbiome and BP in humans. It would be interesting to further understand the similarities and differences in relationships for BP with microbial taxonomy in the gut and mouth from the same individuals, given the mixing of oral and other microbes along the gastrointestinal tract.³²

An important part of interpreting the current results is understanding the functions of the oral microbiota

Table 2. Mean CLR Abundance for 47 (of 245 Total) Bacteria Species That Differed Significantly According to BP and Hypertension Status at Baseline (N=1215)

OTU label	Normal BP (N=429)	Undiagnosed elevated BP (N=306)	Prevalent hypertension (N=480)	P value*
25 Bacteria enriched in elevated BP and hypertension†				
<i>Treponema socranskii</i>	1.58 (2.57)	2.00 (2.48)	2.37 (2.62)	<0.001 ^{†,§}
<i>Oribacterium</i> sp._oral_taxon_078	0.12 (2.67)	0.20 (2.87)	0.88 (2.75)	<0.001 ^{†,§}
<i>Veillonellaceae</i> _[G-1] sp._oral_taxon_155	0.38 (2.93)	0.73 (3.05)	1.12 (3.13)	0.001 ^{†,§}
<i>Prevotella oralis</i>	-0.60 (3.19)	-0.55 (3.26)	0.09 (3.58)	0.003 [†]
<i>Veillonellaceae</i> _[G-1] sp._oral_taxon_150	0.60 (3.06)	0.97 (3.18)	1.26 (3.16)	0.01 [†]
<i>Pseudoramibacter alactolyticus</i>	-2.27 (2.68)	-1.98 (2.82)	-1.61 (2.93)	0.002 ^{†,§}
<i>Bifidobacterium dentium</i>	-2.33 (2.71)	-2.44 (2.56)	-1.70 (3.22)	<0.001 ^{†,§}
<i>Prevotella</i> sp._oral_taxon_292	-1.65 (2.68)	-1.23 (2.97)	-1.02 (3.04)	0.004 [†]
<i>Prevotella buccae</i>	-1.73 (2.42)	-1.67 (2.37)	-1.12 (2.62)	<0.001 ^{†,§}
<i>Tannerella forsythia</i>	1.37 (3.27)	1.68 (3.46)	1.98 (3.56)	0.03 [†]
<i>Fretibacterium</i> sp._oral_taxon_360	2.25 (3.54)	2.63 (3.66)	2.85 (3.81)	0.049 [†]
<i>Scardovia wiggisiae</i>	-2.45 (2.75)	-2.18 (3.10)	-1.86 (3.37)	0.02 [†]
<i>Anaeroglobus geminatus</i>	1.58 (3.52)	1.73 (3.40)	2.17 (3.59)	0.03 [†]
<i>Peptostreptococcaceae</i> _[X][G-1] [Eubacterium]_infi	-1.76 (2.15)	-1.74 (2.29)	-1.25 (2.45)	0.001 ^{†,§}
<i>Fretibacterium</i> sp._oral_taxon_362	-2.01 (2.57)	-1.53 (3.21)	-1.50 (2.93)	0.02 [†]
<i>Peptostreptococcaceae</i> _[X][G-6] [Eubacterium]_noda	-2.31 (2.49)	-1.92 (2.88)	-1.82 (2.85)	0.02 [†]
<i>Fusobacterium nucleatum</i> _subsp._nucleatum	-0.68 (2.64)	-0.46 (2.76)	-0.19 (2.76)	0.03 [†]
<i>Treponema maltophilum</i>	-0.97 (2.47)	-0.74 (2.60)	-0.52 (2.79)	0.03 [†]
<i>Shuttleworthia satelles</i>	-2.51 (2.34)	-2.47 (2.26)	-2.15 (2.45)	0.045 [†]
<i>Mycoplasma salivarium</i>	-2.22 (2.31)	-2.05 (2.50)	-1.78 (2.62)	0.03 [†]
<i>Stomatobaculum longum</i>	-1.22 (2.42)	-0.83 (2.65)	-0.80 (2.58)	0.03 [†]
<i>Campylobacter gracilis</i>	4.87 (1.59)	4.88 (1.70)	5.25 (1.82)	0.001 ^{†,§}
<i>Streptococcus constellatus</i>	-0.17 (3.36)	0.09 (3.44)	0.40 (3.55)	0.045 [†]
<i>Leptotrichia</i> sp._oral_taxon_215	-0.45 (2.73)	0.11 (2.94)	-0.37 (2.72)	0.02
<i>Atopobium rimae</i>	-0.21 (3.02)	-0.22 (3.07)	0.28 (3.29)	0.03 [†]
22 Bacteria enriched in normal BP†				
<i>TM7</i> _[G-1] sp._oral_taxon_869	-1.37 (3.46)	-2.00 (3.07)	-2.14 (2.94)	<0.001 ^{†,§,}
<i>Leptotrichia</i> sp._oral_taxon_212	1.59 (3.05)	1.21 (3.11)	0.83 (3.22)	0.001 ^{†,§}
<i>Rothia aerea</i>	2.26 (3.12)	2.15 (3.09)	1.53 (3.28)	0.001 ^{†,§}
<i>Leptotrichia</i> sp._oral_taxon_225	-0.64 (3.42)	-1.05 (3.31)	-1.31 (3.29)	0.01 [†]
<i>Streptococcus sanguinis</i>	5.07 (2.37)	4.69 (2.62)	4.43 (2.72)	<0.001 ^{†,§}
<i>Fusobacterium nucleatum</i> _subsp._polymorphum	5.15 (2.16)	5.04 (2.16)	4.78 (2.43)	0.04 [†]
<i>TM7</i> _[G-1] sp._oral_taxon_952	2.67 (3.16)	2.40 (3.23)	2.04 (3.43)	0.02 [†]
<i>Cardiobacterium hominis</i>	2.31 (2.86)	2.10 (2.71)	1.70 (2.76)	0.004 [†]
<i>Corynebacterium durum</i> [#]	1.13 (2.84)	0.63 (2.98)	0.54 (2.85)	0.01 [†]
<i>Neisseria elongata</i>	1.74 (3.64)	1.40 (3.43)	1.16 (3.56)	0.046 [†]
<i>Lautropia mirabilis</i>	0.94 (3.13)	0.72 (3.06)	0.36 (3.05)	0.02 [†]
<i>Porphyromonas catoniae</i>	-0.92 (3.13)	-0.99 (3.08)	-1.49 (2.91)	0.01 [†]
<i>Abiotrophia defectiva</i>	-0.05 (3.04)	-0.46 (2.94)	-0.60 (2.88)	0.02 [†]
<i>Aggregatibacter paraphrophilus</i>	-1.79 (3.26)	-2.05 (3.10)	-2.33 (2.83)	0.03 [†]

(Continued)

Table 2. Continued

OTU label	Normal BP (N=429)	Undiagnosed elevated BP (N=306)	Prevalent hypertension (N=480)	P value*
<i>Actinomyces massiliensis</i>	1.47 (2.44)	1.18 (2.50)	0.95 (2.33)	0.01 [†]
<i>Gemella morbillorum</i>	3.18 (3.00)	2.87 (3.05)	2.66 (3.24)	0.04 [†]
<i>TM7_[G-2] sp._oral_taxon_350</i>	-1.88 (3.04)	-1.93 (3.13)	-2.35 (2.88)	0.04
<i>Actinomyces sp._oral_taxon_171</i>	0.69 (2.72)	0.42 (2.77)	0.24 (2.72)	0.047 [†]
<i>Cardiobacterium valvarum</i>	1.57 (3.00)	1.13 (2.90)	1.12 (3.11)	0.045
<i>TM7_[G-1] sp._oral_taxon_348</i>	-0.65 (2.85)	-0.52 (2.95)	-1.02 (2.80)	0.03
<i>Lachnospiraceae_[G-3] sp._oral_taxon_100</i>	0.46 (2.67)	0.62 (2.76)	0.12 (2.85)	0.03
<i>Leptotrichia sp._oral_taxon_417</i>	0.57 (3.18)	0.90 (3.32)	0.32 (3.01)	0.045

Data are mean (SD) CLR bacteria relative abundance. BP indicates blood pressure; CLR, centered log(2)-ratio; and OTU, operational taxonomic unit.

*P value from ANOVA F-tests; superscripts from post hoc pairwise significance tests.

[†]OTUs sorted according to the magnitude of the difference between prevalent hypertension and normal BP. The CLR abundance can be interpreted as a log₂ fold difference for the given bacteria abundance relative to the overall compositional geometric mean. A CLR of 3 indicates an 8-fold (2³) higher abundance, and a CLR of -3 indicates an 8-fold lower abundance.

[‡]Normal vs prevalent hypertension.

[§]Significant (P<0.05) after Benjamini-Hochberg correction.

^{||}Bacteria previously identified within human atherosclerotic plaque (atheroma).

[¶]Normal vs undiagnosed elevated BP.

[#]Bacteria with nitrate-reductase capability for reducing nitrate to nitrite in the oral cavity.

we identified related to BP and hypertension. Our study did not directly evaluate microbial functional characteristics through metabolomics or transcriptomics profiling.³³ However, on the basis of published work, some general observations can be made. One functional pathway through which human microbiota are thought to affect BP regulation is NO homeostasis.⁶⁻⁸ Duncan proposed that salivary nitrite concentrations were enriched by nitrate-reducing oral microbiota, ultimately leading to increased formation of NO,³⁴ a potent vasodilator. Interestingly, women have more effective oral nitrate reduction than men.³⁵ Oral microbiota have been identified that have the genetic make-up to produce nitrate reductase,³⁶⁻³⁸ the key enzyme catalyzing reduction of dietary nitrate to nitrite in the oral cavity. Microbiota are critical to human NO homeostasis because mammalian cells cannot effectively reduce nitrate anions. Nitrate-reducing microbiota, which are listed in Table S6, have been identified at various sites in the oral cavity, including the tongue, hard palate, sublingual, dental plaque, and saliva.³⁶⁻³⁸ Because these previous studies were based on cultivation methods, it is possible that uncultivable bacteria are capable of producing nitrate reductase. Of the 25 bacterial species uniquely identified in these previous studies as having nitrate-reducing capability, 13 were among the 245 subgingival microbiota identified in our Buffalo OsteoPerio study cohort^{16,17} (Table S3). Of these 13, one species (*Corynebacterium durum*) differed significantly with baseline BP categories (higher in normotensive women), and one species (*Neisseria subflava*) was significantly inversely associated with incident hypertension. It is unclear why an association

with BP and hypertension was not seen for the other 11 nitrate-reducing bacteria in our cohort. Given that previous studies characterized microbiota at several oral different sites, and our study focused only on subgingival microbiota, it is possible that a BP influence is attributed to site-specific nitrate-reducing microbiota within the oral cavity. Differences in microbiota composition and diversity have been reported across oral sites.^{39,40} Saliva potentially provides a reflection of the overall oral microbiome at sites not colonized on teeth,⁴⁰ including the tongue, where nitrate-reducing microbiota are abundant. The salivary microbiome has not yet been characterized in our OsteoPerio study cohort; thus, comparison of its microbial composition with BP phenotypes was not possible. We have stored saliva available and will explore this hypothesis in the future as it requires more evaluation.

We previously identified significantly higher mean CLR *Corynebacterium durum* abundance among younger (aged 50-59 years) compared with older (aged ≥70 years) women in our cohort.¹⁷ *C durum* functionally is involved in producing acid from available sugar compounds in saliva,⁴¹ and given the critical role of acidification in converting nitrite to NO,³⁴ it is plausible that *C durum* contributes locally to this process during salivary nitrite concentration. Because we found *C durum* to be of significantly higher abundance in younger compared with older women, it is also plausible that this bacterial species plays a role in maintaining normal BP at younger ages, and its lower abundance in later life contributes to BP dysregulation. If this was the case, we might expect to observe an association between *C durum* and incident hypertension,

Table 3. Fifteen (of 245) Baseline Bacterial Species Significantly Associated With the Risk of Incident Hypertension in Cox Regression Analysis Before Correction for Multiple Comparisons

OTU label	Incident hypertension, CLR mean (SD)					
	No (n=360)	Yes (n=375)	Age-adjusted	Model 1	Model 2	Model 3
			HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
10 Positive associations						
<i>Streptococcus anginosus</i>	0.37 (3.57)	1.08 (3.66)	1.16 (1.04–1.29)	1.15 (1.03–1.28)	1.16 (1.04–1.29)	1.15 (1.03–1.28)
<i>Streptococcus salivarius</i>	2.44 (2.82)	3.03 (3.08)	1.15 (1.04–1.28)	1.16 (1.04–1.28)	1.14 (1.03–1.27)	1.14 (1.03–1.27)
<i>Fretibacterium sp._oral_taxon_362</i>	-2.00 (2.54)	-1.62 (3.14)	1.15 (1.04–1.27)	1.14 (1.03–1.26)	1.14 (1.03–1.27)	1.14 (1.03–1.27)
<i>Selenomonas infelix</i>	0.96 (2.85)	1.50 (2.85)	1.15 (1.03–1.27)	1.14 (1.02–1.26)	1.14 (1.02–1.27)	1.13 (1.01–1.26)
<i>Prevotella sp._oral_taxon_526</i>	-3.03 (2.18)	-2.67 (2.60)	1.13 (1.03–1.25)	1.14 (1.03–1.26)	1.14 (1.03–1.26)	1.14 (1.03–1.26)
<i>Prevotella sp._oral_taxon_292</i>	-1.69 (2.74)	-1.27 (2.87)	1.11 (1.00–1.23)	1.11 (1.00–1.24)	1.10 (0.99–1.22)	1.09 (0.98–1.21)
<i>Megasphaera sp._oral_taxon_123</i>	-3.06 (2.52)	-2.63 (2.72)	1.14 (1.04–1.27)	1.14 (1.03–1.26)	1.14 (1.03–1.26)	1.13 (1.02–1.25)
<i>Capnocytophaga sp._oral_taxon_903</i>	-2.57 (2.59)	-2.21 (2.78)	1.12 (1.01–1.23)	1.11 (1.00–1.22)	1.11 (1.00–1.22)	1.10 (1.00–1.22)
<i>Prevotella sp._oral_taxon_376</i>	-2.91 (2.45)	-2.61 (2.64)	1.11 (1.01–1.23)	1.13 (1.02–1.25)	1.13 (1.03–1.25)	1.14 (1.03–1.25)
<i>Streptococcus lactarius</i>	-1.80 (2.15)	-1.42 (2.48)	1.10 (1.00–1.21)	1.10 (1.00–1.22)	1.08 (0.97–1.20)	1.08 (0.98–1.20)
5 Inverse associations						
<i>Neisseria subflava</i> *	-1.99 (3.15)	-2.40 (2.96)	0.90 (0.81–1.00)	0.89 (0.80–0.98)	0.88 (0.80–0.98)	0.89 (0.80–0.99)
<i>Bergeyella sp._oral_taxon_907</i>	-1.98 (2.31)	-2.19 (2.27)	0.91 (0.81–1.01)	0.89 (0.80–1.00)	0.89 (0.80–0.99)	0.89 (0.79–0.99)
<i>Gemella morbillorum</i>	3.32 (2.95)	2.80 (3.08)	0.88 (0.79–0.97)	0.88 (0.79–0.98)	0.88 (0.79–0.98)	0.89 (0.80–0.99)
<i>Leptotrichia sp._oral_taxon_212</i>	1.74 (2.98)	1.14 (3.15)	0.85 (0.77–0.94)	0.85 (0.76–0.95)	0.86 (0.77–0.96)	0.87 (0.78–0.98)
<i>Aggregatibacter segnis</i>	-0.56 (3.44)	-1.30 (3.13)	0.82 (0.74–0.91)	0.83 (0.75–0.92)	0.83 (0.75–0.93)	0.84 (0.75–0.93)

HR and 95% CI are for a 1-SD increment in baseline CLR bacterial species. Age-adjusted analysis (n=735). Model 1: age, race and ethnicity, education, neighborhood socioeconomic status, and self-rated general health (n=723). Model 2: includes model 1 covariates and history of diabetes treated with medication (n=723). Model 3: includes model 2 covariates and dietary Healthy Eating Index score, physical activity, and statin use (n=715). Uncorrected Wald test of HR=1 in the age-adjusted model. After Benjamini-Hochberg correction, associations no longer were significant. CLR indicates centered log₂-ratio; HR, hazard ratio; and OTU, operational taxonomic unit.

*Bacteria with nitrate-reductase capability for reducing nitrate to nitrite in the oral cavity.

but we did not. Further understanding of how *C durum* might affect BP homeostasis is needed.

Neisseria subflava, another previously identified nitrate-reducing microbiota (Table 4), was significantly inversely associated with the risk of incident hypertension in our cohort. *N subflava* is a commensal microorganism in the healthy oral microbiome that exhibits propensity for biofilm dispersal and translocation.⁴² Our previous cross-sectional evaluation of *N subflava* did not reveal significant differences in its abundance according to age¹⁷ or periodontal disease,¹⁶ nor did we observe differences in *N subflava* according to BP categories at baseline in the present study. Nevertheless, in multivariable adjusted analysis controlling for differences in age and other demographic variables, treated

diabetes, diet, and physical activity levels, each 1-SD increment in baseline *N subflava* was associated with an 11% lower risk of developing hypertension during the 10-year follow-up (Table 3, model 3). It is possible this microorganism plays a particularly prominent role in salivary nitrite formation within the oral cavity or, potentially, through translocation, it might be involved in nitrite production elsewhere in the gastrointestinal tract. Likewise, there could be strain-dependent variation in associations between oral bacterial species and BP homeostasis.⁴³

Limited published data are available from human epidemiological studies on the oral microbiome and BP. Desvarieux¹⁰ conducted a cross-sectional study on 653 adults, mean age 70 years (60%

Table 4. Multivariable HRs for Hypertension Stratified on Baseline Characteristics for the 15 of 245 Bacteria Significantly Associated With Incident Hypertension (N=735)

