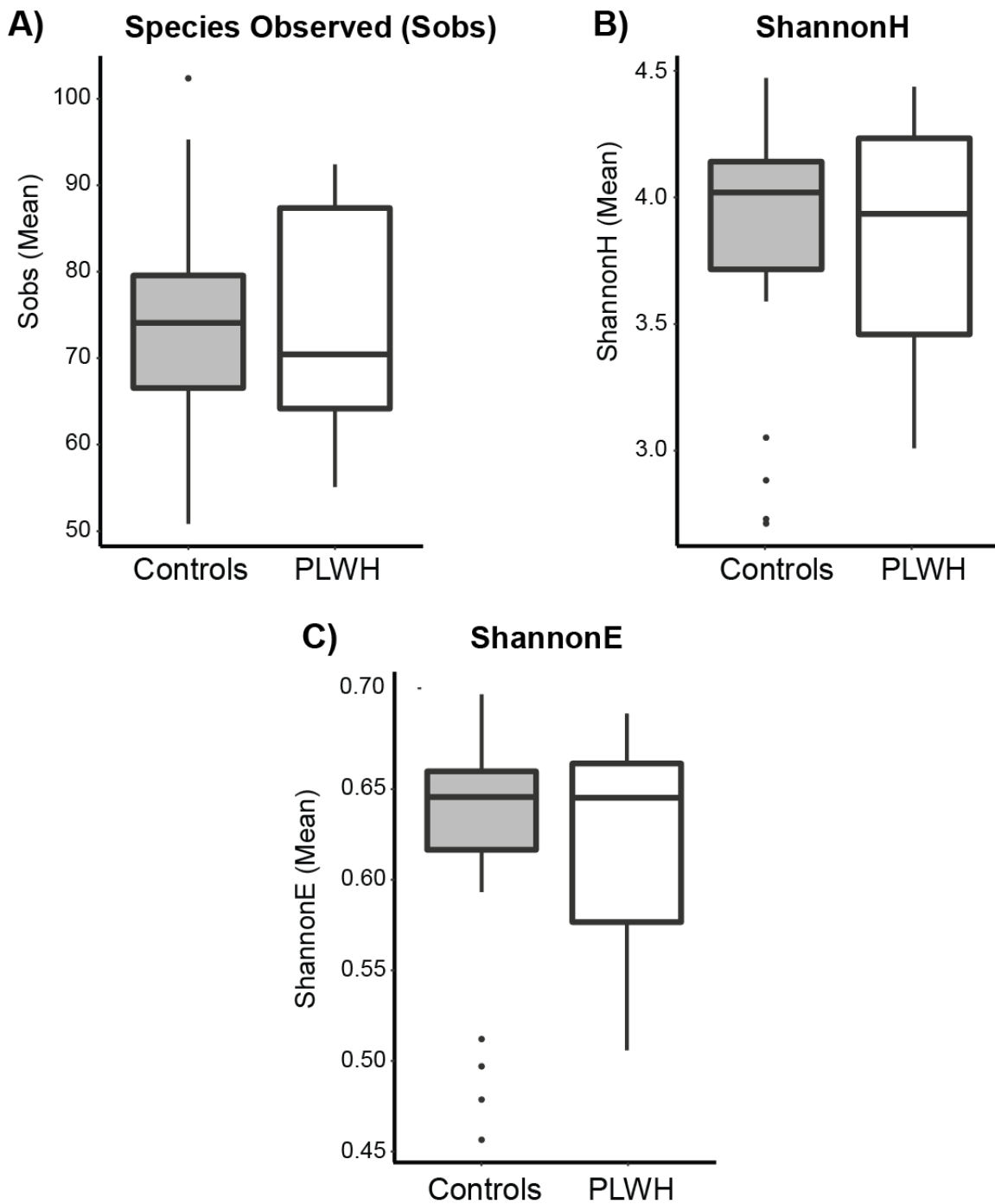


Age-Related Changes in the Stool Microbiome Differ by HIV-1 Serostatus.

