

Oligonucleotides used for Bacterial and Fungal PCR amplification

Name	Sequence (5')
16S fwd	TCGTCGGCAGCGTCAGATGTATAAGAGACAGCCTACGGGNGGCWGCAG
16S rev	GTCTCGTGGCTCGGAGATGTATAAGAGACAGGACTACHVGGGTATCTAATCC
ITS fwd 1	CTTGGTCATTTAGAGGAAGTAA
ITS fwd 2	CTCGGTCAATTAGAGGAAGTAA
ITS fwd 3	CTTGGTCATTTAGAGGAAGTAA
ITS fwd 4	CCCGGTCAATTAGAGGAAGTAA
ITS fwd 5	CTAGGCTATTTAGAGGAAGTAA
ITS fwd 6	CTTAGTTATTTAGAGGAAGTAA
ITS fwd 7	CTACGTCATTTAGAGGAAGTAA
ITS fwd 8	CTTGGTCATTTAGAGGTCGTAAC
ITS rev 1	GCTGCGTTCTTCATCGATGC
ITS rev 2	GCTGCGTTCTTCATCGATGG
ITS rev 3	GCTACGTTCTTCATCGATGC
ITS rev 4	GCTGCGTTCTTCATCGATGT
ITS rev 5	ACTGTGTTCTTCATCGATGT
ITS rev 6	GCTGCGTTCTTCATCGTTGC
ITS rev 7	GCGTTCTTCATCGATGC