OTU label	Overall (n=1215; 387 cases)	Age, y		Smoking status		Blood pressure*		BMI, kg/m ²	
		<65 (n=410; 214 cases)	≥65 (n=325; 173 cases)	Never (n=391; 175 cases)	Ever (n=344; 200 cases)	Normal (n=429; 151 cases)	Elevated (n=306; 224 cases)	<25 (n=382; 168 cases)	≥25 (n=353; 207 cases)
<i>Streptococcus anginosus</i>	1.15 (1.03-1.28)	1.15 (0.99-1.35)	1.13 (0.97-1.31)	1.28 (1.09-1.50)	1.04 (0.90-1.20)	1.24 (1.05-1.48)	1.14 (0.98-1.31)	1.22 (1.04-1.43)	1.08 (0.93-1.25)
<i>Streptococcus salivarius</i>	1.16 (1.04-1.28)	1.21 (1.04-1.40)	1.14 (0.98-1.33)	1.22 (1.05-1.43)	1.10 (0.96-1.27)	1.14 (0.97-1.35)	1.16 (1.01-1.33)	1.21 (1.05-1.41)	1.11 (0.95-1.29)
<i>Fretibacterium sp._oral_taxon_362</i>	1.14 (1.03-1.26)	1.21 (1.06-1.39)	1.04 (0.88-1.23)	1.17 (0.98-1.39)	1.09 (0.96-1.25)	1.20 (1.00-1.44)	1.06 (0.93-1.19)	1.14 (0.94-1.39)	1.12 (0.99-1.26)
<i>Selenomonas infelix</i>	1.14 (1.02-1.26)	1.10 (0.95-1.28)	1.17 (1.00-1.37)	1.11 (0.94-1.30)	1.15 (1.00-1.34)	1.31 (1.10-1.56)	0.99 (0.86-1.14)	1.20 (1.02-1.41)	1.09 (0.94-1.27)
<i>Prevotella sp._oral_taxon_526</i>	1.14 (1.03-1.26)	1.09 (0.94-1.26)	1.17 (1.02-1.35)	1.12 (0.95-1.33)	1.10 (0.97-1.24)	1.23 (1.05-1.43)	1.08 (0.94-1.24)	1.06 (0.88-1.29)	1.14 (1.02-1.29)
<i>Prevotella sp._oral_taxon_292</i>	1.11 (1.00-1.24)	1.18 (1.01-1.38)	1.05 (0.91-1.22)	1.06 (0.90-1.24)	1.12 (0.97-1.28)	1.11 (0.93-1.32)	1.03 (0.90-1.18)	1.24 (1.05-1.45)	1.04 (0.90-1.20)
<i>Megasphaera sp._oral_taxon_123</i>	1.14 (1.03-1.26)	1.18 (1.01-1.37)	1.16 (1.00-1.34)	1.15 (0.99-1.35)	1.08 (0.94-1.24)	1.20 (1.01-1.42)	1.19 (1.04-1.35)	1.05 (0.90-1.23)	1.24 (1.07-1.43)
<i>Capnocytophaga sp._oral_taxon_903</i>	1.11 (1.00-1.22)	1.04 (0.91-1.20)	1.16 (1.00-1.35)	1.07 (0.93-1.24)	1.21 (1.05-1.40)	1.11 (0.95-1.30)	1.16 (1.01-1.33)	0.99 (0.84-1.16)	1.24 (1.08-1.41)
<i>Prevotella sp._oral_taxon_376</i>	1.13 (1.02-1.25)	1.15 (1.01-1.30)	1.09 (0.93-1.27)	1.20 (1.03-1.40)	1.05 (0.92-1.20)	1.17 (1.00-1.36)	1.17 (1.02-1.34)	0.98 (0.81-1.19)	1.18 (1.05-1.32)
<i>Streptococcus lactarius</i>	1.10 (1.00-1.22)	1.09 (0.95-1.26)	1.13 (0.98-1.31)	1.14 (0.99-1.33)	1.06 (0.91-1.22)	1.05 (0.89-1.25)	1.08 (0.95-1.22)	1.18 (1.02-1.37)	1.04 (0.90-1.19)
<i>Neisseria subflava</i> [†]	0.89 (0.80-0.98)	0.94 (0.81-1.09)	0.86 (0.74-1.00)	0.82 (0.69-0.96)	0.97 (0.84-1.11)	0.84 (0.70-1.01)	0.94 (0.82-1.07)	0.78 (0.66-0.93)	0.97 (0.85-1.12)
<i>Bergeyella sp._oral_taxon_907</i>	0.89 (0.80-1.00)	0.92 (0.79-1.07)	0.86 (0.74-1.02)	0.88 (0.75-1.04)	0.92 (0.79-1.06)	0.92 (0.77-1.09)	0.91 (0.79-1.04)	0.82 (0.68-0.97)	0.94 (0.81-1.09)
<i>Gemella morbillorum</i>	0.88 (0.79-0.98)	0.79 (0.67-0.92)	0.95 (0.82-1.11)	0.81 (0.69-0.95)	0.98 (0.85-1.13)	0.83 (0.70-0.98)	0.92 (0.79-1.06)	0.94 (0.80-1.10)	0.86 (0.75-0.99)
<i>Leptotrichia sp._oral_taxon_212</i>	0.85 (0.76-0.95)	0.75 (0.64-0.88)	0.98 (0.84-1.14)	0.79 (0.67-0.92)	0.93 (0.81-1.08)	0.87 (0.73-1.03)	0.90 (0.78-1.03)	0.85 (0.73-0.99)	0.85 (0.73-0.98)
<i>Aggregatibacter segnis</i>	0.83 (0.75-0.92)	0.82 (0.71-0.94)	0.84 (0.72-0.98)	0.80 (0.69-0.93)	0.93 (0.80-1.08)	0.85 (0.71-1.00)	0.84 (0.73-0.96)	0.81 (0.69-0.96)	0.86 (0.75-0.99)

Data are HR (95% CI) for a 1-SD increment in baseline centered log(2)-ratio bacteria abundance adjusted for model 1 covariates in Table 3. The 15 bacteria were significantly associated with hypertension in unstratified results (Table 3) based on an uncorrected Wald test of HR=1 in age-adjusted analysis. Results in the above table are not corrected for multiple comparisons. BMI indicates body mass index; HR, hazard ratio; and OTU, operational taxonomic unit.

*Normal blood pressure (BP)=systolic BP <120 mm Hg and diastolic BP <80 mm Hg, not using BP medication; elevated=undiagnosed elevated BP at examination, systolic BP ≥120 mm Hg or diastolic BP ≥80 mm Hg, not using BP medication and without history of hypertension diagnosis.

[†]Bacteria species with nitrate-reductase capability for reducing nitrate to nitrite in the oral cavity.

women), wherein subgingival plaque was analyzed using targeted measurement of the presence of 11 microbiota (*Aggregatibacter actinomycetemcomitans*, *Porphyromonas gingivalis*, *Tannerella forsythia*, *Treponema denticola*, *Fusobacterium nucleatum*, *Prevotella intermedia*, *Campylobacter rectus*, *Parvimonas micra*, *Eikenella corrodens*, *Veillonella parvula*, and *Actinomyces naeslundii*). Prevalent hypertension was based on measured BP as systolic ≥ 140 mm Hg or diastolic ≥ 90 mm Hg, or self-reported use of BP medication. Mean systolic and diastolic BP was positively ($P < 0.001$) associated with tertiles of bacterial burden score based on presence of *P. gingivalis*, *T. forsythia*, *A. actinomycetemcomitans*, and *T. denticola*. Multivariable adjusted odds ratios for prevalent hypertension across incremental tertiles of the bacteria score were 1.00 (referent), 2.48, and 3.93 (trend, $P < 0.001$). In the present study (Table 2), we observed significant differences in mean *T. forsythia* abundance according to baseline BP categories, higher in women with prevalent hypertension compared with normal BP (corrected $P = 0.03$). Although our finding of a relationship between *T. forsythia* and BP is consistent with the finding of Desvarieux, the other 3 bacteria species included in their bacteria score were not associated with BP in our cohort. The bacteria targeted in the study by Desvarieux were not nitrate reducers. In another human study, Kapil⁴⁴ reported that 7 days of antiseptic mouthwash lowered the abundance of nitrate-reducing microbiota, resulting in a 90% decrease in salivary nitrite concentration ($P < 0.001$) and concomitant increase in systolic and diastolic BP ($P = 0.002$) within 24 hours of oral microbiome disruption. Collectively, the studies by Desvarieux and Kapil, and our present findings, indicate the oral microbiome is correlated with BP and prevalent hypertension in humans.

No other published study has reported prospective associations between oral microbiota and incident hypertension. Thus, our finding of 15 baseline subgingival microbiota associated with future development of treated hypertension is novel (Table 3). Particularly interesting is that only one of these organisms (*N. subflava*) is a known nitrate reducer. So then, how might the remaining oral microbiota influence BP regulation and hypertension development? A major underpinning of essential hypertension is arterial atherosclerosis.⁴⁵ During early stages of atherogenesis, chemical and mechanical insults to the endothelium lead to endothelial dysfunction, which promotes lipid uptake, inflammation, and atheroma formation in the subintimal space and loss of vasodilatory function needed for BP regulation.⁴⁶ It has been hypothesized that oral microbiota translocate through leaky gingival epithelium into the systemic circulation, where they are transported to extraoral sites and contribute to disease, the so-called "mobile microbiome" hypothesis.⁹ Indeed, subgingival

microbiota, including *T. forsythia* and *P. gingivalis*, have been identified as part of a biofilm residing within excised atheroma.⁴⁷ *P. gingivalis* also has been shown to adhere to endothelial cells by way of circulating dendritic cells and induce local proinflammatory signaling via secretion of lipopolysaccharide.⁴⁸ Thus, it seems plausible that a nonnitrate reducing pathway through which oral bacteria might influence BP regulation is arterial atherosclerosis and its effect on endothelial function. Experimental evidence supporting this hypothesis was provided by Tonetti,⁴⁹ who demonstrated significant improvement in endothelial flow-mediated dilation in adults with periodontitis randomized to intensive periodontal therapy compared with usual care. Dental plaque significantly improved in the intensive therapy group, which would be expected to have resulted in a healthier oral microbiome.⁵⁰ In our present study, both *T. forsythia* and *P. gingivalis* were enriched in women with prevalent hypertension compared with normal BP at baseline, although only *T. forsythia* achieved statistical significance.

Strengths of the present study include both cross-sectional and longitudinal analyses, the relatively large cohort of an understudied population (postmenopausal women) on the oral microbiome and its relation to systemic disease, and the community-based enrollment not using oral health status or BP as selection criteria. The findings reported herein provide a comparative benchmark for future studies in clinical and other community populations. Use of untargeted 16S sequencing and well-documented laboratory protocols and quality control minimizing batch-related variation is a strength. Because incident hypertension was documented during 10 years mean following baseline subgingival plaque collection used for microbiome analysis, it is unlikely that reverse causation bias is the explanation for our prospective findings.

Limitations include sampling subgingival plaque on only a portion of teeth present that were not selected on periodontal disease severity at the site. This might have resulted in lower abundance of bacteria species that could be relevant to BP. A different oral site, such as saliva, might provide richer understanding on associations between oral bacteria and BP, especially for those involved with nitrate reduction. We plan to explore this hypothesis in our cohort. We quantified associations for individual bacteria species with BP and hypertension. It is possible that clusters of species with specific functional properties, rather than single taxa, are the more relevant pathogenic factor in BP dysregulation. Studies that assess functionality of the microbiome will help to answer this question. The Women's Health Initiative focused on postmenopausal women; thus, men were not included in our study, but have been in other studies in this area.^{10,35,44}

There is no single agreed upon approach to correct for multiple comparisons, and results can differ based on the approach used.⁵¹ We used the Benjamini-Hochberg²⁹ method, which yielded 12 significant tests of mean bacterial abundance of 47 that achieved significance in uncorrected analysis (Table 2). Debate exists whether correction for multiple testing is needed in epidemiologic studies⁵² because doing so likely results in a conservative understanding of an association,⁵³ herein between microbiota and BP. We provide the corrected results so readers are informed on the range of our findings.

CONCLUSIONS

Specific oral bacteria species are associated with BP status cross sectionally and with development of incident hypertension prospectively in postmenopausal women. Nonnitrate reduction mechanisms could be involved. Additional research is needed to confirm our observations and to characterize mechanisms. Evaluation of the microbiome at other oral sites, such as saliva, and greater understanding of bacteria functionality will further expand existing knowledge on oral microbial composition and BP homeostasis in human populations.

ARTICLE INFORMATION

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Disclosures

None.

Supplemental Material

Tables S1–S6

Figure S1

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SUPPLEMENTAL MATERIAL

Table S1. Baseline characteristics by incident hypertension status (N=735).

	No (N=360)	Yes (N=375)	P-value*
Age (years)	65.3 (6.7)	66.2 (6.8)	0.10
nSES	76.4 (7.0)	76.2 (6.7)	0.68
BMI (kg/m ²)	24.9 (4.2)	26.2 (4.3)	<.001
Systolic BP (mmHg)	110 (13.5)	124 (16.5)	<.001
Diastolic BP (mmHg)	67.2 (7.1)	72.4 (8.7)	<.001
Dietary HEI score	68.5 (10.3)	67.2 (10.1)	0.09
Physical activity (MET-hr/wk)	16.4 (14.6)	14.6 (13.7)	0.09
Whole Mouth CAL	2.4 (0.6)	2.4 (0.7)	0.43
Whole Mouth PPD	2.2 (0.4)	2.2 (0.4)	0.35
Smoking status			<.001
Never	216 (60.0)	175 (46.7)	
Former	133 (36.9)	190 (50.7)	
Current	11 (3.1)	10 (2.7)	
Race-ethnicity			0.29
Other	6 (1.7)	4 (1.1)	
Black or African American	4 (1.1)	1 (0.3)	
White	350 (97.2)	370 (98.7)	
Education			0.52
High school or less	66 (18.6)	77 (20.9)	
College or some college	153 (43.1)	164 (44.6)	
Postgraduate	136 (38.3)	127 (34.5)	
Treated diabetes	4 (1.1)	12 (3.2)	0.05
Statin use	33 (9.2)	37 (9.9)	0.75
HT use			0.16
Never	123 (34.2)	119 (31.7)	
Former	58 (16.1)	81 (21.6)	
Current	179 (49.7)	175 (46.7)	
Self-rated general health			0.18
Excellent	92 (25.8)	69 (18.5)	
Very good	171 (47.9)	204 (54.7)	
Good	85 (23.8)	90 (24.1)	
Fair or poor	9 (2.5)	10 (2.7)	

Data are mean (SD) or N (%) for continuous or categorical variables, respectively.

*P-value from ANOVA F-test and Pearson chi-square test for continuous and categorical variables, respectively.

nSES, neighborhood socioeconomic status; BMI, body mass index; BP, blood pressure; HEI, healthy eating index; MET-hr/wk, metabolic equivalent hours per week; CAL, clinical attachment level; PPD,

probing pocket depth; HT, menopausal hormone therapy. Missing data nSES (10, HEI (8), physical activity (3), PPD (4), CAL (4), education (12), smoking (1), general health (5).

Table S2. Pearson correlations between baseline mean CLR bacterial abundance and baseline systolic and diastolic BP (N=1,215).

OTU Label	Systolic BP	Diastolic BP
<i>Prevotella sp._oral_taxon_292</i>	0.15 [†]	0.08
<i>Treponema socranskii</i>	0.13 [†]	0.05
<i>Anaeroglobus geminatus</i>	0.12 [†]	0.07
<i>Veillonellaceae_[G-1] sp._oral_taxon_150</i>	0.10	0.02
<i>Treponema maltophilum</i>	0.09	0.01
<i>Anaerolineae_[G-1] sp._oral_taxon_439</i>	0.08	0.00
<i>Megasphaera micronuciformis</i>	0.08	0.03
<i>Bifidobacterium dentium</i>	0.08	0.00
<i>Fretibacterium sp._oral_taxon_360</i>	0.08	0.05
<i>Oribacterium sp._oral_taxon_078</i>	0.08	-0.02
<i>Veillonellaceae_[G-1] sp._oral_taxon_155</i>	0.08	0.05
<i>Veillonella atypica</i>	0.08	-0.01
<i>Prevotella oralis</i>	0.08	0.04
<i>Peptostreptococcaceae_[XI][G-1][Eubacterium]_infi</i>	0.08	0.02
<i>Stomatobaculum longum</i>	0.07	-0.04
<i>Scardovia wiggisiae</i>	0.07	-0.01
<i>Campylobacter gracilis</i>	0.07	0.05
<i>Pseudoramibacter alactolyticus</i>	0.07	0.03
<i>Campylobacter curvus</i>	0.07	0.02
<i>Streptococcus constellatus</i>	0.07	0.00
<i>Shuttleworthia satelles</i>	0.07	0.02
<i>Prevotella buccae</i>	0.07	0.03
<i>Tannerella forsythia</i>	0.06	0.02
<i>Veillonella parvula</i>	0.06	-0.01
<i>Atopobium sp._oral_taxon_199</i>	0.06	0.00
<i>Olsenella sp._oral_taxon_807</i>	0.06	0.04
<i>Mycoplasma salivarium</i>	0.06	0.03
<i>Mitsuokella sp._oral_taxon_131</i>	0.06	-0.03
<i>Streptococcus parasanguinis_II</i>	0.06	-0.03
<i>Streptococcus parasanguinis_I</i>	0.06	0.00
<i>Gemella sanguinis</i>	0.06	0.04
<i>Streptococcus mutans</i>	0.05	-0.04
<i>Bacteroidales_[G-2] sp._oral_taxon_274</i>	0.05	0.05
<i>Rothia mucilaginosa</i>	0.05	0.01
<i>Fusobacterium nucleatum_subsp._animalis</i>	0.05	0.03
<i>Dialister invisus</i>	0.05	0.03
<i>Dialister pneumosintes</i>	0.05	0.02
<i>Prevotella salivae</i>	0.05	-0.04
<i>Bacteroidaceae_[G-1] sp._oral_taxon_272</i>	0.04	0.00
<i>Prevotella histicola</i>	0.04	-0.01

<i>Solobacterium moorei</i>	0.04	-0.02
<i>Tannerella sp._oral_taxon_808</i>	0.04	0.00
<i>Veillonellaceae_[G-1] sp._oral_taxon_129</i>	0.04	0.03
<i>Prevotella baroniae</i>	0.04	0.04
<i>Selenomonas sputigena</i>	0.04	0.02
<i>Veillonella dispar</i>	0.04	-0.02
<i>Streptococcus salivarius</i>	0.04	0.00
<i>Fretibacterium sp._oral_taxon_359</i>	0.04	0.01
<i>Atopobium rimae</i>	0.04	0.03
<i>Selenomonas sp._oral_taxon_136</i>	0.04	-0.05
<i>Alloprevotella tannerae</i>	0.04	0.01
<i>Prevotella pallens</i>	0.04	0.01
<i>Parvimonas micra</i>	0.04	0.03
<i>Actinomyces gerencseriae</i>	0.04	0.01
<i>Desulfobulbus sp._oral_taxon_041</i>	0.04	0.00
<i>Prevotella melaninogenica</i>	0.04	0.00
<i>Prevotella denticola</i>	0.04	0.01
<i>Atopobium parvulum</i>	0.04	-0.01
<i>Fretibacterium fastidiosum</i>	0.04	0.00
<i>Peptostreptococcaceae_[XI][G-6] [Eubacterium]_noda</i>	0.03	0.02
<i>Prevotella micans</i>	0.03	-0.01
<i>Selenomonas infelix</i>	0.03	0.04
<i>Fretibacterium sp._oral_taxon_362</i>	0.03	-0.01
<i>Campylobacter concisus</i>	0.03	0.00
<i>Fusobacterium nucleatum_subsp._vincentii</i>	0.03	0.04
<i>Leptotrichia goodfellowii</i>	0.03	0.05
<i>Selenomonas flueggei</i>	0.03	0.01
<i>Leptotrichia shahii</i>	0.03	0.03
<i>Selenomonas sp._oral_taxon_936</i>	0.03	0.01
<i>Leptotrichia sp._oral_taxon_498</i>	0.03	0.00
<i>Actinobaculum sp._oral_taxon_848</i>	0.03	0.01
<i>Porphyromonas gingivalis</i>	0.02	0.04
<i>Prevotella sp._oral_taxon_300</i>	0.02	-0.01
<i>Prevotella dentalis</i>	0.02	0.02
<i>Selenomonas noxia</i>	0.02	-0.02
<i>Johnsonella sp._oral_taxon_166</i>	0.02	0.00
<i>Alloprevotella sp._oral_taxon_308</i>	0.02	0.00
<i>Streptococcus anginosus</i>	0.02	0.00
<i>Actinobaculum sp._oral_taxon_183</i>	0.02	0.04
<i>Selenomonas sp._oral_taxon_134</i>	0.02	0.05
<i>Leptotrichia hofstadii</i>	0.02	0.01
<i>Prevotella maculosa</i>	0.02	-0.02
<i>TM7_[G-1] sp._oral_taxon_349</i>	0.01	0.00
<i>Streptococcus cristatus</i>	0.01	0.02