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Supplementary Figure 1. Alpha-diversity measurements comparing control study participants and people living with HIV (PLWH) and using linear regression models. **(A)** Richness as expressed by species observed (Sobs). **(B)** ShannonH diversity index, a measure of richness. **(C)** ShannonE diversity index, a measure of evenness.

Supplemental Table 1: Impact of HIV on Gut Microbiome

Phylum	Effect	95% CI	FDR p-value
Actinobacteria	0.76	0.41, 1.41	0.52
Bacteroidetes	1.03	0.73, 1.45	0.86
Cyanobacteria	0.16	0.03, 0.82	0.14
Firmicutes	0.91	0.76, 1.07	0.46
Fusobacteria	6.94	1.01, 47.3	0.14
Lentisphaerae	0.21	0.01, 2.30	0.46
Proteobacteria	2.45	1.22, 4.89	0.13
Synergistetes	21.72	1.03, 454.83	0.14
Tenericutes	0.44	0.063, 3.04	0.52
Verrucomicrobia	0.82	0.12, 5.42	0.86
Family	Effect	95% CI	FDR p-value
<i>Phylum Actinobacteria</i>			
Actinomycetaceae	0.86	0.39, 1.84	0.84
Bifidobacteriaceae	0.33	0.10, 1.09	0.23
Coriobacteriaceae	0.94	0.50, 1.75	0.88
<i>Phylum Bacteroidetes</i>			
Bacteroidaceae	0.65	0.32, 1.31	0.45
Porphyromonadaceae	1.11	0.53, 2.28	0.85
Prevotellaceae	2.20	0.62, 7.73	0.45
Rikenellaceae	0.44	0.19, 1.00	0.19
<i>Phylum Firmicutes</i>			
Acidaminococcaceae	1.43	0.49, 4.15	0.69
Christensenellaceae	0.59	0.26, 1.28	0.41
Clostridiaceae	0.85	0.25, 2.90	0.86
Erysipelotrichaceae	2.18	1.09, 4.32	0.12
Lachnospiraceae	0.72	0.58, 0.90	0.03
Lactobacillaceae	3.25	0.79, 13.32	0.29
Peptococcaceae	1.07	0.32, 3.47	0.91
Peptostreptococcaceae	0.45	0.15, 1.26	0.33
Ruminococcaceae	1.05	0.76, 1.44	0.85
Streptococcaceae	1.17	0.43, 3.12	0.85
Veillonellaceae	1.47	0.55, 3.89	0.62
<i>Phylum Fusobacteria</i>			
Fusobacteriaceae	6.10	0.87, 42.33	0.23
Leptotrichiaceae	184.09	4.58, 7386.9	0.04
<i>Phylum Proteobacteria</i>			
Alcaligenaceae	1.58	0.65, 3.83	0.53
Desulfovibrionaceae	2.94	1.3, 6.55	0.047
Enterobacteriaceae	2.31	0.56, 9.40	0.45
Oxalobacteraceae	0.44	0.34, 0.54	<0.0001
Pasteurellaceae	0.36	0.09, 1.36	0.33
Rhodospirillaceae	0.50	0.046, 5.31	0.72
Succinivibrionaceae	7.78	0.78, 76.8	0.24
<i>Phylum Synergistetes</i>			
Synergistaceae	21.72	1.03, 454.8	0.19
<i>Phylum Verrucomicrobia</i>			
Verrucomicrobiaceae	0.85	0.12, 5.74	0.89