Table S3. Patient Characteristics (normal pancreas vs. pancreatic cyst)

	Bacterial analysis			Fungal analysis		
	Normal pancreas	Pancreas cyst	p value	Normal pancreas	Pancreas cyst	p value
Cases	86	86		53	53	
Age (years); mean (range)	60.0 (34.3 - 79.5)	62.6 (33.5 - 87.3)	0.1087	66.6 (40.7 - 79.5)	67.4 (40.2 - 87.3)	0.5726
Sex			0.7594			0.8455
Male (%)	38 (44.2%)	40 (46.5%)		25 (47.2%)	24 (45.3%)	
Female (%)	48 (55.8%)	46 (53.5%)		28 (52.8%)	29 (54.7%)	
Race			0.3868			0.7358
White (%)	81 (94.2%)	77 (89.5%)		49 (92.5%)	49 (92.5%)	
Non-white (%)	5 (5.8%)	6 (7.0%)		4 (7.5%)	3 (5.6%)	
Missing (%)	0 (0%)	3 (3.5%)		0 (0%)	1 (1.9%)	
Smoking status			0.3759			0.5463
Never smoker (%)	61 (70.9%)	60 (69.8%)		39 (73.6%)	34 (64.2%)	
Former smoker (%)	22 (25.6%)	20 (23.2%)		13 (24.5%)	17 (32.0%)	
Current smoker (%)	3 (3.5%)	3 (3.5%)		1 (1.9%)	2 (3.8%)	
Missing (%)	0 (0%)	3 (3.5%)		0 (0%)	0 (0%)	
Alcohol consumption			0.1431			0.4228
Never or occasional (%)	49 (57.0%)	53 (61.6%)		31 (58.5%)	35 (66.0%)	
Regular or heavy (%)	37 (43.0%)	30 (34.9%)		22 (41.5%)	18 (34.0%)	
Missing (%)	0 (0%)	3 (3.5%)		0 (0%)	0 (0%)	
Diabetes			0.227			0.0641
Yes (%)	8 (9.3%)	14 (16.3%)		6 (11.3%)	10 (18.9%)	
No (%)	78 (90.7%)	71 (82.6%)		47 (88.7%)	43 (81.1%)	
Missing (%)	0 (0%)	1 (1.1%)		0 (0%)	0 (0%)	
PPI use			0.4703			1
Regular (%)	22 (25.6%)	18 (20.9%)		10 (18.9%)	10 (18.9%)	
None (%)	64 (74.4%)	68 (79.1%)		43 (81.1%)	43 (81.1%)	