<i>Prevotella oulorum</i>	0.01	0.01
<i>Selenomonas</i> sp._oral_taxon_146	0.01	0.02
<i>Campylobacter showae</i>	0.01	0.00
<i>Leptotrichia</i> sp._oral_taxon_417	0.01	-0.03
<i>Lachnoanaerobaculum umeaense</i>	0.01	0.02
<i>Streptococcus lactarius</i>	0.01	0.05
Veillonellaceae_[G-1] sp._oral_taxon_145	0.01	0.03
<i>Fusobacterium nucleatum</i> _subsp._nucleatum	0.01	-0.02
<i>Neisseria flavescens</i>	0.01	0.00
TM7_[G-1] sp._oral_taxon_352	0.01	0.01
Lachnospiraceae_[G-8] sp._oral_taxon_500	0.01	-0.01
<i>Capnocytophaga</i> sp._oral_taxon_324	0.01	0.02
<i>Leptotrichia</i> sp._oral_taxon_215	0.01	0.04
<i>Fretibacterium</i> sp._oral_taxon_361	0.01	-0.03
<i>Leptotrichia hongkongensis</i>	0.01	0.00
<i>Selenomonas diana</i> e	0.01	-0.01
<i>Leptotrichia</i> sp._oral_taxon_223	0.01	0.00
<i>Leptotrichia buccalis</i>	0.01	0.03
<i>Prevotella</i> sp._oral_taxon_306	0.01	-0.05
<i>Fusobacterium</i> sp._oral_taxon_203	0.01	0.04
<i>Ottowia</i> sp._oral_taxon_894	0.01	0.03
<i>Prevotella veroralis</i>	0.00	0.01
<i>Catonella morbi</i>	0.00	0.03
<i>Capnocytophaga granulosa</i>	0.00	0.02
<i>Kingella oralis</i>	0.00	0.01
<i>Treponema lecithinolyticum</i>	0.00	-0.03
<i>Lachnoanaerobaculum orale</i>	0.00	-0.04
<i>Neisseria subflava</i>	0.00	0.02
Ruminococcaceae_[G-1] sp._oral_taxon_075	0.00	-0.04
<i>Prevotella</i> sp._oral_taxon_526	0.00	-0.02
<i>Selenomonas artemidis</i>	0.00	0.01
<i>Prevotella</i> sp._oral_taxon_313	0.00	0.00
<i>Streptococcus gordonii</i>	0.00	-0.01
<i>Neisseria bacilliformis</i>	0.00	-0.03
<i>Porphyromonas</i> sp._oral_taxon_279	0.00	-0.03
<i>Actinomyces meyeri</i>	0.00	0.03
<i>Kingella denitrificans</i>	0.00	0.00
<i>Streptococcus australis</i>	0.00	0.01
<i>Selenomonas</i> sp._oral_taxon_126	0.00	-0.02
<i>Streptococcus sobrinus</i>	0.00	-0.06
TM7_[G-1] sp._oral_taxon_346	0.00	0.01
<i>Fretibacterium</i> sp._oral_taxon_358	0.00	-0.02
Peptostreptococcaceae_[X1][G-5] [Eubacterium]_saph	-0.01	-0.05
<i>Actinomyces</i> sp._oral_taxon_180	-0.01	-0.02

<i>Streptococcus sp._oral_taxon_074</i>	-0.01	0.02
<i>Veillonella rogosae</i>	-0.01	0.06
<i>Centipeda periodontii</i>	-0.01	0.00
<i>Alloprevotella rava</i>	-0.01	-0.01
<i>Fusobacterium periodonticum</i>	-0.01	0.00
<i>Prevotella sp._oral_taxon_376</i>	-0.01	0.04
<i>Fusobacterium sp._oral_taxon_370</i>	-0.01	-0.03
<i>Capnocytophaga sputigena</i>	-0.01	0.01
<i>Treponema denticola</i>	-0.01	-0.02
<i>Prevotella sp._oral_taxon_317</i>	-0.01	-0.01
<i>TM7_[G-5] sp._oral_taxon_356</i>	-0.01	0.01
<i>Actinomyces johnsonii</i>	-0.01	0.02
<i>TM7_[G-3] sp._oral_taxon_351</i>	-0.01	-0.03
<i>Prevotella multiformis</i>	-0.01	-0.03
<i>Johnsonella ignava</i>	-0.01	-0.02
<i>Porphyromonas sp._oral_taxon_278</i>	-0.01	0.01
<i>Porphyrobacter tepidarius</i>	-0.01	-0.01
<i>Capnocytophaga sp._oral_taxon_338</i>	-0.01	-0.02
<i>Capnocytophaga sp._oral_taxon_903</i>	-0.01	-0.02
<i>Aggregatibacter sp._oral_taxon_458</i>	-0.02	0.02
<i>Peptostreptococcus stomatis</i>	-0.02	0.03
<i>Treponema sp._oral_taxon_231</i>	-0.02	-0.03
<i>Veillonella denticariosi</i>	-0.02	-0.03
<i>Filifactor alocis</i>	-0.02	-0.03
<i>Prevotella oris</i>	-0.02	0.00
<i>Selenomonas sp._oral_taxon_919</i>	-0.02	-0.01
<i>Neisseria sicca</i>	-0.02	-0.03
<i>Neisseria pharyngis</i>	-0.02	0.00
<i>Prevotella nigrescens</i>	-0.02	0.00
<i>Leptotrichia wadei</i>	-0.02	-0.05
<i>Porphyromonas endodontalis</i>	-0.02	0.00
<i>Eikenella corrodens</i>	-0.02	0.02
<i>Aggregatibacter sp._oral_taxon_513</i>	-0.02	0.02
<i>Haemophilus parainfluenzae</i>	-0.02	0.01
<i>Granulicatella adiacens</i>	-0.02	-0.05
<i>TM7_[G-2] sp._oral_taxon_350</i>	-0.03	-0.05
<i>Haemophilus sp._oral_taxon_036</i>	-0.03	0.03
<i>Gemella haemolysans</i>	-0.03	-0.03
<i>Selenomonas sp._oral_taxon_892</i>	-0.03	0.00
<i>TM7_[G-6] sp._oral_taxon_870</i>	-0.03	-0.02
<i>Aggregatibacter aphrophilus</i>	-0.03	0.03
<i>Aggregatibacter segnis</i>	-0.03	0.00
<i>Brevundimonas diminuta</i>	-0.03	-0.04
<i>Prevotella sp._oral_taxon_314</i>	-0.03	-0.05

<i>Sphingomonas</i> sp._oral_taxon_006	-0.03	-0.03
<i>Granulicatella elegans</i>	-0.03	-0.01
<i>Leptotrichia</i> sp._oral_taxon_219	-0.03	0.02
<i>Capnocytophaga</i> sp._oral_taxon_902	-0.03	-0.02
<i>Actinomyces</i> sp._oral_taxon_178	-0.03	-0.02
<i>Capnocytophaga</i> sp._oral_taxon_326	-0.03	0.02
<i>Microbacterium flavescens</i>	-0.03	-0.02
TM7_[G-1] sp._oral_taxon_348	-0.03	-0.01
<i>Selenomonas</i> sp._oral_taxon_133	-0.03	-0.02
<i>Capnocytophaga</i> sp._oral_taxon_336	-0.03	-0.03
<i>Capnocytophaga</i> sp._oral_taxon_412	-0.03	0.00
<i>Actinomyces</i> sp._oral_taxon_169	-0.03	-0.02
<i>Prevotella intermedia</i>	-0.03	-0.03
<i>Bergeyella</i> sp._oral_taxon_322	-0.04	0.02
<i>Capnocytophaga</i> sp._oral_taxon_323	-0.04	-0.03
Peptostreptococcaceae_[XI][G-7] [Eubacterium]_yuri	-0.04	0.03
<i>Prevotella saccharolytica</i>	-0.04	-0.02
TM7_[G-1] sp._oral_taxon_952	-0.04	0.01
<i>Capnocytophaga gingivalis</i>	-0.04	0.03
<i>Porphyromonas</i> sp._oral_taxon_284	-0.04	-0.02
<i>Lachnoanaerobaculum saburreum</i>	-0.04	-0.03
<i>Rothia dentocariosa</i>	-0.04	0.00
Peptostreptococcaceae_[XI][G-9] [Eubacterium]_brac	-0.04	0.00
<i>Neisseria elongata</i>	-0.04	0.03
<i>Bacteroidetes</i> _[G-5] sp._oral_taxon_511	-0.04	-0.07
<i>Megasphaera</i> sp._oral_taxon_123	-0.04	-0.01
<i>Actinomyces oris</i>	-0.04	-0.04
<i>Selenomonas</i> sp._oral_taxon_137	-0.04	-0.04
<i>Capnocytophaga leadbetteri</i>	-0.04	-0.02
<i>Tannerella</i> sp._oral_taxon_286	-0.04	-0.02
<i>Porphyromonas</i> sp._oral_taxon_275	-0.04	0.00
<i>Corynebacterium matruchotii</i>	-0.04	0.02
<i>Actinomyces</i> sp._oral_taxon_171	-0.04	0.01
<i>Aggregatibacter paraphrophilus</i>	-0.05	-0.03
Lachnospiraceae_[G-3] sp._oral_taxon_100	-0.05	0.00
<i>Haemophilus parahaemolyticus</i>	-0.05	-0.01
<i>Actinomyces</i> sp._oral_taxon_170	-0.05	0.00
<i>Sphingomonas echinoides</i>	-0.05	-0.01
<i>Haemophilus haemolyticus</i>	-0.05	-0.03
<i>Bergeyella</i> sp._oral_taxon_907	-0.05	-0.04
<i>Veillonella</i> sp._oral_taxon_780	-0.05	-0.02
<i>Streptococcus</i> sp._oral_taxon_056	-0.05	-0.04
<i>Fusobacterium naviforme</i>	-0.05	-0.02
SR1_[G-1] sp._oral_taxon_874	-0.05	-0.02

<i>Capnocytophaga sp._oral_taxon_332</i>	-0.05	0.00
<i>Streptococcus intermedius</i>	-0.05	0.01
<i>Prevotella loescheii</i>	-0.05	-0.03
<i>Streptococcus oralis</i>	-0.05	0.03
<i>Neisseria oralis</i>	-0.05	-0.01
<i>TM7_[G-1] sp._oral_taxon_488</i>	-0.05	-0.01
<i>Capnocytophaga sp._oral_taxon_864</i>	-0.05	-0.01
<i>TM7_[G-1] sp._oral_taxon_347</i>	-0.05	-0.07
<i>Actinomyces naeslundii</i>	-0.05	0.01
<i>Prevotella pleuritidis</i>	-0.05	-0.04
<i>Leptotrichia sp._oral_taxon_392</i>	-0.05	0.02
<i>Alloprevotella sp._oral_taxon_473</i>	-0.06	-0.05
<i>Parvimonas sp._oral_taxon_393</i>	-0.06	-0.04
<i>Cardiobacterium valvarum</i>	-0.06	0.05
<i>Prevotella sp._oral_taxon_472</i>	-0.06	0.04
<i>Treponema sp._oral_taxon_237</i>	-0.06	-0.06
<i>Cardiobacterium hominis</i>	-0.06	0.00
<i>Lautropia mirabilis</i>	-0.06	0.00
<i>Leptotrichia sp._oral_taxon_212</i>	-0.07	0.02
<i>Actinomyces massiliensis</i>	-0.07	0.01
<i>TM7_[G-1] sp._oral_taxon_869</i>	-0.07	-0.06
<i>Fusobacterium nucleatum_subsp._polymorphum</i>	-0.07	0.00
<i>Abiotrophia defectiva</i>	-0.07	-0.04
<i>Corynebacterium durum</i>	-0.08	0.00
<i>Porphyromonas catoniae</i>	-0.08	0.02
<i>Leptotrichia sp._oral_taxon_225</i>	-0.08	-0.03
<i>Rothia aeria</i>	-0.08	0.03
<i>Streptococcus sanguinis</i>	-0.08	0.00
<i>Gemella morbillorum</i>	-0.09	0.00

Table is sorted according to magnitude of correlations with systolic blood pressure (BP).

Uncorrected $P < 0.05$ for $|r| \geq 0.06$.

$P < 0.05$ after Benjamini-Hochberg[†] correction for multiple testing.

Table S3. Mean CLR abundance for all 245 bacteria species according to BP and HTN status at baseline (N=1,215).

OTU Label	Normal BP (N=429)	Undiagnosed Elevated BP (N=306)	Prevalent HTN (N=480)	P-value†
122 Bacteria enriched in elevated BP and HTN*				
<i>Prevotella oulorum</i>	0.90 (3.04)	0.87 (3.04)	1.07 (3.12)	0.62
<i>Treponema socranskii</i>	1.58 (2.57)	2.00 (2.48)	2.37 (2.62)	<0.001 ^{a¶}
<i>Oribacterium sp._oral_taxon_078</i>	0.12 (2.67)	0.20 (2.87)	0.88 (2.75)	<0.001 ^{a¶}
<i>Veillonellaceae_[G-1] sp._oral_taxon_155</i>	0.38 (2.93)	0.73 (3.05)	1.12 (3.13)	0.001 ^{a¶}
<i>Pseudoramibacter alactolyticus</i>	-2.27 (2.68)	-1.98 (2.82)	-1.61 (2.93)	0.002 ^{a¶}
<i>Veillonellaceae_[G-1] sp._oral_taxon_150</i>	0.60 (3.06)	0.97 (3.18)	1.26 (3.16)	0.01 ^a
<i>Bifidobacterium dentium</i>	-2.33 (2.71)	-2.44 (2.56)	-1.70 (3.22)	<0.001 ^{a¶}
<i>Prevotella sp._oral_taxon_292</i>	-1.65 (2.68)	-1.23 (2.97)	-1.02 (3.04)	0.004 ^a
<i>Prevotella buccae</i>	-1.73 (2.42)	-1.67 (2.37)	-1.12 (2.62)	<0.001 ^{a¶}
<i>Tannerella forsythia</i> ¶	1.37 (3.27)	1.68 (3.46)	1.98 (3.56)	0.03 ^a
<i>Streptococcus anginosus</i>	0.71 (3.63)	0.76 (3.65)	1.10 (3.89)	0.24
<i>Fretibacterium sp._oral_taxon_360</i>	2.25 (3.54)	2.63 (3.66)	2.85 (3.81)	0.049 ^a
<i>Scardovia wiggisiae</i>	-2.45 (2.75)	-2.18 (3.10)	-1.86 (3.37)	0.02 ^a
<i>Anaeroglobus geminatus</i>	1.58 (3.52)	1.73 (3.40)	2.17 (3.59)	0.03 ^a
<i>Peptostreptococcaceae_[XI][G-1] [Eubacterium]_infi</i>	-1.76 (2.15)	-1.74 (2.29)	-1.25 (2.45)	0.001 ^{a§}
<i>Prevotella oralis</i>	-0.60 (3.19)	-0.55 (3.26)	0.09 (3.58)	0.003 ^a
<i>Fretibacterium sp._oral_taxon_362</i>	-2.01 (2.57)	-1.53 (3.21)	-1.50 (2.93)	0.02 ^a
<i>Bacteroidales_[G-2] sp._oral_taxon_274</i>	2.55 (3.21)	2.80 (3.28)	3.05 (3.36)	0.08
<i>Streptococcus mutans</i>	0.88 (3.93)	1.17 (3.72)	1.38 (4.07)	0.16
<i>Peptostreptococcaceae_[XI][G-6] [Eubacterium]_noda</i>	-2.31 (2.49)	-1.92 (2.88)	-1.82 (2.85)	0.02 ^a
<i>Fusobacterium nucleatum_subsp._nucleatum</i> ¶	-0.68 (2.64)	-0.46 (2.76)	-0.19 (2.76)	0.03 ^a
<i>Treponema maltophilum</i>	-0.97 (2.47)	-0.74 (2.60)	-0.52 (2.79)	0.03 ^a
<i>Mycoplasma salivarium</i>	-2.22 (2.31)	-2.05 (2.50)	-1.78 (2.62)	0.03 ^a
<i>Stomatobaculum longum</i>	-1.22 (2.42)	-0.83 (2.65)	-0.80 (2.58)	0.03 ^a
<i>Actinomyces gerencseriae</i>	0.16 (2.64)	0.26 (2.48)	0.57 (2.67)	0.06
<i>Campylobacter gracilis</i>	4.87 (1.59)	4.88 (1.70)	5.25 (1.82)	0.001 ^{a¶}
<i>Dialister invisus</i>	3.14 (2.60)	3.20 (2.49)	3.52 (2.70)	0.06
<i>Fusobacterium nucleatum_subsp._polymorphum</i>	5.15 (2.16)	5.04 (2.16)	4.78 (2.43)	0.04 ^a
<i>Leptotrichia wadei</i>	1.74 (3.55)	1.80 (3.66)	2.11 (3.80)	0.27
<i>TM7_[G-1] sp._oral_taxon_349</i>	2.59 (3.32)	2.75 (3.45)	2.96 (3.56)	0.29
<i>Shuttleworthia satelles</i>	-2.51 (2.34)	-2.47 (2.26)	-2.15 (2.45)	0.045
<i>Desulfobulbus sp._oral_taxon_041</i>	-1.01 (3.26)	-0.88 (3.33)	-0.66 (3.45)	0.29
<i>Solobacterium moorei</i>	-0.85 (2.24)	-0.81 (2.18)	-0.52 (2.30)	0.06
<i>Fusobacterium nucleatum_subsp._vincentii</i>	6.13 (2.56)	6.10 (2.48)	6.46 (2.79)	0.09
<i>Olsenella sp._oral_taxon_807</i>	-0.93 (2.27)	-0.63 (2.40)	-0.60 (2.48)	0.09
<i>Mitsuokella sp._oral_taxon_131</i>	-2.15 (2.88)	-2.20 (2.82)	-1.82 (3.25)	0.14
<i>Anaerolineae_[G-1] sp._oral_taxon_439</i>	-2.56 (2.44)	-2.30 (2.71)	-2.23 (2.78)	0.15
<i>Prevotella histicola</i>	-1.26 (2.98)	-1.01 (3.20)	-0.94 (3.25)	0.30
<i>Atopobium parvulum</i>	-0.69 (2.67)	-0.61 (2.62)	-0.38 (2.75)	0.20