Genus	SCFA producers ^{[1-3]*}	Effect	95% CI	FDR p-value
<i>Phylum Actinobacteria</i>				
Bifidobacterium		0.34	0.10, 1.12	0.26
Collinsella		0.94	0.40, 2.19	0.93
Eggerthella		0.17	0.044, 0.62	0.047
Enterorhabdus		1.56	0.33, 7.18	0.74
Slackia		0.70	0.11, 4.25	0.83
Varibaculum		0.02	5e-04, 0.90	0.17
<i>Phylum Bacteroidetes</i>				
Alistipes	propionate	0.32	0.13, 0.77	0.06
Bacteroides	propionate	0.65	0.32, 1.31	0.48
Barnesiella		0.09	0.03, 0.26	0.0011
Odoribacter		0.70	0.65, 0.73	<0.0001
Parabacteroides		1.45	0.62, 3.37	0.59
Paraprevotella		1.53	1.36, 1.72	<0.0001
Prevotella	propionate	2.08	0.58, 7.32	0.50
<i>Phylum Firmicutes</i>				
Acidaminococcus		2.61	0.30, 22.74	0.59
Allisonella		2.85	2.51, 3.23	<0.0001
Anaerostipes	butyrate	0.62	0.29, 1.32	0.47
Anaerotruncus		1.58	0.76, 3.24	0.47
Anaerovibrio		421.75	42.4, 4190.8	<0.0001
Blautia	propionate	0.81	0.56, 1.15	0.49
Butyrivibrio	butyrate	0.84	0.099, 7.15	0.93
Catenibacterium		2.85	0.64, 12.66	0.43
Clostridium		0.85	0.25, 2.90	0.90
Coprococcus	butyrate, propionate	0.88	0.53, 1.46	0.78
Dialister	propionate	1.30	0.36, 4.63	0.83
Dorea		1.42	0.66, 3.03	0.58
Erysipelotrichaceae		1.59	0.91, 2.77	0.32
Faecalibacterium	butyrate	0.79	0.42, 1.46	0.62
Flavonifractor		1.92	0.52, 7.00	0.56
Holdemania		0.92	0.37, 2.22	0.93
Howardella		1.74	1.5, 1.95	<0.0001
Lachnospira		0.85	0.34, 2.12	0.86
Lactobacillus		3.25	0.79, 13.32	0.32
Marvinbryantia		1.63	0.61, 4.34	0.56
Megamonas		0.57	0.056, 5.75	0.78
Megasphaera		2.93	0.48, 17.75	0.49
Mitsuokella		1.06	0.043, 25.95	0.98
Mogibacterium		6.45	1.17, 35.55	0.13
Oribacterium		4.96	0.70, 34.66	0.32
Oscillospira		0.01	6e-04, 0.091	0.001
Peptococcus		5.58	0.55, 56.23	0.41
Phascolarctobacterium	propionate	1.04	0.30, 3.57	0.97
Pseudobutyrvibrio		0.55	0.21, 1.38	0.47
Roseburia	butyrate, propionate	0.44	0.22, 0.85	0.073
Ruminococcus		0.51	0.19, 1.31	0.43
Solobacterium		2.47	0.18, 33.49	0.66
Streptococcus		1.17	0.43, 3.18	0.86
Subdoligranulum	butyrate	0.70	0.29, 1.69	0.62
Turicibacter		2.68	0.59, 11.96	0.46

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Veillonella	0.50	0.12, 2.08	0.58
<i>Phylum Fusobacteria</i>			
Fusobacterium	6.10	0.87, 42.29	0.24
<i>Phylum Proteobacteria</i>			
Bilophila	1.48	0.54, 4.03	0.62
Desulfovibrio	4.71	1.19, 18.49	0.12
Enterobacter	73.70	8.08, 671.52	0.0011
Escherichia	0.84	0.19, 3.58	0.90
Haemophilus	0.39	0.10, 1.45	0.43
Oxalobacter	0.43	0.34, 0.53	<0.0001
Parasutterella	1.77	0.37, 8.41	0.64
Succinivibrio	7.81	0.79, 77.22	0.26
Sutterella	1.55	0.49, 4.84	0.62
Thalassospira	0.50	0.046, 5.31	0.74
<i>Phylum Verrucomicrobia</i>			
Akkermansia	propionate	0.85	0.12, 5.74

HIV effect on relative abundance of taxa, with effect size > 1 indicating higher abundance and values <1 indicating lower abundance. **Bold:** taxa with FDR p-value <0.1. FDR = false discovery rate; CI = confidence interval. *SCFA producers: reflects genera known to contain species with the capacity to produce butyrate or propionate. In some instances, different species within the same genus produce either butyrate or propionate.