<i>Veillonella atypica</i> ‡	2.36 (3.08)	2.81 (2.99)	2.66 (3.03)	0.12
<i>Prevotella maculosa</i>	1.09 (2.61)	1.12 (2.57)	1.39 (2.66)	0.16
<i>Campylobacter showae</i>	2.50 (2.66)	2.75 (2.67)	2.80 (2.69)	0.21
<i>Streptococcus oralis</i>	7.99 (1.74)	7.92 (1.92)	7.70 (1.94)	0.05
<i>Fusobacterium nucleatum</i> _subsp._ <i>animalis</i>	5.05 (2.21)	5.10 (2.34)	5.34 (2.35)	0.14
<i>Campylobacter curvus</i>	-2.09 (2.47)	-1.74 (2.57)	-1.81 (2.61)	0.13
<i>Veillonella denticariosi</i>	-1.69 (3.10)	-1.86 (2.74)	-1.42 (3.25)	0.12
<i>Peptostreptococcus stomatis</i>	-1.28 (2.92)	-1.13 (2.86)	-1.01 (3.00)	0.37
<i>Megasphaera micronuciformis</i>	0.24 (2.85)	0.44 (2.90)	0.51 (2.99)	0.38
<i>Streptococcus parasanguinis</i> _11	0.35 (3.12)	0.55 (3.06)	0.62 (3.19)	0.41
<i>Parvimonas micra</i>	4.02 (2.57)	3.97 (2.71)	4.28 (2.65)	0.19
<i>Prevotella baroniae</i>	-2.41 (2.47)	-2.26 (2.49)	-2.15 (2.67)	0.31
<i>Fretibacterium sp.</i> _oral_taxon_359	-0.33 (3.57)	-0.03 (3.84)	0.08 (3.77)	0.23
<i>Porphyromonas gingivalis</i>	-0.99 (3.98)	-0.56 (4.32)	-0.74 (4.36)	0.38
<i>Streptococcus constellatus</i>	-0.17 (3.36)	0.09 (3.44)	0.40 (3.55)	0.045 ^a
<i>Atopobium sp.</i> _oral_taxon_199	-2.65 (2.28)	-2.43 (2.62)	-2.42 (2.65)	0.32
<i>Selenomonas sputigena</i>	5.20 (2.67)	5.28 (2.93)	5.43 (2.89)	0.48
<i>Selenomonas sp.</i> _oral_taxon_134	0.43 (3.34)	0.50 (3.18)	0.66 (3.55)	0.57
<i>Leptotrichia goodfellowii</i>	-2.50 (2.45)	-2.37 (2.62)	-2.28 (2.65)	0.44
<i>Selenomonas sp.</i> _oral_taxon_136	1.43 (2.89)	1.63 (3.09)	1.64 (2.98)	0.53
<i>Selenomonas flueggei</i>	0.40 (2.74)	0.72 (2.78)	0.60 (2.85)	0.29
<i>Fretibacterium sp.</i> _oral_taxon_358	-3.17 (2.17)	-3.17 (2.21)	-2.97 (2.54)	0.34
<i>Fretibacterium fastidiosum</i>	0.90 (3.27)	1.22 (3.50)	1.10 (3.47)	0.43
<i>Veillonellaceae</i> _ [G-1] <i>sp.</i> _oral_taxon_129	-2.05 (2.56)	-1.88 (2.85)	-1.85 (2.72)	0.49
<i>Capnocytophaga sp.</i> _oral_taxon_336	0.35 (3.02)	0.57 (3.07)	0.55 (3.40)	0.55
<i>Treponema lecithinolyticum</i>	-2.38 (2.67)	-2.25 (2.80)	-2.18 (2.93)	0.57
<i>Prevotella pallens</i>	-1.46 (2.50)	-1.17 (2.78)	-1.27 (2.79)	0.31
<i>Veillonella dispar</i> ‡	7.90 (2.13)	7.97 (2.12)	8.08 (2.14)	0.48
<i>Prevotella micans</i>	-2.48 (2.29)	-2.27 (2.43)	-2.31 (2.44)	0.44
<i>Dialister pneumosintes</i>	0.17 (3.16)	0.39 (3.02)	0.34 (3.35)	0.60
<i>Streptococcus salivarius</i>	2.70 (2.99)	2.80 (2.94)	2.87 (2.89)	0.68
<i>Prevotella denticola</i>	1.42 (3.52)	1.47 (3.65)	1.59 (3.66)	0.75
<i>Actinobaculum sp.</i> _oral_taxon_848	-0.98 (2.76)	-1.02 (2.63)	-0.72 (2.76)	0.22
<i>Prevotella sp.</i> _oral_taxon_300	1.15 (2.94)	1.05 (3.03)	1.31 (3.00)	0.47
<i>Veillonella parvula</i> ‡	7.22 (2.25)	7.39 (2.34)	7.38 (2.37)	0.48
<i>Tannerella sp.</i> _oral_taxon_808	-2.10 (2.33)	-1.88 (2.38)	-1.95 (2.40)	0.42
<i>TM7</i> _ [G-1] <i>sp.</i> _oral_taxon_346	3.41 (2.84)	3.67 (3.07)	3.55 (3.12)	0.50
<i>Fusobacterium sp.</i> _oral_taxon_203	3.88 (3.57)	4.39 (3.37)	4.01 (3.52)	0.14
<i>Campylobacter concisus</i>	2.01 (2.24)	2.31 (2.27)	2.14 (2.26)	0.22
<i>Neisseria sicca</i>	1.48 (3.81)	1.16 (3.86)	1.61 (3.80)	0.27
<i>Bacteroidaceae</i> _ [G-1] <i>sp.</i> _oral_taxon_272	-2.42 (2.47)	-2.53 (2.39)	-2.30 (2.56)	0.42
<i>Capnocytophaga sp.</i> _oral_taxon_324	-2.63 (2.46)	-2.24 (2.79)	-2.52 (2.42)	0.11
<i>Actinomyces sp.</i> _oral_taxon_180	1.14 (2.44)	1.25 (2.32)	1.25 (2.32)	0.73
<i>Veillonellaceae</i> _ [G-1] <i>sp.</i> _oral_taxon_145	-2.16 (2.59)	-2.12 (2.85)	-2.05 (2.80)	0.85
<i>Leptotrichia hongkongensis</i>	1.87 (3.24)	1.56 (3.21)	1.90 (3.20)	0.30
<i>Lachnoanaerobaculum orale</i>	-1.65 (2.17)	-1.59 (2.33)	-1.55 (2.40)	0.79

<i>Lachnospiraceae</i> _[G-8] sp._oral_taxon_500	-2.27 (2.40)	-2.17 (2.49)	-2.17 (2.56)	0.79
<i>Selenomonas noxia</i> ‡	4.41 (2.62)	4.68 (2.63)	4.50 (2.69)	0.38
<i>Prevotella nigrescens</i>	4.08 (3.42)	3.92 (3.51)	4.17 (3.65)	0.64
<i>Streptococcus cristatus</i>	2.98 (2.58)	3.14 (2.59)	3.07 (2.51)	0.71
<i>Leptotrichia</i> sp._oral_taxon_215	-0.45 (2.73)	0.11 (2.94)	-0.37 (2.72)	0.02 ^b
<i>Kingella oralis</i>	2.44 (2.82)	2.33 (2.83)	2.52 (2.78)	0.67
<i>Prevotella</i> sp._oral_taxon_526	-2.89 (2.33)	-2.78 (2.51)	-2.81 (2.44)	0.81
<i>Selenomonas</i> sp._oral_taxon_936	-1.27 (2.66)	-1.22 (2.81)	-1.19 (2.83)	0.91
<i>Atopobium rimae</i>	-0.21 (3.02)	-0.22 (3.07)	0.28 (3.29)	0.03 ^a
<i>Prevotella melaninogenica</i> ‡	1.46 (2.91)	1.70 (2.72)	1.53 (2.82)	0.53
<i>Gemella sanguinis</i>	-0.56 (2.33)	-0.26 (2.37)	-0.50 (2.45)	0.21
<i>Megasphaera</i> sp._oral_taxon_123	-2.74 (2.68)	-2.99 (2.57)	-2.68 (3.17)	0.31
<i>Prevotella veroralis</i>	-2.08 (2.86)	-2.18 (2.75)	-2.02 (2.94)	0.74
<i>Centipeda periodontii</i>	-0.87 (2.65)	-0.92 (2.59)	-0.81 (2.56)	0.85
<i>Prevotella</i> sp._oral_taxon_306	-2.50 (2.33)	-2.50 (2.39)	-2.44 (2.37)	0.92
<i>Lachnoanaerobaculum umeaense</i>	-0.76 (2.50)	-0.73 (2.69)	-0.70 (2.49)	0.94
<i>Capnocytophaga</i> sp._oral_taxon_412	-2.10 (2.83)	-2.27 (2.70)	-2.05 (2.90)	0.57
<i>Streptococcus lactarius</i>	-1.67 (2.23)	-1.51 (2.47)	-1.62 (2.41)	0.68
<i>Filifactor alocis</i>	-1.15 (3.55)	-1.38 (3.53)	-1.11 (3.74)	0.57
<i>Porphyrobacter tepidarius</i>	-3.84 (1.28)	-3.90 (1.20)	-3.80 (1.33)	0.58
<i>Prevotella</i> sp._oral_taxon_314	-2.59 (2.50)	-2.61 (2.60)	-2.55 (2.64)	0.94
<i>Peptostreptococcaceae</i> _[XI][G-9] [Eubacterium]_brac	1.55 (2.76)	1.40 (2.72)	1.58 (2.89)	0.66
<i>Johnsonella</i> sp._oral_taxon_166	-3.08 (2.23)	-2.94 (2.39)	-3.05 (2.22)	0.70
<i>Actinomyces johnsonii</i>	0.72 (2.41)	0.83 (2.53)	0.75 (2.53)	0.82
<i>Fusobacterium</i> sp._oral_taxon_370	-2.43 (2.00)	-2.44 (2.02)	-2.40 (2.09)	0.95
<i>Actinobaculum</i> sp._oral_taxon_183	0.08 (2.79)	0.14 (2.94)	0.11 (2.73)	0.96
<i>Brevundimonas diminuta</i>	-3.51 (1.45)	-3.59 (1.46)	-3.49 (1.45)	0.63
<i>Capnocytophaga</i> sp._oral_taxon_902	-1.94 (2.74)	-1.80 (3.07)	-1.92 (2.88)	0.80
<i>Prevotella salivae</i>	-0.04 (2.86)	0.09 (3.01)	0.06 (2.83)	0.82
<i>Prevotella</i> sp._oral_taxon_313	-1.92 (2.62)	-1.68 (2.74)	-1.91 (2.57)	0.41
TM7_[G-1] sp._oral_taxon_352	-1.57 (2.23)	-1.42 (2.48)	-1.56 (2.33)	0.66
<i>Streptococcus sobrinus</i>	-3.27 (2.29)	-3.33 (2.15)	-3.26 (2.41)	0.91
<i>Sphingomonas</i> sp._oral_taxon_006	-3.80 (1.29)	-3.82 (1.29)	-3.79 (1.38)	0.93
<i>Lachnoanaerobaculum saburreum</i>	0.82 (2.74)	0.89 (2.78)	0.83 (2.76)	0.94
<i>Prevotella multiformis</i>	-3.25 (2.00)	-3.48 (1.90)	-3.25 (2.20)	0.22
<i>Streptococcus parasanguinis</i> _I	-0.61 (2.60)	-0.31 (2.53)	-0.61 (2.71)	0.23
<i>Prevotella dentalis</i>	-2.01 (2.81)	-1.76 (2.99)	-2.01 (2.84)	0.42
<i>Rothia mucilaginosa</i>	1.66 (2.67)	1.73 (2.67)	1.66 (2.63)	0.93
123 Bacteria enriched in normal BP*				
TM7_[G-1] sp._oral_taxon_869	-1.37 (3.46)	-2.00 (3.07)	-2.14 (2.94)	<0.001 ^{ab¶}
<i>Leptotrichia</i> sp._oral_taxon_212	1.59 (3.05)	1.21 (3.11)	0.83 (3.22)	0.001 ^{a¶}
<i>Rothia aeria</i>	2.26 (3.12)	2.15 (3.09)	1.53 (3.28)	0.001 ^{a¶}
<i>Leptotrichia</i> sp._oral_taxon_225	-0.64 (3.42)	-1.05 (3.31)	-1.31 (3.29)	0.01 ^a
<i>Streptococcus sanguinis</i> II	5.07 (2.37)	4.69 (2.62)	4.43 (2.72)	<0.001 ^{a¶}
TM7_[G-1] sp._oral_taxon_952	2.67 (3.16)	2.4 (3.23)	2.04 (3.43)	0.02 ^a

<i>Cardiobacterium hominis</i>	2.31 (2.86)	2.10 (2.71)	1.70 (2.76)	0.004 ^a
<i>Corynebacterium durum</i> ‡	1.13 (2.84)	0.63 (2.98)	0.54 (2.85)	0.006 ^a
<i>Lautropia mirabilis</i>	0.94 (3.13)	0.72 (3.06)	0.36 (3.05)	0.02 ^a
<i>Neisseria elongata</i>	1.74 (3.64)	1.40 (3.43)	1.16 (3.56)	0.046 ^a
<i>Porphyromonas catoniae</i>	-0.92 (3.13)	-0.99 (3.08)	-1.49 (2.91)	0.01 ^a
<i>Abiotrophia defectiva</i>	-0.05 (3.04)	-0.46 (2.94)	-0.6 (3.08)	0.02 ^a
<i>Aggregatibacter paraphrophilus</i>	-1.79 (3.26)	-2.05 (3.10)	-2.33 (2.83)	0.03 ^a
<i>Actinomyces massiliensis</i>	1.47 (2.44)	1.18 (2.50)	0.95 (2.33)	0.005 ^a
<i>Gemella morbillorum</i>	3.18 (3.00)	2.87 (3.05)	2.66 (3.24)	0.04 ^a
TM7_[G-2] sp._oral_taxon_350	-1.88 (3.04)	-1.93 (3.13)	-2.35 (2.88)	0.04 ^a
<i>Actinomyces</i> sp._oral_taxon_171	0.69 (2.72)	0.42 (2.77)	0.24 (2.72)	0.047 ^a
<i>Cardiobacterium valvarum</i>	1.57 (3.00)	1.13 (2.90)	1.12 (3.11)	0.045
TM7_[G-1] sp._oral_taxon_347	-0.96 (3.21)	-1.19 (3.14)	-1.41 (3.04)	0.09
<i>Veillonella rogosae</i>	0.74 (3.12)	0.75 (3.23)	0.34 (3.20)	0.09
<i>Aggregatibacter segnis</i>	-0.79 (3.30)	-1.15 (3.31)	-1.19 (3.30)	0.15
<i>Haemophilus parahaemolyticus</i>	-2.32 (2.82)	-2.68 (2.57)	-2.70 (2.61)	0.07
<i>Streptococcus</i> sp._oral_taxon_056	-0.49 (2.98)	-0.77 (3.07)	-0.87 (2.82)	0.14
TM7_[G-1] sp._oral_taxon_348	-0.65 (2.85)	-0.52 (2.95)	-1.02 (2.80)	0.03
<i>Haemophilus</i> sp._oral_taxon_036	-1.00 (3.12)	-1.28 (3.11)	-1.37 (3.11)	0.18
<i>Bacteroidetes</i> _[G-5] sp._oral_taxon_511	-1.56 (3.08)	-1.73 (3.21)	-1.93 (3.11)	0.19
<i>Capnocytophaga gingivalis</i>	3.39 (2.58)	3.04 (2.69)	3.03 (2.80)	0.09
<i>Prevotella intermedia</i>	-1.55 (3.81)	-1.51 (3.88)	-1.91 (3.69)	0.24
SR1_[G-1] sp._oral_taxon_874	-2.04 (2.44)	-2.24 (2.35)	-2.39 (2.22)	0.08
TM7_[G-6] sp._oral_taxon_870	-1.81 (2.81)	-1.96 (2.75)	-2.16 (2.56)	0.16
<i>Lachnospiraceae</i> _[G-3] sp._oral_taxon_100	0.46 (2.67)	0.62 (2.76)	0.12 (2.85)	0.03
<i>Ruminococcaceae</i> _[G-1] sp._oral_taxon_075	-0.92 (2.69)	-0.93 (2.83)	-1.26 (2.63)	0.11
<i>Bergeyella</i> sp._oral_taxon_322	2.04 (2.37)	1.87 (2.47)	1.72 (2.26)	0.11
<i>Selenomonas</i> sp._oral_taxon_137	0.91 (3.90)	0.60 (3.86)	0.60 (4.09)	0.43
<i>Capnocytophaga</i> sp._oral_taxon_864	-1.27 (3.00)	-1.76 (2.83)	-1.57 (2.94)	0.07
<i>Johnsonella ignava</i>	-0.50 (3.23)	-0.46 (3.30)	-0.80 (3.29)	0.26
TM7_[G-3] sp._oral_taxon_351	-1.89 (2.15)	-1.83 (2.16)	-1.60 (2.17)	0.11
<i>Granulicatella adiacens</i> ‡	4.03 (2.05)	3.94 (2.21)	3.74 (2.11)	0.11
<i>Neisseria oralis</i>	0.30 (3.67)	-0.08 (3.74)	0.01 (3.67)	0.33
<i>Porphyromonas</i> sp._oral_taxon_284	0.05 (3.39)	-0.23 (3.26)	-0.33 (3.29)	0.22
<i>Aggregatibacter aphrophilus</i>	-0.41 (3.89)	-0.24 (3.91)	-0.69 (3.78)	0.25
<i>Peptostreptococcaceae</i> _[XI][G-7] [<i>Eubacterium</i>]_yuri	0.10 (3.36)	-0.25 (3.32)	-0.37 (3.34)	0.09
<i>Actinomyces naeslundii</i> ‡	3.81 (2.06)	3.62 (2.08)	3.54 (2.16)	0.14
<i>Porphyromonas</i> sp._oral_taxon_275	-2.18 (2.69)	-2.48 (2.53)	-2.45 (2.57)	0.19
<i>Haemophilus parainfluenzae</i> ‡	3.62 (3.00)	3.61 (3.01)	3.35 (3.15)	0.32
<i>Capnocytophaga leadbetteri</i>	2.77 (3.04)	2.77 (3.08)	2.50 (3.15)	0.34
<i>Rothia dentocariosa</i>	4.21 (2.97)	4.13 (3.08)	3.94 (3.04)	0.36
<i>Streptococcus intermedius</i>	3.86 (3.26)	3.58 (3.41)	3.59 (3.41)	0.39
<i>Parvimonas</i> sp._oral_taxon_393	0.52 (3.76)	0.30 (3.56)	0.25 (3.70)	0.52
<i>Capnocytophaga</i> sp._oral_taxon_326	0.37 (3.55)	0.16 (3.55)	-0.11 (3.43)	0.12
<i>Leptotrichia</i> sp._oral_taxon_417	0.57 (3.18)	0.90 (3.32)	0.32 (3.01)	0.045
<i>Selenomonas</i> sp._oral_taxon_892	0.81 (2.81)	0.79 (3.03)	0.56 (2.87)	0.36

<i>Prevotella sp._oral_taxon_472</i>	0.35 (3.54)	0.21 (3.64)	0.10 (3.53)	0.56
<i>Veillonella sp._oral_taxon_780</i>	-1.97 (2.87)	-2.39 (2.57)	-2.21 (2.82)	0.12
<i>Leptotrichia sp._oral_taxon_392</i>	0.32 (3.11)	0.12 (3.03)	-0.08 (3.14)	0.16
<i>Sphingomonas echinoides</i>	-2.02 (2.39)	-2.18 (2.20)	-2.24 (2.36)	0.36
<i>Actinomyces sp._oral_taxon_170</i>	-1.34 (2.97)	-1.60 (2.98)	-1.56 (3.03)	0.40
<i>Prevotella sp._oral_taxon_317</i>	2.58 (3.59)	2.61 (3.54)	2.36 (3.74)	0.55
<i>Fusobacterium periodonticum</i>	-0.31 (2.50)	-0.10 (2.68)	-0.52 (2.51)	0.08
<i>Leptotrichia sp._oral_taxon_223</i>	-1.92 (2.78)	-2.21 (2.67)	-2.13 (2.83)	0.33
<i>Treponema sp._oral_taxon_237</i>	-2.32 (2.83)	-2.65 (2.80)	-2.52 (2.81)	0.27
<i>Corynebacterium matruchotii</i>	4.72 (2.41)	4.48 (2.49)	4.53 (2.53)	0.35
<i>Selenomonas sp._oral_taxon_146</i>	-0.14 (2.77)	-0.23 (2.76)	-0.33 (2.94)	0.62
<i>Kingella denitrificans</i>	0.42 (3.13)	0.28 (3.03)	0.23 (3.00)	0.63
<i>Gemella haemolysans</i>	1.97 (2.95)	1.89 (3.10)	1.78 (3.03)	0.64
<i>Tannerella sp._oral_taxon_286</i>	-0.13 (2.53)	0.06 (2.43)	-0.31 (2.49)	0.12
<i>Alloprevotella sp._oral_taxon_473</i>	-1.97 (2.81)	-2.25 (2.78)	-2.15 (2.79)	0.37
<i>Leptotrichia sp._oral_taxon_219</i>	-1.43 (2.65)	-1.52 (2.51)	-1.61 (2.61)	0.58
<i>Prevotella loescheii</i>	-1.37 (3.29)	-1.51 (3.32)	-1.55 (3.26)	0.69
<i>Streptococcus australis</i>	-1.70 (2.49)	-1.81 (2.44)	-1.87 (2.51)	0.58
<i>Granulicatella elegans</i>	-1.75 (2.67)	-1.81 (2.64)	-1.92 (2.57)	0.60
<i>Selenomonas sp._oral_taxon_919</i>	0.28 (2.90)	0.24 (2.87)	0.11 (2.90)	0.64
<i>Capnocytophaga granulosa</i>	2.48 (3.08)	2.81 (3.10)	2.32 (3.34)	0.12
<i>Fusobacterium naviforme</i>	3.56 (2.70)	3.16 (2.86)	3.40 (2.90)	0.17
<i>Leptotrichia buccalis</i>	0.19 (3.35)	0.43 (3.49)	-0.03 (3.31)	0.18
<i>Aggregatibacter sp._oral_taxon_513</i>	-2.81 (2.50)	-2.97 (2.38)	-2.97 (2.38)	0.54
<i>Actinomyces meyeri</i>	-0.17 (2.72)	-0.21 (2.81)	-0.33 (2.86)	0.68
<i>Leptotrichia shahii</i>	-0.29 (3.40)	-0.19 (3.64)	-0.13 (3.78)	0.79
<i>Neisseria subflava</i> ‡	-2.28 (2.91)	-2.08 (3.26)	-2.43 (2.80)	0.27
<i>Capnocytophaga sp._oral_taxon_332</i>	-2.64 (2.41)	-2.80 (2.52)	-2.79 (2.54)	0.62
<i>Treponema sp._oral_taxon_231</i>	-1.29 (3.02)	-1.48 (3.07)	-1.44 (3.19)	0.66
<i>Leptotrichia sp._oral_taxon_498</i>	-1.18 (3.28)	-1.32 (3.25)	-1.33 (3.13)	0.76
<i>Actinomyces sp._oral_taxon_178</i>	-1.09 (2.11)	-1.18 (2.17)	-1.23 (2.16)	0.59
<i>Leptotrichia hofstadii</i>	-0.07 (3.45)	0.13 (3.49)	-0.18 (3.47)	0.48
<i>Streptococcus gordonii</i>	3.96 (2.79)	4.05 (2.59)	3.85 (2.89)	0.59
<i>TM7_[G-1] sp._oral_taxon_488</i>	-0.57 (3.48)	-0.45 (3.42)	-0.68 (3.53)	0.66
<i>Capnocytophaga sp._oral_taxon_323</i>	-2.10 (2.89)	-2.26 (2.80)	-2.21 (2.68)	0.69
<i>Neisseria bacilliformis</i>	-2.08 (3.11)	-2.02 (3.08)	-2.19 (3.17)	0.73
<i>Prevotella saccharolytica</i>	-0.54 (2.52)	-0.58 (2.69)	-0.65 (2.54)	0.79
<i>Ottowia sp._oral_taxon_894</i>	-1.43 (2.89)	-1.46 (2.77)	-1.54 (3.01)	0.84
<i>Bergeyella sp._oral_taxon_907</i>	-1.98 (2.29)	-2.23 (2.28)	-2.08 (2.50)	0.38
<i>Actinomyces oris</i>	2.20 (2.56)	2.14 (2.87)	2.10 (2.74)	0.85
<i>Capnocytophaga sp._oral_taxon_903</i>	-2.36 (2.75)	-2.43 (2.62)	-2.46 (2.69)	0.86
<i>Haemophilus haemolyticus</i>	-2.00 (2.76)	-2.13 (2.74)	-2.09 (2.81)	0.81
<i>TM7_[G-5] sp._oral_taxon_356</i>	0.32 (3.53)	0.15 (3.68)	0.23 (3.80)	0.82
<i>Alloprevotella tanneriae</i>	2.56 (3.84)	2.39 (3.91)	2.47 (4.25)	0.85
<i>Selenomonas sp._oral_taxon_126</i>	-0.81 (2.73)	-0.88 (2.71)	-0.90 (2.91)	0.87
<i>Selenomonas diana</i>	-2.52 (2.34)	-2.83 (2.17)	-2.60 (2.31)	0.17

<i>Aggregatibacter sp._oral_taxon_458</i>	-0.41 (3.10)	-0.61 (3.01)	-0.49 (3.18)	0.70
<i>Prevotella sp._oral_taxon_376</i>	-2.73 (2.58)	-2.79 (2.52)	-2.80 (2.51)	0.92
<i>Neisseria pharyngis</i>	-3.17 (2.01)	-3.00 (2.36)	-3.23 (2.01)	0.33
<i>Porphyromonas endodontalis</i>	0.28 (3.99)	0.31 (4.05)	0.22 (4.17)	0.96
<i>Eikenella corrodens</i> ‡	2.67 (2.33)	2.78 (2.19)	2.62 (2.56)	0.64
<i>Capnocytophaga sputigena</i> ‡	1.98 (3.37)	1.76 (3.33)	1.93 (3.28)	0.67
<i>Actinomyces sp._oral_taxon_169</i>	1.75 (3.06)	1.65 (3.18)	1.70 (3.11)	0.89
<i>Fretibacterium sp._oral_taxon_361</i>	-3.17 (1.99)	-3.22 (2.13)	-3.22 (2.20)	0.90
<i>Prevotella oris</i>	4.94 (2.86)	4.72 (3.02)	4.90 (3.26)	0.60
<i>Treponema denticola</i>	-0.54 (3.41)	-0.47 (3.57)	-0.58 (3.69)	0.92
<i>Catonella morbi</i>	1.67 (2.61)	1.60 (2.56)	1.63 (2.68)	0.94
<i>Selenomonas sp._oral_taxon_133</i>	-2.59 (2.70)	-2.59 (2.80)	-2.63 (2.74)	0.98
<i>Prevotella pleuritidis</i>	-0.27 (4.16)	-0.53 (4.00)	-0.30 (4.32)	0.68
<i>Selenomonas infelix</i>	1.19 (2.81)	1.29 (2.92)	1.16 (2.96)	0.84
<i>Porphyromonas sp._oral_taxon_278</i>	-2.46 (2.46)	-2.76 (2.21)	-2.48 (2.51)	0.19
<i>Alloprevotella sp._oral_taxon_308</i>	-1.48 (2.31)	-1.35 (2.34)	-1.50 (2.34)	0.62
<i>Capnocytophaga sp._oral_taxon_338</i>	-1.29 (3.02)	-1.49 (3.09)	-1.31 (3.14)	0.66
<i>Selenomonas artemidis</i>	2.24 (3.75)	2.39 (3.61)	2.22 (3.78)	0.82
<i>Streptococcus sp._oral_taxon_074</i>	-0.14 (2.34)	-0.11 (2.51)	-0.16 (2.44)	0.97
<i>Porphyromonas sp._oral_taxon_279</i>	1.07 (3.19)	1.54 (2.97)	1.06 (3.25)	0.08
<i>Microbacterium flavescens</i>	-3.08 (1.55)	-3.23 (1.60)	-3.09 (1.57)	0.38
<i>Alloprevotella rava</i>	-0.97 (2.79)	-1.11 (2.72)	-0.98 (2.88)	0.79
<i>Neisseria flavescens</i>	0.99 (3.20)	0.85 (3.24)	0.99 (3.47)	0.80
<i>Peptostreptococcaceae_[XI][G-5][Eubacterium]_saph</i>	-2.44 (2.66)	-2.43 (2.73)	-2.44 (2.72)	0.99

Data are mean (SD) CLR bacteria relative abundance.

*OTUs sorted according to the magnitude of the difference between prevalent HTN and normal BP.

The CLR abundance can be interpreted as a log₂ fold-difference for the given bacteria abundance relative to the overall compositional geometric mean. A CLR of 3 indicates an 8-fold (2³) higher abundance, and a CLR of -3 indicates a 8-fold lower abundance.

†P-value from ANOVA F-tests; superscripts from post-hoc pairwise significance tests: ^a normal vs prevalent HTN, ^b normal vs undiagnosed elevated BP.

¶Significant (P<0.05) after Benjamini-Hochberg correction.

‡Bacteria with nitrate-reductase capability for reducing nitrate to nitrite in the oral cavity.

||Bacteria previously identified within human atherosclerotic plaque (atheroma).

Table S4. Associations† for each baseline bacterial species with incident hypertension (N=735).

OTU Label	Incident Hypertension		Age-adjusted HR (95% CI)	Model 1 HR (95% CI)	Model 2 HR (95% CI)	Model 3 HR (95% CI)
	No (n=360)	Yes (n=375)				
	CLR Mean (SD)	CLR Mean (SD)				
Positive associations						
<i>Streptococcus anginosus</i>	0.37 (3.57)	1.08 (3.66)	1.16 (1.04-1.29)	1.15 (1.03-1.28)	1.16 (1.04-1.29)	1.15 (1.03-1.27)
<i>Streptococcus salivarius</i>	2.44 (2.82)	3.03 (3.08)	1.15 (1.04-1.28)	1.16 (1.04-1.28)	1.14 (1.03-1.27)	1.14 (1.03-1.27)
<i>Fretibacterium sp._oral_taxon_362</i>	-2.00 (2.54)	-1.62 (3.14)	1.15 (1.04-1.27)	1.14 (1.03-1.26)	1.14 (1.03-1.27)	1.14 (1.03-1.27)
<i>Selenomonas infelix</i>	0.96 (2.85)	1.50 (2.85)	1.15 (1.03-1.27)	1.14 (1.02-1.26)	1.14 (1.02-1.27)	1.12 (1.01-1.25)
<i>Prevotella sp._oral_taxon_526</i>	-3.03 (2.18)	-2.67 (2.60)	1.13 (1.03-1.25)	1.14 (1.03-1.26)	1.14 (1.03-1.26)	1.14 (1.03-1.26)
<i>Prevotella sp._oral_taxon_292</i>	-1.69 (2.74)	-1.27 (2.87)	1.11 (1.00-1.23)	1.11 (1.00-1.24)	1.10 (0.99-1.22)	1.09 (0.98-1.21)
<i>Megasphaera sp._oral_taxon_123</i>	-3.06 (2.52)	-2.63 (2.72)	1.14 (1.04-1.27)	1.14 (1.03-1.26)	1.14 (1.03-1.26)	1.13 (1.02-1.25)
<i>Capnocytophaga sp._oral_taxon_903</i>	-2.57 (2.59)	-2.21 (2.78)	1.12 (1.01-1.23)	1.11 (1.00-1.22)	1.11 (1.00-1.22)	1.11 (1.00-1.22)
<i>Prevotella sp._oral_taxon_376</i>	-2.91 (2.45)	-2.61 (2.64)	1.11 (1.01-1.23)	1.13 (1.02-1.25)	1.13 (1.03-1.25)	1.13 (1.02-1.25)
<i>Streptococcus lactarius</i>	-1.80 (2.15)	-1.42 (2.48)	1.10 (0.99-1.21)	1.10 (1.00-1.22)	1.08 (0.97-1.20)	1.08 (0.98-1.20)
<i>Streptococcus mutans</i>	0.74 (3.79)	1.24 (3.88)	1.10 (0.99-1.21)	1.10 (0.99-1.22)	1.08 (0.98-1.20)	1.07 (0.97-1.19)
<i>Megasphaera micronuciformis</i>	0.08 (2.78)	0.56 (2.94)	1.10 (0.99-1.22)	1.09 (0.98-1.21)	1.08 (0.98-1.20)	1.08 (0.97-1.20)
<i>Veillonella atypica</i>	2.36 (3.03)	2.73 (3.05)	1.09 (0.99-1.21)	1.06 (0.96-1.18)	1.06 (0.95-1.17)	1.07 (0.96-1.19)
<i>Veillonellaceae_[G-1] sp._oral_taxon_155</i>	0.38 (2.92)	0.67 (3.04)	1.09 (0.98-1.22)	1.07 (0.96-1.19)	1.07 (0.96-1.19)	1.04 (0.94-1.16)
<i>Stomatobaculum longum</i>	-1.23 (2.49)	-0.90 (2.55)	1.09 (0.99-1.20)	1.08 (0.97-1.19)	1.07 (0.96-1.18)	1.07 (0.96-1.18)
<i>Prevotella histicola</i>	-1.34 (2.97)	-0.97 (3.16)	1.09 (0.98-1.20)	1.06 (0.96-1.18)	1.06 (0.96-1.18)	1.09 (0.98-1.21)
<i>Streptococcus parasanguinis_II</i>	0.28 (3.02)	0.58 (3.17)	1.09 (0.98-1.20)	1.08 (0.97-1.20)	1.07 (0.96-1.19)	1.07 (0.96-1.19)
<i>Selenomonas sp._oral_taxon_133</i>	-2.79 (2.57)	-2.40 (2.88)	1.11 (1.00-1.22)	1.09 (0.98-1.20)	1.09 (0.99-1.21)	1.08 (0.98-1.20)
<i>Prevotella denticola</i>	1.23 (3.56)	1.64 (3.58)	1.08 (0.98-1.20)	1.08 (0.97-1.20)	1.07 (0.96-1.19)	1.06 (0.96-1.18)
<i>Prevotella oralis</i>	-0.66 (3.19)	-0.50 (3.24)	1.09 (0.98-1.21)	1.10 (0.98-1.22)	1.08 (0.97-1.20)	1.06 (0.95-1.18)
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<i>Fretibacterium fastidiosum</i>	0.91 (3.29)	1.15 (3.45)	1.09 (0.98-1.21)	1.10 (0.98-1.22)	1.09 (0.98-1.22)	1.07 (0.96-1.19)
<i>Campylobacter curvus</i>	-2.09 (2.53)	-1.80 (2.51)	1.09 (0.98-1.20)	1.10 (0.99-1.22)	1.11 (1.00-1.24)	1.10 (0.99-1.22)
<i>Veillonellaceae_[G-1] sp._oral_taxon_145</i>	-2.30 (2.57)	-1.98 (2.81)	1.08 (0.98-1.19)	1.08 (0.98-1.20)	1.08 (0.98-1.20)	1.07 (0.97-1.19)

<i>Treponema socranskii</i>	1.68 (2.49)	1.81 (2.58)	1.06 (0.96-1.18)	1.06 (0.95-1.18)	1.05 (0.94-1.17)	1.04 (0.93-1.16)
<i>Prevotella baroniae</i>	-2.44 (2.52)	-2.26 (2.44)	1.08 (0.98-1.20)	1.09 (0.98-1.21)	1.10 (0.99-1.22)	1.09 (0.98-1.21)
<i>Alloprevotella sp._oral_taxon_308</i>	-1.58 (2.31)	-1.28 (2.33)	1.09 (0.99-1.21)	1.09 (0.99-1.21)	1.08 (0.98-1.19)	1.09 (0.99-1.21)
<i>Prevotella salivae</i>	-0.15 (2.96)	0.17 (2.87)	1.06 (0.96-1.17)	1.05 (0.95-1.16)	1.04 (0.94-1.15)	1.03 (0.93-1.14)
<i>Mycoplasma salivarium</i>	-2.23 (2.27)	-2.07 (2.50)	1.09 (0.97-1.21)	1.10 (0.98-1.23)	1.11 (0.99-1.24)	1.10 (0.99-1.23)
<i>Parvimonas micra</i>	3.90 (2.63)	4.10 (2.63)	1.08 (0.97-1.21)	1.08 (0.97-1.21)	1.07 (0.96-1.20)	1.07 (0.95-1.19)
<i>Actinomyces gerencseriae</i>	0.08 (2.45)	0.32 (2.69)	1.06 (0.96-1.18)	1.07 (0.96-1.19)	1.06 (0.95-1.18)	1.07 (0.96-1.18)
<i>Mitsuokella sp._oral_taxon_131</i>	-2.26 (2.77)	-2.09 (2.94)	1.04 (0.94-1.16)	1.04 (0.93-1.16)	1.03 (0.92-1.16)	1.03 (0.92-1.15)
<i>Atopobium parvulum</i>	-0.79 (2.57)	-0.53 (2.71)	1.07 (0.97-1.18)	1.04 (0.94-1.16)	1.03 (0.92-1.14)	1.04 (0.93-1.15)
<i>Olsenella sp._oral_taxon_807</i>	-0.85 (2.34)	-0.76 (2.31)	1.05 (0.94-1.16)	1.05 (0.94-1.16)	1.04 (0.93-1.16)	1.03 (0.93-1.15)
<i>Atopobium sp._oral_taxon_199</i>	-2.66 (2.40)	-2.47 (2.46)	1.06 (0.96-1.18)	1.05 (0.94-1.17)	1.06 (0.95-1.18)	1.05 (0.95-1.17)
<i>Scardovia wiggisiae</i>	-2.43 (2.78)	-2.25 (3.02)	1.05 (0.95-1.17)	1.03 (0.92-1.15)	1.03 (0.92-1.15)	1.02 (0.91-1.14)
<i>Prevotella sp._oral_taxon_313</i>	-1.97 (2.57)	-1.67 (2.76)	1.09 (0.99-1.20)	1.08 (0.98-1.20)	1.08 (0.97-1.19)	1.07 (0.97-1.18)
<i>Selenomonas noxia</i>	4.46 (2.64)	4.58 (2.62)	1.05 (0.94-1.16)	1.02 (0.92-1.14)	1.02 (0.91-1.13)	1.02 (0.92-1.14)
<i>Fretibacterium sp._oral_taxon_359</i>	-0.28 (3.69)	-0.14 (3.70)	1.08 (0.97-1.19)	1.07 (0.97-1.19)	1.07 (0.96-1.19)	1.06 (0.95-1.18)
<i>Johnsonella sp._oral_taxon_166</i>	-3.16 (2.18)	-2.88 (2.40)	1.06 (0.96-1.16)	1.05 (0.95-1.16)	1.05 (0.95-1.16)	1.06 (0.96-1.17)
<i>Streptococcus parasanguinis_I</i>	-0.60 (2.53)	-0.38 (2.61)	1.05 (0.95-1.17)	1.04 (0.94-1.16)	1.04 (0.93-1.16)	1.05 (0.95-1.17)
<i>Actinomyces sp._oral_taxon_180</i>	1.03 (2.48)	1.33 (2.30)	1.08 (0.98-1.19)	1.09 (0.98-1.20)	1.07 (0.97-1.19)	1.07 (0.96-1.18)
<i>Porphyromonas gingivalis</i>	-1.00 (4.05)	-0.63 (4.21)	1.07 (0.96-1.18)	1.08 (0.97-1.19)	1.07 (0.97-1.19)	1.07 (0.96-1.18)
<i>Centipeda periodontii</i>	-0.98 (2.63)	-0.80 (2.62)	1.05 (0.95-1.16)	1.06 (0.96-1.17)	1.06 (0.96-1.17)	1.06 (0.95-1.17)
<i>Capnocytophaga sp._oral_taxon_324</i>	-2.55 (2.62)	-2.38 (2.59)	1.05 (0.96-1.15)	1.05 (0.95-1.16)	1.05 (0.95-1.15)	1.04 (0.95-1.15)
<i>Porphyrobacter tepidarius</i>	-3.93 (1.19)	-3.81 (1.29)	1.07 (0.96-1.19)	1.06 (0.95-1.18)	1.06 (0.95-1.18)	1.08 (0.97-1.20)
<i>Prevotella oulorum</i>	0.83 (3.05)	0.95 (3.03)	1.06 (0.95-1.17)	1.04 (0.93-1.15)	1.04 (0.94-1.16)	1.03 (0.93-1.14)
<i>Veillonellaceae_[G-1] sp._oral_taxon_150</i>	0.75 (3.14)	0.77 (3.09)	1.03 (0.93-1.14)	1.01 (0.91-1.12)	1.00 (0.90-1.11)	0.98 (0.88-1.09)
<i>Alloprevotella rava</i>	-1.09 (2.78)	-0.97 (2.74)	1.07 (0.96-1.19)	1.06 (0.95-1.18)	1.06 (0.96-1.18)	1.06 (0.95-1.18)
<i>Oribacterium sp._oral_taxon_078</i>	0.15 (2.68)	0.16 (2.82)	1.03 (0.92-1.14)	1.01 (0.91-1.13)	1.01 (0.91-1.12)	1.01 (0.91-1.13)
<i>Peptostreptococcaceae_[XI][G-6] [Eubacterium]_noda</i>	-2.22 (2.57)	-2.08 (2.74)	1.06 (0.96-1.18)	1.07 (0.96-1.19)	1.08 (0.97-1.20)	1.09 (0.98-1.21)
<i>Bacteroidaceae_[G-1] sp._oral_taxon_272</i>	-2.51 (2.35)	-2.42 (2.51)	1.05 (0.95-1.16)	1.06 (0.95-1.18)	1.05 (0.95-1.17)	1.05 (0.94-1.16)
<i>Anaerolineae_[G-1] sp._oral_taxon_439</i>	-2.52 (2.49)	-2.40 (2.63)	1.04 (0.94-1.15)	1.04 (0.93-1.15)	1.05 (0.94-1.16)	1.05 (0.95-1.16)