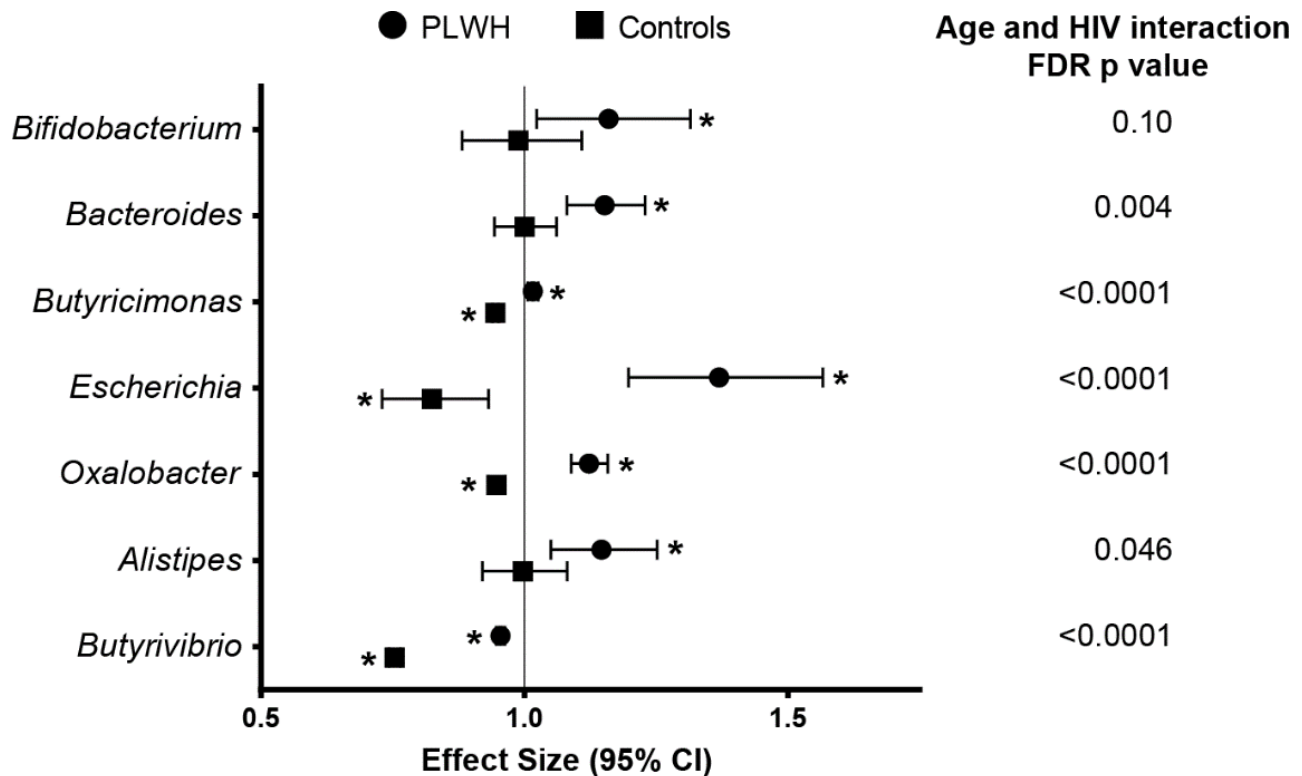
Supplemental Table 2: Impact of age on Gut Microbiome