<i>Solobacterium moorei</i>	-0.84 (2.27)	-0.83 (2.16)	1.06 (0.96-1.18)	1.06 (0.95-1.18)	1.06 (0.95-1.18)	1.05 (0.94-1.17)
<i>Rothia mucilaginosa</i>	1.62 (2.52)	1.75 (2.81)	1.06 (0.95-1.17)	1.05 (0.95-1.17)	1.05 (0.95-1.17)	1.07 (0.96-1.19)
<i>Rothia dentocariosa</i>	4.02 (2.83)	4.33 (3.18)	1.07 (0.96-1.19)	1.05 (0.95-1.17)	1.05 (0.94-1.16)	1.05 (0.95-1.17)
<i>Prevotella pallens</i>	-1.43 (2.59)	-1.25 (2.65)	1.05 (0.95-1.16)	1.05 (0.94-1.17)	1.03 (0.93-1.15)	1.05 (0.94-1.16)
<i>Fusobacterium nucleatum_subsp._animalis</i>	5.04 (2.20)	5.10 (2.33)	1.03 (0.93-1.15)	1.03 (0.93-1.15)	1.03 (0.92-1.14)	1.03 (0.92-1.14)
<i>Streptococcus sobrinus</i>	-3.33 (2.23)	-3.26 (2.23)	1.04 (0.93-1.15)	1.03 (0.93-1.15)	1.03 (0.92-1.14)	1.03 (0.93-1.14)
<i>Fusobacterium nucleatum_subsp._vincentii</i>	6.11 (2.40)	6.13 (2.64)	1.04 (0.94-1.16)	1.06 (0.95-1.18)	1.05 (0.94-1.17)	1.03 (0.92-1.15)
<i>Peptostreptococcaceae_[XI][G-9] [Eubacterium]_brac</i>	1.41 (2.79)	1.56 (2.70)	1.07 (0.97-1.19)	1.07 (0.96-1.19)	1.06 (0.95-1.18)	1.06 (0.95-1.18)
<i>Parvimonas sp._oral_taxon_393</i>	0.24 (3.67)	0.61 (3.67)	1.07 (0.97-1.19)	1.10 (0.99-1.22)	1.10 (0.99-1.22)	1.11 (1.00-1.23)
<i>Bacteroidales_[G-2] sp._oral_taxon_274</i>	2.56 (3.20)	2.75 (3.28)	1.04 (0.94-1.15)	1.06 (0.95-1.18)	1.06 (0.95-1.18)	1.06 (0.95-1.18)
<i>Fusobacterium sp._oral_taxon_370</i>	-2.58 (1.97)	-2.29 (2.03)	1.05 (0.96-1.16)	1.07 (0.97-1.17)	1.07 (0.97-1.18)	1.07 (0.97-1.18)
<i>Bifidobacterium dentium</i>	-2.43 (2.70)	-2.32 (2.59)	1.03 (0.92-1.15)	1.01 (0.90-1.13)	1.01 (0.90-1.13)	1.00 (0.89-1.12)
<i>Lachnoanaerobaculum saburreum</i>	0.78 (2.81)	0.91 (2.69)	1.04 (0.94-1.15)	1.04 (0.93-1.15)	1.03 (0.93-1.14)	1.04 (0.93-1.15)
<i>Sphingomonas sp._oral_taxon_006</i>	-3.85 (1.20)	-3.76 (1.37)	1.05 (0.94-1.17)	1.04 (0.93-1.16)	1.04 (0.93-1.16)	1.06 (0.95-1.18)
<i>Veillonella parvula</i>	7.26 (2.27)	7.33 (2.31)	1.03 (0.93-1.14)	1.02 (0.92-1.13)	1.01 (0.91-1.12)	1.01 (0.91-1.12)
<i>Prevotella melaninogenica</i>	1.46 (2.84)	1.65 (2.83)	1.04 (0.94-1.15)	1.04 (0.93-1.15)	1.02 (0.92-1.14)	1.02 (0.92-1.13)
<i>Prevotella sp._oral_taxon_472</i>	0.13 (3.53)	0.45 (3.62)	1.07 (0.97-1.18)	1.08 (0.97-1.20)	1.08 (0.97-1.19)	1.06 (0.96-1.18)
<i>Prevotella sp._oral_taxon_300</i>	1.07 (3.03)	1.15 (2.92)	1.03 (0.93-1.14)	1.02 (0.92-1.14)	1.01 (0.91-1.13)	1.01 (0.91-1.13)
<i>Treponema maltophilum</i>	-0.93 (2.50)	-0.83 (2.55)	1.03 (0.92-1.15)	1.03 (0.92-1.15)	1.03 (0.92-1.15)	1.02 (0.91-1.14)
<i>TM7_[G-3] sp._oral_taxon_351</i>	-1.93 (2.12)	-1.80 (2.19)	1.03 (0.93-1.15)	1.04 (0.94-1.15)	1.03 (0.93-1.15)	1.04 (0.94-1.15)
<i>Anaeroglobus geminatus</i>	1.66 (3.44)	1.63 (3.51)	1.01 (0.91-1.12)	1.01 (0.91-1.13)	1.00 (0.90-1.11)	0.99 (0.89-1.10)
<i>Actinomyces sp._oral_taxon_169</i>	1.56 (3.02)	1.85 (3.19)	1.06 (0.96-1.18)	1.06 (0.96-1.18)	1.06 (0.95-1.17)	1.06 (0.96-1.18)
<i>Leptotrichia shahii</i>	-0.33 (3.47)	-0.16 (3.53)	1.03 (0.93-1.15)	1.02 (0.92-1.14)	1.02 (0.91-1.13)	1.00 (0.90-1.11)
<i>Lachnoanaerobaculum orale</i>	-1.70 (2.21)	-1.56 (2.26)	1.03 (0.93-1.14)	1.01 (0.91-1.12)	0.99 (0.89-1.11)	0.99 (0.89-1.10)
<i>Johnsonella ignava</i>	-0.63 (3.26)	-0.34 (3.25)	1.05 (0.95-1.16)	1.05 (0.95-1.16)	1.05 (0.95-1.17)	1.06 (0.96-1.18)
<i>Fusobacterium nucleatum_subsp._nucleatum</i>	-0.68 (2.70)	-0.50 (2.69)	1.03 (0.93-1.14)	1.03 (0.93-1.14)	1.03 (0.94-1.14)	1.04 (0.94-1.15)
<i>Neisseria bacilliformis</i>	-2.16 (3.08)	-1.95 (3.11)	1.04 (0.94-1.15)	1.06 (0.95-1.17)	1.07 (0.96-1.18)	1.06 (0.95-1.17)
<i>Capnocytophaga sp._oral_taxon_902</i>	-1.94 (2.81)	-1.83 (2.95)	1.04 (0.94-1.15)	1.02 (0.92-1.13)	1.02 (0.92-1.13)	1.02 (0.92-1.13)

<i>Dialister pneumosintes</i>	0.29 (3.19)	0.23 (3.02)	1.03 (0.93-1.14)	1.01 (0.91-1.13)	1.02 (0.92-1.14)	1.01 (0.90-1.12)
<i>Pseudoramibacter alactolyticus</i>	-2.15 (2.71)	-2.14 (2.77)	1.01 (0.91-1.13)	1.01 (0.90-1.13)	1.00 (0.89-1.11)	0.99 (0.89-1.10)
<i>Alloprevotella tanneriae</i>	2.45 (3.84)	2.52 (3.90)	1.04 (0.94-1.16)	1.03 (0.92-1.14)	1.05 (0.94-1.17)	1.03 (0.92-1.15)
<i>Kingella oralis</i>	2.36 (2.83)	2.43 (2.82)	1.04 (0.94-1.15)	1.04 (0.94-1.15)	1.03 (0.92-1.14)	1.04 (0.94-1.15)
<i>Selenomonas flueggei</i>	0.50 (2.79)	0.56 (2.73)	1.02 (0.92-1.13)	1.02 (0.92-1.12)	1.02 (0.92-1.12)	1.00 (0.90-1.11)
<i>Actinomyces sp._oral_taxon_170</i>	-1.58 (2.95)	-1.32 (3.00)	1.06 (0.96-1.17)	1.04 (0.94-1.15)	1.04 (0.94-1.15)	1.07 (0.96-1.18)
<i>Gemella sanguinis</i>	-0.45 (2.30)	-0.42 (2.39)	1.03 (0.92-1.14)	1.00 (0.90-1.12)	1.01 (0.91-1.13)	1.02 (0.92-1.14)
<i>Peptostreptococcus stomatis</i>	-1.35 (2.90)	-1.09 (2.90)	1.05 (0.95-1.17)	1.05 (0.95-1.17)	1.05 (0.95-1.17)	1.06 (0.95-1.17)
<i>TM7_[G-1] sp._oral_taxon_346</i>	3.45 (2.95)	3.59 (2.93)	1.02 (0.92-1.14)	1.02 (0.92-1.13)	1.02 (0.92-1.14)	0.99 (0.89-1.10)
<i>Prevotella sp._oral_taxon_314</i>	-2.73 (2.42)	-2.48 (2.64)	1.03 (0.93-1.14)	1.01 (0.91-1.12)	1.01 (0.91-1.12)	1.00 (0.90-1.11)
<i>Fusobacterium sp._oral_taxon_203</i>	4.00 (3.45)	4.19 (3.54)	1.04 (0.93-1.15)	1.06 (0.95-1.17)	1.05 (0.95-1.16)	1.04 (0.94-1.16)
<i>Dialister invisus</i>	3.15 (2.57)	3.17 (2.54)	1.01 (0.91-1.12)	1.02 (0.91-1.13)	1.01 (0.90-1.12)	1.00 (0.89-1.11)
<i>Atopobium rimae</i>	-0.26 (3.13)	-0.17 (2.95)	1.02 (0.92-1.14)	1.02 (0.91-1.13)	1.00 (0.90-1.12)	1.00 (0.90-1.12)
<i>Peptostreptococcaceae_[XI][G-5] [Eubacterium]_saph</i>	-2.47 (2.57)	-2.41 (2.79)	1.02 (0.92-1.13)	1.02 (0.92-1.14)	1.03 (0.92-1.14)	1.03 (0.92-1.14)
<i>Leptotrichia sp._oral_taxon_498</i>	-1.31 (3.19)	-1.17 (3.33)	1.01 (0.91-1.11)	1.00 (0.91-1.11)	1.00 (0.90-1.10)	1.01 (0.92-1.12)
<i>Catonella morbi</i>	1.58 (2.65)	1.69 (2.53)	1.04 (0.94-1.16)	1.02 (0.92-1.14)	1.03 (0.92-1.15)	1.04 (0.93-1.16)
<i>Fretibacterium sp._oral_taxon_360</i>	2.41 (3.42)	2.41 (3.76)	1.02 (0.91-1.13)	1.02 (0.92-1.14)	1.02 (0.92-1.14)	1.01 (0.91-1.12)
<i>Veillonella dispar</i>	7.92 (2.02)	7.95 (2.23)	1.02 (0.92-1.13)	1.00 (0.90-1.12)	0.99 (0.89-1.11)	0.99 (0.89-1.10)
<i>Prevotella maculosa</i>	1.12 (2.61)	1.08 (2.58)	1.01 (0.91-1.12)	1.01 (0.91-1.12)	1.01 (0.90-1.12)	0.99 (0.89-1.11)
<i>Prevotella sp._oral_taxon_306</i>	-2.53 (2.29)	-2.47 (2.41)	1.01 (0.91-1.12)	1.00 (0.90-1.11)	1.00 (0.90-1.11)	1.01 (0.91-1.13)
<i>Selenomonas diana</i>	-2.72 (2.14)	-2.58 (2.40)	1.03 (0.93-1.14)	1.02 (0.92-1.13)	1.03 (0.93-1.15)	1.03 (0.93-1.14)
<i>Selenomonas sp._oral_taxon_134</i>	0.49 (3.38)	0.43 (3.16)	1.01 (0.91-1.12)	1.01 (0.91-1.12)	1.01 (0.91-1.12)	0.99 (0.89-1.10)
<i>Prevotella veroralis</i>	-2.19 (2.83)	-2.06 (2.80)	1.04 (0.94-1.15)	1.04 (0.94-1.16)	1.05 (0.95-1.17)	1.05 (0.95-1.16)
<i>Selenomonas artemidis</i>	2.30 (3.71)	2.30 (3.67)	1.02 (0.92-1.13)	1.01 (0.91-1.13)	1.01 (0.91-1.12)	1.02 (0.91-1.13)
<i>TM7_[G-2] sp._oral_taxon_350</i>	-2.01 (3.06)	-1.79 (3.09)	1.02 (0.92-1.12)	1.02 (0.92-1.12)	1.02 (0.92-1.13)	1.01 (0.91-1.11)
<i>Veillonellaceae_[G-1] sp._oral_taxon_129</i>	-1.99 (2.63)	-1.97 (2.74)	1.01 (0.91-1.11)	0.99 (0.89-1.10)	1.00 (0.90-1.11)	0.99 (0.89-1.10)
<i>Aggregatibacter aphrophilus</i>	-0.49 (3.91)	-0.19 (3.88)	1.04 (0.95-1.15)	1.06 (0.96-1.17)	1.07 (0.97-1.18)	1.07 (0.97-1.18)
<i>Neisseria pharyngis</i>	-3.14 (2.21)	-3.06 (2.12)	1.01 (0.92-1.11)	1.00 (0.91-1.11)	1.01 (0.91-1.11)	1.02 (0.93-1.13)
<i>TM7_[G-1] sp._oral_taxon_347</i>	-1.21 (3.06)	-0.91 (3.30)	1.02 (0.93-1.13)	1.01 (0.92-1.12)	1.02 (0.92-1.13)	1.02 (0.92-1.13)
<i>Streptococcus constellatus</i>	-0.07 (3.35)	-0.06 (3.44)	1.01 (0.91-1.13)	1.01 (0.91-1.13)	1.00 (0.90-1.12)	1.00 (0.90-1.11)
<i>Filifactor alocis</i>	-1.32 (3.44)	-1.18 (3.64)	1.03 (0.93-1.14)	1.05 (0.94-1.17)	1.06 (0.95-1.18)	1.06 (0.95-1.18)