Phylum	Effect	95% CI	FDR p-value	
Actinobacteria	0.97	0.92, 1.01	0.36	
Bacteroidetes	1.00	0.97, 1.02	0.99	
Cyanobacteria	0.95	0.85, 1.07	0.66	
Firmicutes	1.00	0.99, 1.01	0.66	
Fusobacteria	0.85	0.74, 0.97	0.10	
Lentisphaerae	0.88	0.74, 1.03	0.35	
Proteobacteria	1.00	0.94, 1.04	0.99	
Synergistetes	1.62	1.28, 2.04	0.0007	
Tenericutes	0.93	0.80, 1.06	0.46	
Verrucomicrobia	1.00	0.87, 1.14	0.99	
Family	Effect	95% CI	FDR p-value	
<i>Phylum Actinobacteria</i>				
Actinomycetaceae	0.96	0.91, 1.01	0.35	
Bifidobacteriaceae	0.99	0.91, 1.08	0.96	
Coriobacteriaceae	0.96	0.92, 1.00	0.26	
<i>Phylum Bacteroidetes</i>				
Bacteroidaceae	1.03	0.98, 1.09	0.35	
Porphyromonadaceae	1.07	1.02, 1.12	0.03	
Prevotellaceae	0.93	0.85, 1.01	0.32	
Rikenellaceae	0.99	0.93, 1.05	0.93	
<i>Phylum Firmicutes</i>				
Acidaminococcaceae	1.04	0.96, 1.12	0.46	
Christensenellaceae	1.01	0.95, 1.06	0.86	
Clostridiaceae	0.92	0.85, 1.00	0.26	
Erysipelotrichaceae	0.96	0.92, 1.01	0.42	
Lachnospiraceae	1.01	0.99, 1.02	0.40	
Lactobacillaceae	1.14	1.04, 1.26	0.03	
Peptococcaceae	1.01	0.93, 1.10	0.91	
Peptostreptococcaceae	1.03	0.96, 1.11	0.57	
Ruminococcaceae	1.00	0.98, 1.02	0.92	
Streptococcaceae	0.95	0.89, 1.02	0.40	
Veillonellaceae	0.97	0.90, 1.03	0.57	
<i>Phylum Fusobacteria</i>				
Fusobacteriaceae	0.81	0.71, 0.92	0.01	
Leptotrichiaceae	1.28	0.97, 1.68	0.26	
<i>Phylum Proteobacteria</i>				
Alcaligenaceae	1.00	0.93, 1.06	0.98	
Desulfovibrionaceae	1.04	0.97, 1.10	0.41	
Enterobacteriaceae	0.96	0.86, 1.061	0.61	
Pasteurellaceae	0.93	0.84, 1.01	0.32	
Succinivibrionaceae	1.05	0.88, 1.23	0.81	
<i>Phylum Synergistetes</i>				
Synergistaceae	1.62	1.28, 2.04	0.002	
<i>Phylum Verrucomicrobia</i>				
Verrucomicrobia	1.01	0.88, 1.15	0.94	
Genus	<i>SCFA producers</i> ^{[1-3]*}	Effect	95% CI	FDR p-value
<i>Phylum Actinobacteria</i>				
Bifidobacterium		1.00	0.91, 1.08	0.95
Collinsella		0.97	0.91, 1.02	0.56

Eggerthella		0.91	0.82, 1.00	0.25
Enterorhabdus		0.90	0.81, 1.00	0.25
Slackia		0.96	0.84, 1.08	0.77
<i>Phylum Bacteroidetes</i>				
Alistipes	propionate	1.01	0.94, 1.08	0.88
Bacteroides	propionate	1.04	0.98, 1.09	0.37
Barnesiella		0.99	0.91, 1.07	0.92
Butyricimonas		0.96	0.96, 0.97	<0.0001
Parabacteroides		1.09	1.03, 1.15	0.01
Prevotella	propionate	0.93	0.85, 1.01	0.36
<i>Phylum Firmicutes</i>				
Acidaminococcus		1.11	0.95, 1.28	0.45
Allisonella		0.95	0.83, 1.08	0.72
Anaerostipes	butyrate	1.00	0.94, 1.05	0.94
Anaerotruncus		0.99	0.93, 1.03	0.81
Anaerovibrio		1.02	0.82, 1.2	0.92
Blautia	propionate	1.02	0.99, 1.04	0.48
Butyrivibrio	butyrate	0.84	0.73, 0.97	0.12
Catenibacterium		0.91	0.82, 1.01	0.28
Clostridium		0.93	0.85, 1.00	0.27
Coprococcus	butyrate, propionate	1.01	0.97, 1.04	0.88
Dialister	propionate	0.98	0.89, 1.07	0.88
Dorea		0.98	0.92, 1.03	0.71
Faecalibacterium	butyrate	1.00	0.96, 1.05	0.92
Flavonifractor		1.08	0.98, 1.17	0.34
Holdemania		1.03	0.96, 1.09	0.63
Howardella		0.96	0.95, 0.97	<0.0001
Lachnospira		1.02	0.95, 1.09	0.73
Lactobacillus		1.15	1.04, 1.26	0.03
Marvinbryantia		0.97	0.90, 1.0	0.59
Megamonas		0.91	0.77, 1.06	0.51
Megasphaera		0.98	0.86, 1.11	0.88
Mogibacterium		0.96	0.84, 1.07	0.79
Oribacterium		1.00	0.87, 1.15	0.95
Oscillospira		1.11	0.98, 1.34	0.56
Peptococcus		1.01	0.84, 1.19	0.95
Phascolarctobacterium	propionate	1.02	0.93, 1.11	0.85
Pseudobutyrvibrio		1.04	0.97, 1.11	0.45
Roseburia	butyrate, propionate	0.99	0.94, 1.04	0.88
Ruminococcus		0.99	0.92, 1.05	0.88
Streptococcus		0.95	0.88, 1.02	0.44
Subdoligranulum	butyrate	1.04	0.97, 1.10	0.48
Turcibacter		1.12	1.00, 1.24	0.16
Veillonella		1.10	0.99, 1.21	0.24
<i>Phylum Fusobacteria</i>				
Fusobacterium		0.81	0.71, 0.92	0.01
Sneathia		1.44	1.41, 1.47	<0.0001
<i>Phylum Proteobacteria</i>				
Actinobacillus		0.10	0.05, 0.20	<0.0001
Bilophila		1.05	0.97, 1.12	0.42
Desulfovibrio		1.04	1.03, 1.04	<0.0001
Enterobacter		0.75	0.62, 0.9	0.03

Escherichia		1.03	0.92, 1.13	0.83
Haemophilus		0.93	0.84, 1.02	0.37
Oxalobacter		0.99	0.97, 1.00	0.25
Parasutterella		1.07	0.96, 1.19	0.45
Succinivibrio		1.05	0.88, 1.23	0.83
Sutterella		0.97	0.89, 1.05	0.72
<i>Phylum Verrucomicrobia</i>				
Akkermansia	propionate	1.01	0.88, 1.15	0.94

Age effect on relative abundance of taxa. For every 1 year increase in age, effect size > 1 means higher abundance; effect size < 1 means lower abundance. **Bold:** taxa with FDR p-value < 0.1. FDR = false discovery rate; CI = confidence interval. *SCFA producers: reflects genera known to contain species with the capacity to produce butyrate or propionate. In some instances, different species within the same genus produce either butyrate or propionate.



Supplementary Figure 2. Age Effect by HIV Serostatus on Genus Taxonomic Rank. The effect size can be interpreted as the per year increase (if >1) or decrease (if <1) in relative abundance of each taxa. * indicates when the Age effect is significantly different (all FDR p < 0.05) among PLWH (Circles) or Controls (Squares); the Age HIV interaction tests whether the effect of age differs between PLWH and controls. CI = confidence interval.

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