<i>Prevotella loescheii</i>	-1.49 (3.30)	-1.36 (3.30)	1.02 (0.93-1.13)	1.03 (0.93-1.14)	1.04 (0.94-1.15)	1.03 (0.93-1.14)
<i>Actinomyces oris</i>	2.15 (2.51)	2.20 (2.86)	1.03 (0.93-1.14)	1.02 (0.92-1.13)	1.00 (0.90-1.12)	1.02 (0.91-1.13)
<i>Peptostreptococcaceae_[XI][G-1] [Eubacterium]_infi</i>	-1.73 (2.25)	-1.78 (2.17)	1.00 (0.90-1.11)	1.01 (0.91-1.13)	1.01 (0.91-1.13)	1.02 (0.92-1.14)
<i>TM7_[G-1] sp._oral_taxon_349</i>	2.68 (3.35)	2.63 (3.41)	1.00 (0.90-1.11)	1.00 (0.90-1.11)	1.01 (0.91-1.12)	1.00 (0.90-1.11)
<i>TM7_[G-1] sp._oral_taxon_488</i>	-0.60 (3.49)	-0.44 (3.41)	1.01 (0.91-1.11)	1.01 (0.91-1.12)	1.00 (0.90-1.11)	1.02 (0.92-1.13)
<i>Leptotrichia wadei</i>	1.78 (3.60)	1.75 (3.59)	1.00 (0.91-1.11)	1.00 (0.90-1.11)	1.00 (0.90-1.11)	1.00 (0.90-1.11)
<i>Leptotrichia hongkongensis</i>	1.69 (3.23)	1.79 (3.23)	1.00 (0.90-1.10)	1.01 (0.91-1.12)	1.02 (0.92-1.13)	1.02 (0.92-1.13)
<i>Actinomyces sp._oral_taxon_178</i>	-1.12 (2.15)	-1.13 (2.12)	1.00 (0.90-1.11)	1.00 (0.90-1.11)	0.98 (0.88-1.09)	1.00 (0.90-1.12)
<i>Aggregatibacter sp._oral_taxon_513</i>	-2.90 (2.46)	-2.86 (2.44)	1.01 (0.91-1.11)	1.01 (0.91-1.12)	1.01 (0.91-1.12)	1.01 (0.92-1.12)
<i>Prevotella multiformis</i>	-3.32 (1.97)	-3.37 (1.96)	1.00 (0.90-1.12)	1.01 (0.90-1.13)	1.01 (0.90-1.13)	1.01 (0.90-1.13)
<i>Desulfobulbus sp._oral_taxon_041</i>	-0.93 (3.26)	-0.99 (3.32)	1.00 (0.90-1.11)	1.02 (0.92-1.14)	1.02 (0.92-1.13)	1.01 (0.91-1.12)
<i>Prevotella intermedia</i>	-1.46 (3.92)	-1.61 (3.75)	1.01 (0.91-1.12)	1.01 (0.91-1.12)	1.01 (0.91-1.12)	1.00 (0.90-1.11)
<i>Leptotrichia buccalis</i>	0.32 (3.43)	0.26 (3.40)	1.00 (0.91-1.11)	1.00 (0.91-1.11)	1.01 (0.91-1.11)	1.00 (0.91-1.11)
<i>Streptococcus oralis</i>	7.93 (1.73)	7.99 (1.90)	1.02 (0.92-1.14)	1.03 (0.92-1.15)	1.02 (0.91-1.14)	1.03 (0.92-1.15)
<i>Fretibacterium sp._oral_taxon_361</i>	-3.18 (2.17)	-3.20 (1.93)	1.00 (0.91-1.11)	1.01 (0.91-1.13)	1.02 (0.91-1.13)	1.03 (0.92-1.14)
<i>Capnocytophaga sp._oral_taxon_332</i>	-2.76 (2.39)	-2.66 (2.52)	1.01 (0.91-1.12)	1.00 (0.90-1.11)	1.00 (0.90-1.11)	1.00 (0.90-1.10)
<i>Actinomyces meyeri</i>	-0.25 (2.72)	-0.13 (2.79)	1.02 (0.91-1.13)	1.03 (0.92-1.14)	1.02 (0.91-1.13)	1.01 (0.91-1.13)
<i>Tannerella sp._oral_taxon_808</i>	-1.99 (2.36)	-2.04 (2.35)	0.98 (0.89-1.09)	1.00 (0.90-1.11)	1.00 (0.90-1.11)	0.99 (0.89-1.10)
<i>Prevotella nigrescens</i>	4.01 (3.44)	4.02 (3.47)	1.00 (0.90-1.12)	1.01 (0.90-1.12)	1.00 (0.90-1.12)	0.99 (0.89-1.10)
<i>Capnocytophaga sp._oral_taxon_412</i>	-2.16 (2.80)	-2.19 (2.75)	1.02 (0.92-1.13)	1.01 (0.91-1.12)	1.01 (0.91-1.13)	1.04 (0.93-1.15)
<i>Porphyromonas endodontalis</i>	0.40 (4.02)	0.19 (4.00)	1.00 (0.90-1.12)	1.00 (0.90-1.12)	1.01 (0.91-1.13)	1.01 (0.91-1.13)
<i>Lachnospiraceae_[G-8] sp._oral_taxon_500</i>	-2.24 (2.40)	-2.22 (2.46)	0.98 (0.89-1.09)	0.99 (0.89-1.10)	1.00 (0.90-1.11)	1.00 (0.90-1.11)
<i>Capnocytophaga sp._oral_taxon_338</i>	-1.36 (3.03)	-1.39 (3.07)	0.99 (0.89-1.10)	1.00 (0.90-1.11)	1.01 (0.91-1.12)	1.01 (0.91-1.13)
<i>Treponema sp._oral_taxon_231</i>	-1.38 (3.01)	-1.36 (3.07)	0.99 (0.89-1.09)	1.00 (0.90-1.12)	1.01 (0.91-1.12)	1.00 (0.90-1.11)
<i>Sphingomonas echinoides</i>	-2.07 (2.33)	-2.10 (2.30)	1.00 (0.91-1.11)	1.00 (0.91-1.11)	0.99 (0.90-1.10)	1.01 (0.91-1.12)
<i>Microbacterium flavescens</i>	-3.17 (1.54)	-3.13 (1.60)	1.00 (0.90-1.10)	0.99 (0.90-1.10)	0.99 (0.90-1.10)	1.01 (0.91-1.12)
<i>Leptotrichia sp._oral_taxon_219</i>	-1.40 (2.71)	-1.54 (2.47)	0.97 (0.88-1.08)	0.99 (0.90-1.10)	1.01 (0.91-1.11)	1.01 (0.91-1.12)
<i>Streptococcus australis</i>	-1.72 (2.50)	-1.76 (2.44)	0.98 (0.89-1.09)	0.99 (0.90-1.10)	1.01 (0.91-1.12)	1.03 (0.93-1.14)
<i>Streptococcus sanguinis</i>	4.88 (2.44)	4.94 (2.52)	1.01 (0.90-1.13)	1.01 (0.90-1.13)	1.00 (0.90-1.12)	1.01 (0.91-1.13)
<i>Leptotrichia goodfellowii</i>	-2.39 (2.59)	-2.50 (2.46)	0.99 (0.89-1.10)	1.01 (0.90-1.12)	1.00 (0.90-1.11)	1.01 (0.91-1.13)
<i>Haemophilus parainfluenzae</i>	3.70 (2.98)	3.54 (3.03)	0.99 (0.89-1.09)	1.00 (0.90-1.11)	1.00 (0.90-1.11)	1.02 (0.92-1.14)

<i>Ruminococcaceae</i> [G-1] <i>sp._oral_taxon_075</i>	-0.92 (2.74)	-0.93 (2.76)	0.99 (0.89-1.09)	0.99 (0.90-1.10)	1.00 (0.90-1.11)	1.00 (0.90-1.11)
Inversely associated						
<i>Neisseria subflava</i> *	-1.99 (3.15)	-2.40 (2.96)	0.90 (0.81-1.00)	0.89 (0.80-0.98)	0.88 (0.80-0.98)	0.89 (0.80-0.99)
<i>Bergeyella sp._oral_taxon_907</i>	-1.98 (2.31)	-2.19 (2.27)	0.91 (0.81-1.01)	0.89 (0.80-1.00)	0.89 (0.80-0.99)	0.89 (0.79-0.99)
<i>Gemella morbillorum</i>	3.32 (2.95)	2.80 (3.08)	0.88 (0.79-0.97)	0.88 (0.79-0.98)	0.88 (0.79-0.98)	0.89 (0.80-0.99)
<i>Leptotrichia sp._oral_taxon_212</i>	1.74 (2.98)	1.14 (3.15)	0.85 (0.77-0.94)	0.85 (0.76-0.95)	0.86 (0.77-0.96)	0.88 (0.79-0.98)
<i>Aggregatibacter segnis</i>	-0.56 (3.44)	-1.30 (3.13)	0.82 (0.74-0.91)	0.83 (0.75-0.92)	0.83 (0.75-0.93)	0.84 (0.75-0.93)
<i>Neisseria flavescens</i>	1.15 (3.30)	0.73 (3.13)	0.92 (0.83-1.02)	0.91 (0.82-1.01)	0.92 (0.82-1.02)	0.94 (0.84-1.04)
<i>Prevotella buccae</i>	-1.68 (2.51)	-1.73 (2.29)	0.99 (0.89-1.10)	0.99 (0.89-1.10)	0.98 (0.88-1.10)	0.98 (0.88-1.09)
<i>Selenomonas sputigena</i>	5.27 (2.64)	5.20 (2.91)	0.99 (0.89-1.10)	0.98 (0.88-1.09)	0.97 (0.87-1.08)	0.96 (0.87-1.07)
<i>Selenomonas sp._oral_taxon_136</i>	1.48 (2.99)	1.54 (2.96)	0.99 (0.90-1.10)	0.96 (0.86-1.07)	0.95 (0.86-1.06)	0.96 (0.86-1.07)
<i>Leptotrichia sp._oral_taxon_417</i>	0.72 (3.10)	0.70 (3.38)	0.99 (0.90-1.10)	0.98 (0.88-1.08)	0.97 (0.87-1.07)	0.97 (0.88-1.08)
<i>Selenomonas sp._oral_taxon_126</i>	-0.80 (2.80)	-0.88 (2.65)	1.01 (0.91-1.12)	0.99 (0.89-1.10)	0.98 (0.89-1.09)	0.97 (0.87-1.07)
<i>Lachnoanaerobaculum umeaense</i>	-0.71 (2.57)	-0.78 (2.59)	0.97 (0.88-1.08)	0.96 (0.86-1.06)	0.96 (0.86-1.07)	0.96 (0.87-1.07)
<i>Capnocytophaga sp._oral_taxon_336</i>	0.53 (3.06)	0.35 (3.02)	0.97 (0.87-1.08)	0.96 (0.87-1.07)	0.96 (0.86-1.07)	0.95 (0.85-1.05)
<i>Tannerella forsythia</i>	1.63 (3.16)	1.38 (3.52)	0.97 (0.87-1.08)	0.98 (0.88-1.09)	0.98 (0.88-1.09)	0.96 (0.86-1.07)
<i>Treponema denticola</i>	-0.50 (3.49)	-0.53 (3.46)	0.98 (0.88-1.09)	0.98 (0.88-1.09)	0.98 (0.88-1.10)	0.97 (0.87-1.08)
<i>Capnocytophaga sp._oral_taxon_323</i>	-2.13 (2.76)	-2.20 (2.94)	0.98 (0.89-1.08)	0.99 (0.89-1.09)	0.98 (0.89-1.09)	0.99 (0.89-1.09)
<i>Eikenella corrodens</i>	2.79 (2.23)	2.65 (2.32)	0.98 (0.89-1.09)	0.98 (0.88-1.09)	0.98 (0.88-1.09)	0.98 (0.88-1.09)
<i>Prevotella micans</i>	-2.35 (2.35)	-2.44 (2.35)	0.97 (0.87-1.07)	0.97 (0.87-1.08)	0.97 (0.87-1.08)	0.98 (0.88-1.09)
<i>Corynebacterium matruchotii</i>	4.61 (2.44)	4.63 (2.45)	0.99 (0.90-1.10)	0.97 (0.87-1.08)	0.97 (0.87-1.07)	0.97 (0.88-1.08)
<i>Brevundimonas diminuta</i>	-3.50 (1.48)	-3.59 (1.43)	0.97 (0.87-1.07)	0.96 (0.86-1.06)	0.96 (0.87-1.07)	0.98 (0.88-1.09)
<i>Actinomyces naeslundii</i>	3.74 (2.00)	3.73 (2.13)	0.96 (0.86-1.07)	0.96 (0.87-1.07)	0.96 (0.86-1.06)	0.98 (0.88-1.09)
<i>Actinobaculum sp._oral_taxon_183</i>	0.18 (2.84)	0.03 (2.87)	0.96 (0.87-1.06)	0.96 (0.87-1.06)	0.96 (0.87-1.06)	0.97 (0.88-1.07)
<i>Bacteroidetes</i> [G-5] <i>sp._oral_taxon_511</i>	-1.56 (3.17)	-1.70 (3.10)	0.96 (0.86-1.06)	0.96 (0.86-1.07)	0.96 (0.87-1.07)	0.96 (0.87-1.07)
<i>Selenomonas sp._oral_taxon_146</i>	-0.18 (2.76)	-0.18 (2.77)	0.96 (0.87-1.07)	0.95 (0.86-1.06)	0.96 (0.86-1.07)	0.95 (0.85-1.05)
<i>Selenomonas sp._oral_taxon_919</i>	0.36 (2.85)	0.17 (2.92)	0.98 (0.88-1.08)	0.97 (0.87-1.07)	0.95 (0.86-1.06)	0.94 (0.85-1.05)
<i>Tannerella sp._oral_taxon_286</i>	0.04 (2.51)	-0.14 (2.47)	0.96 (0.87-1.07)	0.96 (0.87-1.07)	0.96 (0.87-1.07)	0.96 (0.86-1.06)

<i>Leptotrichia sp._oral_taxon_215</i>	-0.15 (2.74)	-0.29 (2.91)	0.98 (0.88-1.09)	0.97 (0.88-1.08)	0.97 (0.87-1.07)	0.97 (0.88-1.08)
<i>Treponema lecithinolyticum</i>	-2.27 (2.77)	-2.37 (2.67)	0.97 (0.88-1.08)	0.99 (0.89-1.10)	0.99 (0.89-1.10)	0.99 (0.89-1.10)
<i>Prevotella pleuritidis</i>	-0.36 (4.13)	-0.40 (4.06)	0.96 (0.87-1.07)	0.95 (0.85-1.05)	0.95 (0.85-1.06)	0.96 (0.86-1.06)
<i>Prevotella oris</i>	4.96 (2.78)	4.74 (3.06)	0.98 (0.88-1.09)	0.97 (0.87-1.08)	0.96 (0.86-1.07)	0.95 (0.86-1.06)
<i>Capnocytophaga granulosa</i>	2.72 (3.05)	2.51 (3.12)	0.96 (0.86-1.06)	0.97 (0.87-1.08)	0.98 (0.88-1.09)	0.97 (0.87-1.08)
<i>Haemophilus parahaemolyticus</i>	-2.45 (2.81)	-2.49 (2.64)	0.97 (0.88-1.08)	0.98 (0.89-1.08)	0.99 (0.89-1.09)	1.00 (0.90-1.10)
<i>Capnocytophaga sputigena</i>	1.99 (3.44)	1.78 (3.27)	0.96 (0.87-1.06)	0.96 (0.87-1.07)	0.97 (0.87-1.07)	0.97 (0.88-1.07)
<i>Leptotrichia hofstadii</i>	0.15 (3.45)	-0.11 (3.48)	0.94 (0.85-1.04)	0.94 (0.85-1.05)	0.94 (0.85-1.04)	0.93 (0.84-1.03)
<i>Porphyromonas sp._oral_taxon_275</i>	-2.30 (2.70)	-2.31 (2.56)	0.95 (0.86-1.05)	0.96 (0.87-1.07)	0.97 (0.88-1.08)	0.97 (0.87-1.07)
<i>Veillonella sp._oral_taxon_780</i>	-2.07 (2.89)	-2.21 (2.62)	0.97 (0.88-1.08)	0.96 (0.87-1.07)	0.97 (0.87-1.07)	0.97 (0.87-1.08)
<i>Prevotella sp._oral_taxon_317</i>	2.77 (3.57)	2.42 (3.57)	0.94 (0.85-1.04)	0.95 (0.85-1.05)	0.95 (0.86-1.05)	0.95 (0.85-1.05)
<i>Cardiobacterium valvarum</i>	1.49 (2.95)	1.29 (2.97)	0.95 (0.86-1.05)	0.94 (0.85-1.05)	0.95 (0.85-1.05)	0.94 (0.84-1.04)
<i>Prevotella saccharolytica</i>	-0.46 (2.53)	-0.65 (2.65)	0.95 (0.85-1.05)	0.95 (0.86-1.05)	0.96 (0.87-1.06)	0.95 (0.86-1.06)
<i>Fusobacterium naviforme</i>	3.50 (2.69)	3.29 (2.85)	0.95 (0.86-1.05)	0.95 (0.86-1.06)	0.95 (0.86-1.06)	0.94 (0.85-1.05)
<i>Porphyromonas sp._oral_taxon_279</i>	1.38 (3.10)	1.16 (3.12)	0.95 (0.86-1.05)	0.94 (0.85-1.04)	0.94 (0.85-1.04)	0.95 (0.85-1.05)
<i>Lachnospiraceae_[G-3] sp._oral_taxon_100</i>	0.63 (2.72)	0.43 (2.69)	0.95 (0.86-1.06)	0.96 (0.86-1.07)	0.96 (0.87-1.07)	0.96 (0.86-1.07)
<i>Selenomonas sp._oral_taxon_137</i>	0.93 (3.87)	0.63 (3.90)	0.95 (0.85-1.05)	0.95 (0.85-1.05)	0.95 (0.85-1.05)	0.95 (0.86-1.06)
<i>Veillonella denticariosi</i>	-1.63 (3.15)	-1.89 (2.75)	0.93 (0.84-1.04)	0.94 (0.84-1.05)	0.94 (0.84-1.05)	0.95 (0.85-1.06)
<i>Actinobaculum sp._oral_taxon_848</i>	-0.88 (2.70)	-1.11 (2.71)	0.92 (0.83-1.03)	0.92 (0.83-1.02)	0.93 (0.84-1.03)	0.94 (0.85-1.04)
<i>Fretibacterium sp._oral_taxon_358</i>	-3.07 (2.36)	-3.27 (2.00)	0.94 (0.84-1.05)	0.94 (0.84-1.06)	0.95 (0.84-1.07)	0.95 (0.85-1.07)
<i>TM7_[G-6] sp._oral_taxon_870</i>	-1.86 (2.85)	-1.89 (2.72)	0.99 (0.90-1.09)	0.99 (0.90-1.10)	0.99 (0.89-1.09)	0.99 (0.90-1.10)
<i>Prevotella dentalis</i>	-1.85 (2.95)	-1.96 (2.83)	0.98 (0.89-1.09)	0.98 (0.89-1.09)	0.99 (0.89-1.10)	0.99 (0.89-1.10)
<i>Actinomyces johnsonii</i>	0.76 (2.42)	0.77 (2.49)	0.99 (0.90-1.10)	1.00 (0.90-1.11)	0.99 (0.89-1.10)	0.98 (0.88-1.08)
<i>Rothia aeria</i>	2.26 (3.14)	2.17 (3.08)	0.96 (0.87-1.07)	0.97 (0.87-1.08)	0.98 (0.88-1.09)	1.00 (0.90-1.12)
<i>Campylobacter gracilis</i>	4.93 (1.40)	4.82 (1.84)	0.98 (0.88-1.10)	0.98 (0.87-1.10)	0.97 (0.86-1.08)	0.97 (0.87-1.09)
<i>TM7_[G-1] sp._oral_taxon_352</i>	-1.55 (2.32)	-1.48 (2.36)	0.99 (0.90-1.10)	0.99 (0.89-1.11)	0.99 (0.89-1.10)	1.01 (0.91-1.12)
<i>Campylobacter concisus</i>	2.16 (2.17)	2.12 (2.33)	0.98 (0.89-1.09)	0.96 (0.86-1.07)	0.96 (0.86-1.07)	0.97 (0.88-1.08)
<i>Granulicatella adiacens</i>	4.02 (1.97)	3.96 (2.25)	0.99 (0.89-1.10)	0.98 (0.88-1.09)	0.97 (0.87-1.08)	0.98 (0.89-1.09)
<i>Streptococcus cristatus</i>	3.04 (2.60)	3.05 (2.58)	1.00 (0.90-1.10)	0.99 (0.90-1.10)	0.99 (0.90-1.10)	0.99 (0.90-1.10)
<i>Streptococcus intermedius</i>	3.79 (3.28)	3.70 (3.37)	0.98 (0.88-1.09)	0.99 (0.89-1.10)	0.99 (0.89-1.10)	0.98 (0.88-1.08)
<i>Streptococcus gordonii</i>	3.99 (2.76)	4.01 (2.66)	0.99 (0.90-1.10)	1.00 (0.90-1.11)	0.99 (0.89-1.10)	0.98 (0.88-1.09)

<i>Shuttleworthia satelles</i>	-2.45 (2.41)	-2.53 (2.20)	0.97 (0.87-1.08)	0.95 (0.86-1.06)	0.96 (0.86-1.08)	0.96 (0.86-1.07)
<i>Selenomonas sp._oral_taxon_936</i>	-1.22 (2.66)	-1.27 (2.78)	0.99 (0.89-1.10)	0.98 (0.88-1.09)	0.98 (0.89-1.09)	0.97 (0.87-1.08)
<i>TM7_[G-1] sp._oral_taxon_348</i>	-0.63 (2.84)	-0.57 (2.95)	0.99 (0.89-1.09)	0.97 (0.88-1.08)	0.98 (0.88-1.09)	0.97 (0.88-1.08)
<i>Gemella haemolysans</i>	2.05 (3.01)	1.82 (3.01)	0.95 (0.86-1.05)	0.95 (0.86-1.05)	0.95 (0.85-1.05)	0.95 (0.85-1.05)
<i>Capnocytophaga sp._oral_taxon_864</i>	-1.39 (3.03)	-1.55 (2.86)	0.94 (0.85-1.04)	0.94 (0.85-1.04)	0.93 (0.84-1.03)	0.92 (0.83-1.03)
<i>Porphyromonas sp._oral_taxon_278</i>	-2.45 (2.53)	-2.71 (2.19)	0.94 (0.84-1.04)	0.93 (0.84-1.04)	0.94 (0.85-1.04)	0.94 (0.85-1.05)
<i>Aggregatibacter sp._oral_taxon_458</i>	-0.39 (3.09)	-0.60 (3.03)	0.94 (0.85-1.05)	0.94 (0.85-1.05)	0.95 (0.86-1.06)	0.95 (0.86-1.06)
<i>Capnocytophaga sp._oral_taxon_326</i>	0.46 (3.63)	0.11 (3.47)	0.95 (0.85-1.05)	0.97 (0.87-1.07)	0.96 (0.87-1.07)	0.96 (0.87-1.07)
<i>Treponema sp._oral_taxon_237</i>	-2.36 (2.86)	-2.55 (2.79)	0.95 (0.85-1.06)	0.95 (0.85-1.06)	0.95 (0.85-1.06)	0.96 (0.86-1.07)
<i>Streptococcus sp._oral_taxon_074</i>	-0.03 (2.44)	-0.22 (2.38)	0.94 (0.85-1.04)	0.93 (0.83-1.03)	0.93 (0.84-1.04)	0.95 (0.85-1.06)
<i>Cardiobacterium hominis</i>	2.33 (2.80)	2.12 (2.81)	0.94 (0.85-1.04)	0.96 (0.87-1.07)	0.96 (0.87-1.06)	0.98 (0.88-1.08)
<i>Campylobacter showae</i>	2.72 (2.52)	2.49 (2.79)	0.94 (0.85-1.04)	0.96 (0.86-1.06)	0.96 (0.86-1.06)	0.93 (0.84-1.04)
<i>TM7_[G-1] sp._oral_taxon_952</i>	2.65 (3.19)	2.46 (3.19)	0.94 (0.85-1.04)	0.94 (0.85-1.05)	0.94 (0.85-1.05)	0.95 (0.86-1.06)
<i>Neisseria elongata</i>	1.67 (3.62)	1.54 (3.49)	0.93 (0.84-1.03)	0.94 (0.85-1.04)	0.94 (0.85-1.04)	0.95 (0.85-1.05)
<i>Haemophilus sp._oral_taxon_036</i>	-0.94 (3.25)	-1.28 (2.98)	0.94 (0.85-1.04)	0.95 (0.85-1.05)	0.96 (0.86-1.06)	0.96 (0.86-1.06)
<i>Leptotrichia sp._oral_taxon_223</i>	-1.90 (2.84)	-2.18 (2.63)	0.92 (0.83-1.03)	0.93 (0.83-1.03)	0.94 (0.84-1.05)	0.94 (0.85-1.05)
<i>TM7_[G-5] sp._oral_taxon_356</i>	0.47 (3.68)	0.03 (3.50)	0.92 (0.82-1.02)	0.92 (0.82-1.02)	0.92 (0.83-1.03)	0.91 (0.82-1.02)
<i>Capnocytophaga leadbetteri</i>	2.91 (2.99)	2.64 (3.11)	0.93 (0.84-1.03)	0.94 (0.85-1.05)	0.95 (0.85-1.05)	0.95 (0.85-1.05)
<i>Veillonella rogosae</i>	0.91 (3.17)	0.59 (3.15)	0.95 (0.85-1.05)	0.95 (0.85-1.06)	0.94 (0.85-1.05)	0.96 (0.86-1.06)
<i>Selenomonas sp._oral_taxon_892</i>	0.89 (2.86)	0.72 (2.94)	0.93 (0.84-1.04)	0.95 (0.85-1.05)	0.95 (0.85-1.05)	0.92 (0.83-1.02)
<i>Fusobacterium periodonticum</i>	-0.08 (2.55)	-0.36 (2.59)	0.93 (0.84-1.04)	0.93 (0.83-1.03)	0.93 (0.83-1.03)	0.95 (0.85-1.06)
<i>Ottowia sp._oral_taxon_894</i>	-1.31 (2.85)	-1.57 (2.83)	0.92 (0.82-1.02)	0.93 (0.84-1.03)	0.94 (0.84-1.04)	0.95 (0.85-1.05)
<i>Kingella denitrificans</i>	0.56 (3.13)	0.17 (3.03)	0.90 (0.81-0.99)	0.91 (0.82-1.00)	0.92 (0.83-1.01)	0.92 (0.83-1.02)
<i>TM7_[G-1] sp._oral_taxon_869</i>	-1.45 (3.53)	-1.80 (3.08)	0.91 (0.83-1.01)	0.92 (0.83-1.02)	0.93 (0.84-1.03)	0.94 (0.85-1.04)
<i>Fusobacterium nucleatum_subsp._polymorphum</i>	5.25 (2.10)	4.96 (2.21)	0.92 (0.83-1.03)	0.92 (0.83-1.02)	0.92 (0.83-1.03)	0.92 (0.83-1.03)
<i>Capnocytophaga gingivalis</i>	3.40 (2.54)	3.09 (2.71)	0.92 (0.83-1.02)	0.92 (0.83-1.03)	0.92 (0.83-1.03)	0.92 (0.83-1.03)
<i>Actinomyces massiliensis</i>	1.43 (2.41)	1.27 (2.52)	0.93 (0.84-1.03)	0.94 (0.85-1.04)	0.94 (0.85-1.04)	0.96 (0.86-1.06)
<i>Granulicatella elegans</i>	-1.61 (2.83)	-1.93 (2.47)	0.92 (0.83-1.02)	0.91 (0.82-1.01)	0.92 (0.83-1.02)	0.92 (0.83-1.02)
<i>Corynebacterium durum</i>	1.01 (2.92)	0.83 (2.90)	0.94 (0.85-1.04)	0.94 (0.84-1.04)	0.94 (0.85-1.05)	0.95 (0.86-1.06)
<i>Leptotrichia sp._oral_taxon_392</i>	0.36 (3.15)	0.11 (3.00)	0.93 (0.84-1.03)	0.94 (0.85-1.05)	0.95 (0.85-1.05)	0.96 (0.86-1.06)
<i>Porphyromonas sp._oral_taxon_284</i>	0.13 (3.44)	-0.25 (3.24)	0.92 (0.83-1.02)	0.93 (0.84-1.03)	0.93 (0.84-1.03)	0.92 (0.83-1.02)

<i>Neisseria subflava</i>	-1.99 (3.15)	-2.40 (2.96)	0.90 (0.81-1.00)	0.89 (0.80-0.98)	0.88 (0.80-0.98)	0.89 (0.80-0.99)
<i>Peptostreptococcaceae_[XI][G-7]</i> <i>[Eubacterium]_yuri</i>	0.11 (3.47)	-0.20 (3.22)	0.93 (0.84-1.03)	0.93 (0.84-1.04)	0.94 (0.85-1.05)	0.95 (0.85-1.05)
<i>Haemophilus haemolyticus</i>	-1.92 (2.85)	-2.19 (2.64)	0.91 (0.82-1.01)	0.92 (0.83-1.02)	0.93 (0.83-1.03)	0.93 (0.84-1.03)
<i>Streptococcus sp._oral_taxon_056</i>	-0.49 (3.01)	-0.72 (3.02)	0.91 (0.83-1.01)	0.93 (0.84-1.03)	0.93 (0.84-1.03)	0.92 (0.83-1.02)
<i>Bergeyella sp._oral_taxon_322</i>	2.16 (2.34)	1.79 (2.46)	0.92 (0.83-1.01)	0.93 (0.84-1.02)	0.93 (0.84-1.03)	0.94 (0.85-1.04)
<i>Neisseria sicca</i>	1.58 (3.78)	1.12 (3.87)	0.91 (0.82-1.00)	0.92 (0.83-1.02)	0.93 (0.83-1.03)	0.92 (0.83-1.02)
<i>Aggregatibacter paraphrophilus</i>	-1.76 (3.30)	-2.02 (3.09)	0.92 (0.83-1.02)	0.94 (0.84-1.04)	0.94 (0.85-1.04)	0.95 (0.85-1.05)
<i>Alloprevotella sp._oral_taxon_473</i>	-1.93 (2.87)	-2.23 (2.72)	0.91 (0.82-1.02)	0.92 (0.83-1.03)	0.93 (0.84-1.04)	0.95 (0.85-1.05)
<i>Actinomyces sp._oral_taxon_171</i>	0.71 (2.71)	0.45 (2.77)	0.91 (0.82-1.01)	0.91 (0.82-1.01)	0.90 (0.81-0.99)	0.91 (0.82-1.01)
<i>Abiotrophia defectiva</i>	-0.06 (3.12)	-0.38 (2.88)	0.91 (0.82-1.00)	0.92 (0.83-1.02)	0.93 (0.84-1.03)	0.93 (0.84-1.03)
<i>Neisseria oralis</i>	0.43 (3.76)	-0.13 (3.63)	0.90 (0.82-1.00)	0.91 (0.82-1.01)	0.92 (0.83-1.02)	0.92 (0.83-1.02)
<i>Porphyromonas catoniae</i>	-0.75 (3.20)	-1.14 (3.00)	0.90 (0.82-1.00)	0.91 (0.82-1.01)	0.92 (0.83-1.02)	0.93 (0.84-1.03)
<i>Lautropia mirabilis</i>	1.05 (3.18)	0.66 (3.01)	0.90 (0.81-0.99)	0.92 (0.83-1.02)	0.93 (0.84-1.03)	0.94 (0.85-1.05)
<i>SR1_[G-1] sp._oral_taxon_874</i>	-1.96 (2.49)	-2.29 (2.31)	0.89 (0.81-0.99)	0.90 (0.82-1.00)	0.91 (0.82-1.01)	0.91 (0.82-1.01)
<i>Leptotrichia sp._oral_taxon_225</i>	-0.55 (3.44)	-1.07 (3.30)	0.89 (0.80-0.99)	0.90 (0.81-1.00)	0.90 (0.81-1.00)	0.89 (0.80-0.99)

HR, hazard ratio; CI, confidence interval. HR and CI are for a 1-standard deviation increment in baseline CLR bacterial species.

Age-adjusted analysis (n=735).

Model 1: age, race-ethnicity, education, nSES, self-rated general health (n=723).

Model 2: includes model 1 covariates and history of treated diabetes (n=723).

Model 3: includes model 2 covariates and dietary HEI score, physical activity (n=715).

†**Bolded** bacterial species are significantly associated with incident hypertension based on an uncorrected Wald test of hazard ratio = 1.

After Benjamini-Hochberg correction, associations no longer were significant.

Table S5. Sensitivity analysis on hypertension risk in those with normal blood pressure at baseline (n=429) for the 15 bacteria found to be significant in primary results.

OTU Label	Incident Hypertension		Age-adjusted HR (95% CI) †	Multivariable HR (95% CI) †
	No (n=278)	Yes (n=151)		
	CLR Mean (SD)	CLR Mean (SD)		
10 positive associations				
<i>Streptococcus anginosus</i>	0.41 (3.62)	1.26 (3.59)	1.25 (1.06-1.48)	1.28 (1.08-1.53)
<i>Streptococcus salivarius</i>	2.56 (2.84)	2.95 (3.25)	1.16 (0.98-1.36)	1.12 (0.95-1.32)
<i>Fretibacterium sp._oral_taxon_362</i>	-2.14 (2.39)	-1.77 (2.86)	1.17 (0.99-1.39)	1.19 (0.99-1.44)
<i>Selenomonas infelix</i>	0.84 (2.91)	1.84 (2.51)	1.34 (1.13-1.58)	1.30 (1.09-1.56)
<i>Prevotella sp._oral_taxon_526</i>	-3.08 (2.10)	-2.54 (2.68)	1.23 (1.06-1.42)	1.22 (1.05-1.42)
<i>Prevotella sp._oral_taxon_292</i>	-1.74 (2.70)	-1.48 (2.66)	1.11 (0.93-1.31)	1.06 (0.88-1.26)
<i>Megasphaera sp._oral_taxon_123</i>	-2.95 (2.49)	-2.34 (2.95)	1.20 (1.02-1.40)	1.18 (1.00-1.39)
<i>Capnocytophaga sp._oral_taxon_903</i>	-2.51 (2.63)	-2.08 (2.96)	1.14 (0.98-1.32)	1.14 (0.97-1.33)
<i>Prevotella sp._oral_taxon_376</i>	-2.86 (2.43)	-1.48 (2.66)	1.15 (0.99-1.33)	1.17 (1.01-1.36)
<i>Streptococcus lactarius</i>	-1.73 (2.12)	-1.55 (2.42)	1.07 (0.90-1.26)	0.98 (0.82-1.17)
5 inverse associations				
<i>Neisseria subflava</i> *	-2.08 (3.03)	-2.66 (2.64)	0.83 (0.70-1.00)	0.86 (0.72-1.03)
<i>Bergeyella sp._oral_taxon_907</i>	-1.95 (2.24)	-2.04 (2.39)	0.93 (0.78-1.10)	0.93 (0.78-1.11)
<i>Gemella morbillorum</i>	3.35 (2.94)	2.88 (3.10)	0.85 (0.72-0.99)	0.85 (0.72-1.01)
<i>Leptotrichia sp._oral_taxon_212</i>	1.72 (3.03)	1.34 (3.07)	0.84 (0.71-1.00)	0.91 (0.76-1.09)
<i>Aggregatibacter segnis</i>	-0.61 (3.41)	-1.11 (3.08)	0.83 (0.71-0.98)	0.84 (0.71-1.00)

HR, hazard ratio; CI, confidence interval. HR and CI are for a 1-standard deviation increment in baseline CLR bacterial species.

Multivariable model: age, race-ethnicity, education, nSES, self-rated general health, history of diabetes treated with medication, diet score, physical activity, statin use. (Covariates as in fully adjusted Model 3, Table 3)

* Bacteria with nitrate-reductase capability for reducing nitrate to nitrite in the oral cavity.

†Uncorrected Wald test of hazard ratio = 1. After Benjamini-Hochberg correction, associations no longer were significant.

Table S6. Nitrate-reducing oral bacteria species identified in previous studies.

Species Identified in Previous Studies	Among the 245 Identified Species in the Buffalo OsteoPerio Study*	Associated [†] with BP or HTN in the present Buffalo OsteoPerio Study	
		Prevalent HTN or BP‡	Incident HTN
Doel et al. 2005 [36]			
<i>Actinomyces naeslundii</i>	Yes	No	No
<i>A. adontolyticus</i>	No	---	---
<i>A. viscosus</i>	No	---	---
<i>Capnocytophaga sputigena</i>	Yes	No	No
<i>Corynebacterium matruchotti</i>	No	---	---
<i>C. durum</i>	Yes	Yes§	No
<i>Eikenella corrodens</i>	Yes	No	No
<i>Granulicatella adiacens</i>	Yes	No	No
<i>Haemophilus parainfluenzae</i>	Yes	No	No
<i>H. segnis</i>	No	---	---
<i>Microbacterium oxydans</i>	No	---	---
<i>Propionibacterium acnes</i>	No	---	---
<i>Rothia denticariosa</i>	No	---	---
<i>R. mucilaginosa</i>	No	---	---
<i>Selenomonas noxia</i>	YES	No	No
<i>S. hemolyticus</i>	No	---	---
<i>Staphylococcus epidermidis</i>	No	---	---
<i>Veillonella atypica</i>	YES	No	No
<i>V. dispar</i>	YES	No	No
<i>V. parvula</i>	YES	No	No
Hyde et al., 2014 [37]			
<i>Actinomyces adonotolyticus</i>	No	---	---
<i>A. orisa</i>	No	---	---
<i>A. viscosus</i>	No	---	---
<i>Granulicatella adiacens</i>	No	---	---
<i>Haemophilus parainfluenza</i>	YES	No	No
<i>Neisseria mucosa</i>	No	---	---
<i>N. subflava</i>	YES	No	YES¶
Liddle et al. 2019 [38]			
<i>Haemophilus parainfluenza</i>	YES	No	No
<i>Neisseria subflava</i>	YES	No	No
<i>Prevotella melaninogenica</i>	YES	No	No
<i>Rothia denticariosa</i>	No	---	---
<i>R. mucilaginosa</i>	No	---	---
<i>Veillonella dispar</i>	YES	No	No
<i>Veillonella parvula</i>	YES	No	No

*See Table S3 for list of the 245 bacteria species identified in the Buffalo OsteoPerio Study. †CLR bacteria abundance differed across baseline BP categories (Table 2) or was associated with incident HTN (Table 3).

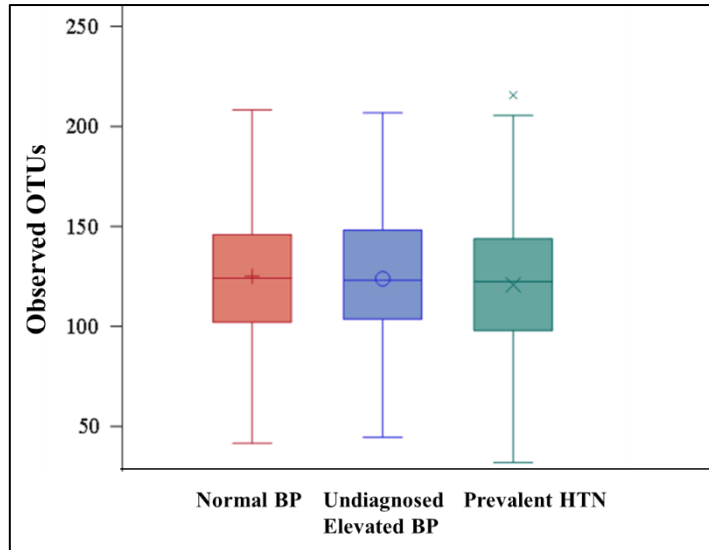
‡See Table 1 for BP category definitions.

§See Table 2 CLR mean differences in *Corynebacterium durum* according to baseline BP categories.

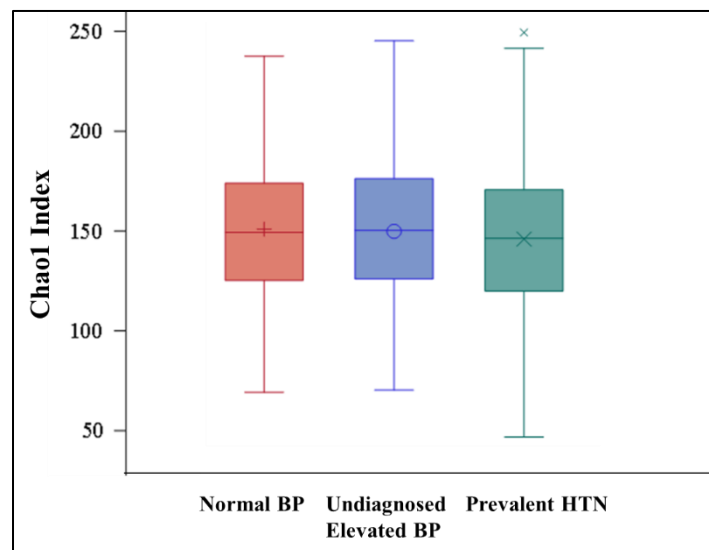
¶See Table 3 hazard ratio for incident HTN associated with baseline CLR mean *Neisseria subflava*.

Figure S1. Alpha diversity indices according to baseline BP and HTN status. (N=1,215). Tests for differences in (a) Observed OTUs, (b) Chao1 Index, and (c) Shannon Index across BP/HTN groups did not achieve statistical significance ($P > 0.05$, all).

A. Observed OTUs



B. Chao1 Index



C. Shannon Index