Probiotics			0.5603			0.1534
Yes (%)	1 (1.2%)	2 (2.3%)		0 (0%)	2 (3.8%)	
No (%)	85 (98.8%)	84 (97.7%)		53 (100%)	51 (96.2%)	
Antibiotics			0.5603			1
Yes (%)	1 (1.2%)	2 (2.3%)		1 (1.9%)	1 (1.9%)	
No (%)	85 (98.8%)	84 (97.7%)		52 (98.1%)	52 (98.1%)	
Cyst location						
head (%)	33 (38.4%)			18 (34.0%)		
body (%)	34 (39.5%)			24 (45.3%)		
tail (%)	19 (22.1%)			11 (20.8%)		
Cyst size (cm); mean (range)	1.24 (0.16-8.0)			1.14 (0.16-8.0)		
Number of cysts; mean (range)	2.2 (1-8)			2.4 (1-8)		
Worrisome features						
Yes (%)	8 (9.3%)			4 (7.5%)		
MPD dilation	4			0		
Mural nodule	4			4		
No (%)	78 (90.7%)			49 (92.5%)		

Table S2; PPI use and age in normal controls

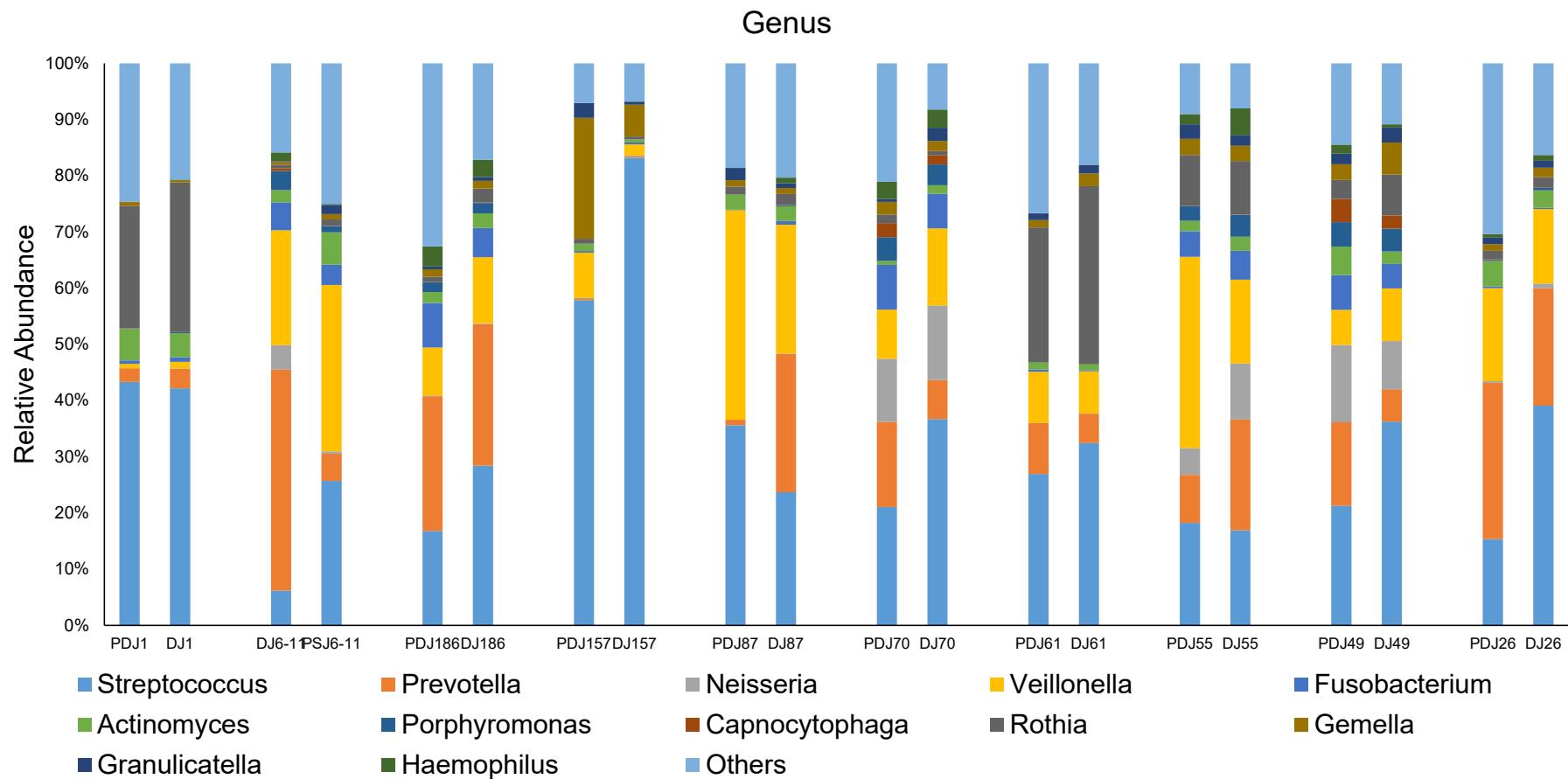
	non-users	low dose users
<i>for analysis of bacteria</i>		
Cases	98	10
Age (years)	53.8 (20.3-79.5)	53.0 (34.3-76.4)
<i>for analysis of fungal</i>		
Cases	31	4
Age (years)	57.0 (40.7-79.5)	58.7 (48.0-76.4)

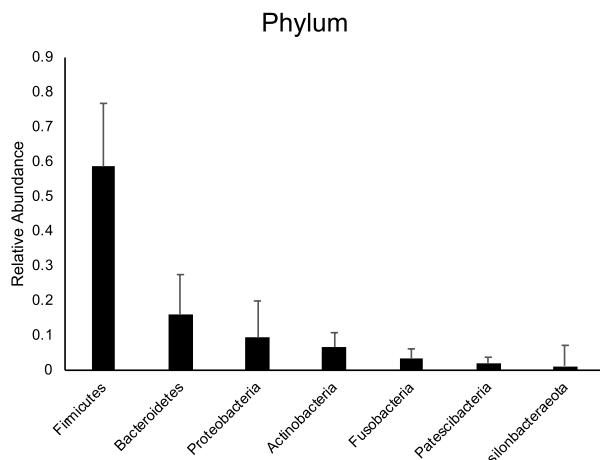
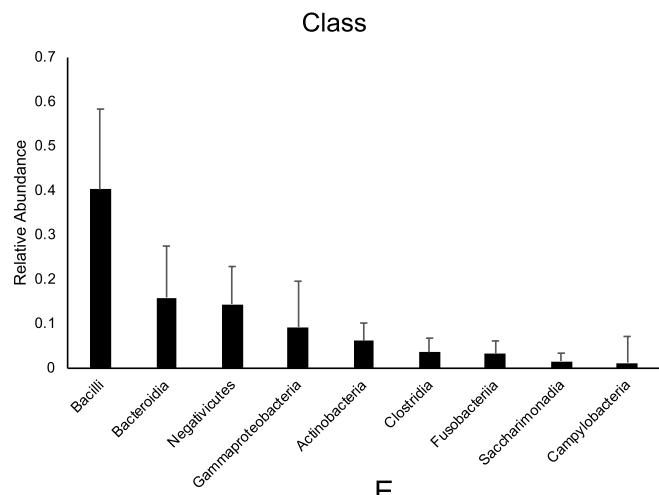
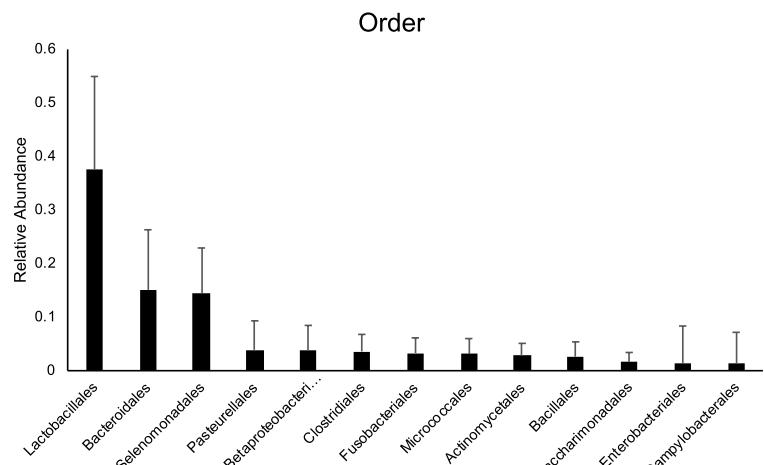
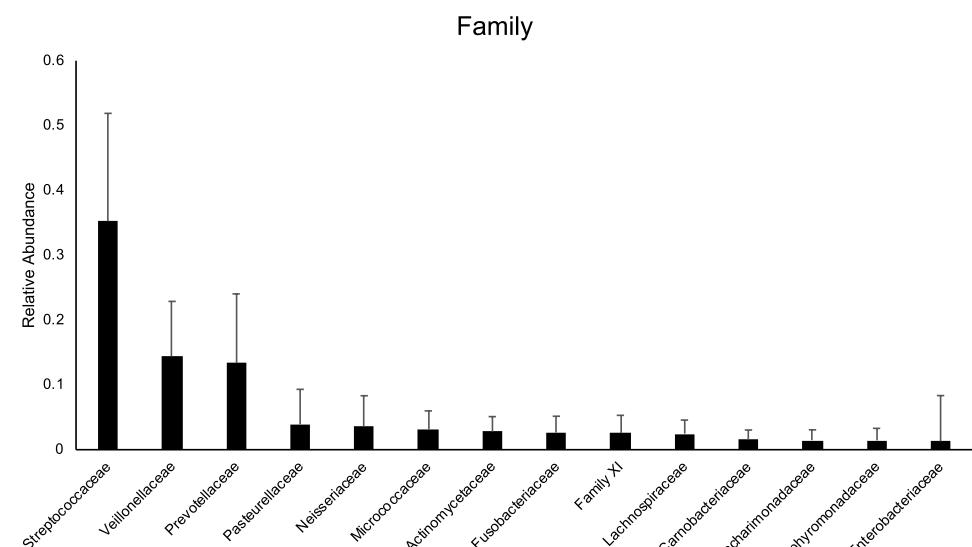
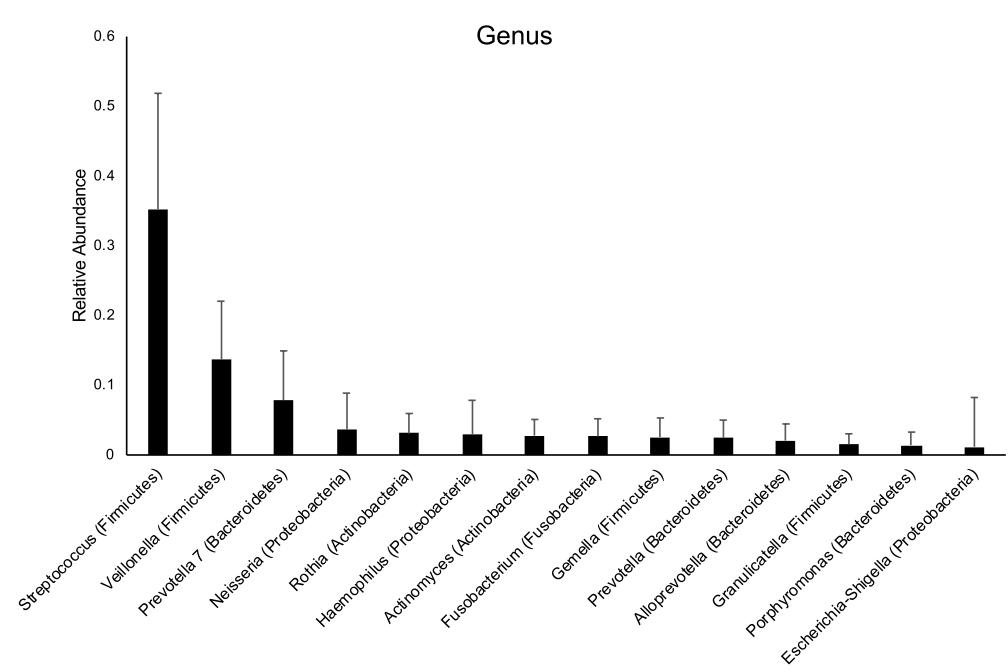
regular or high dose users	p value
19 56.8 (38.9-77.3)	0.60
6 56.6 (44.2-77.3)	0.91

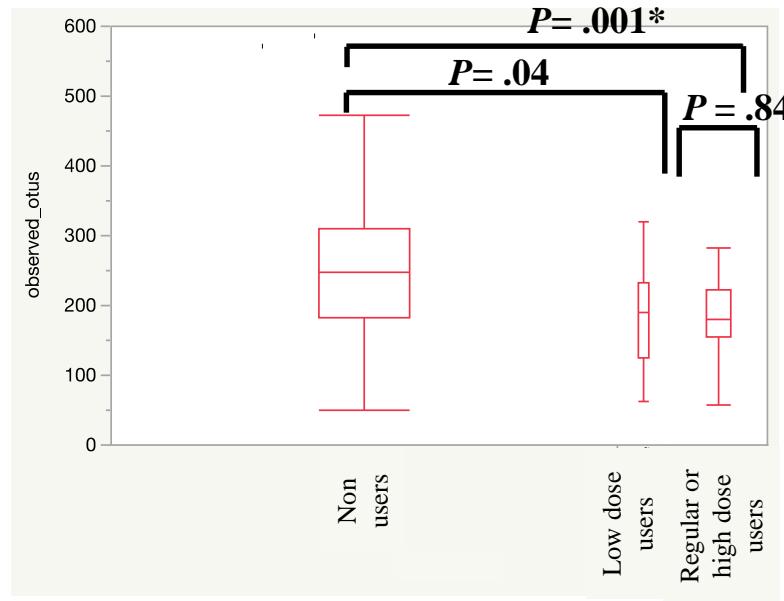
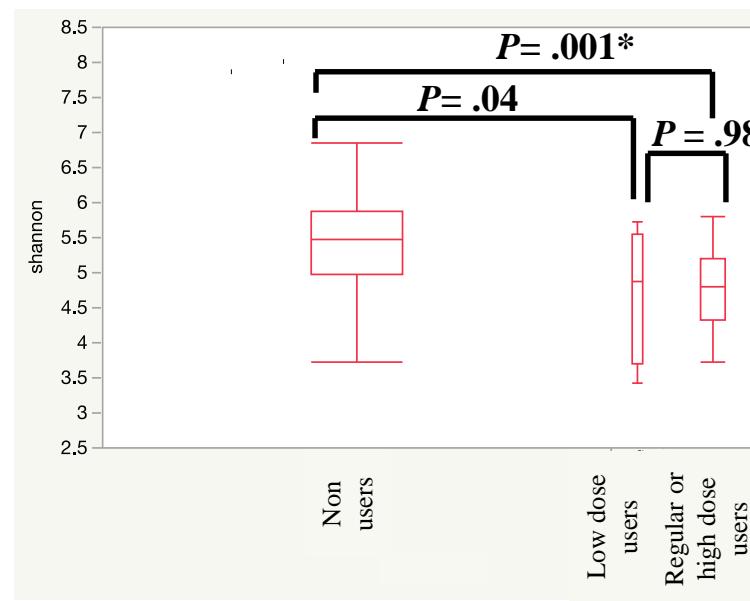
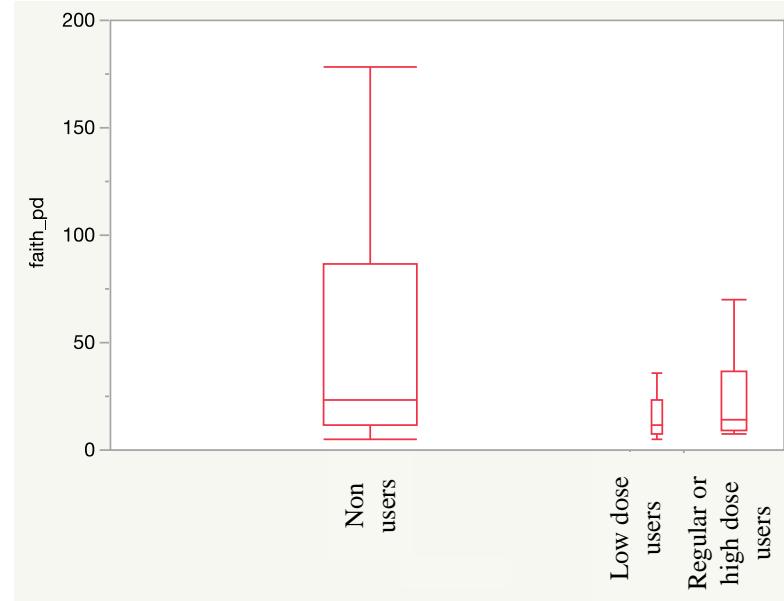
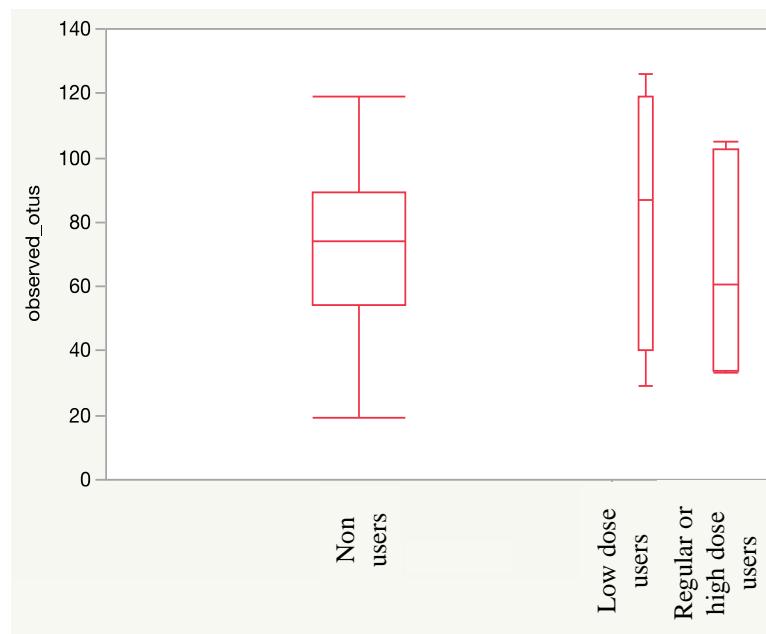
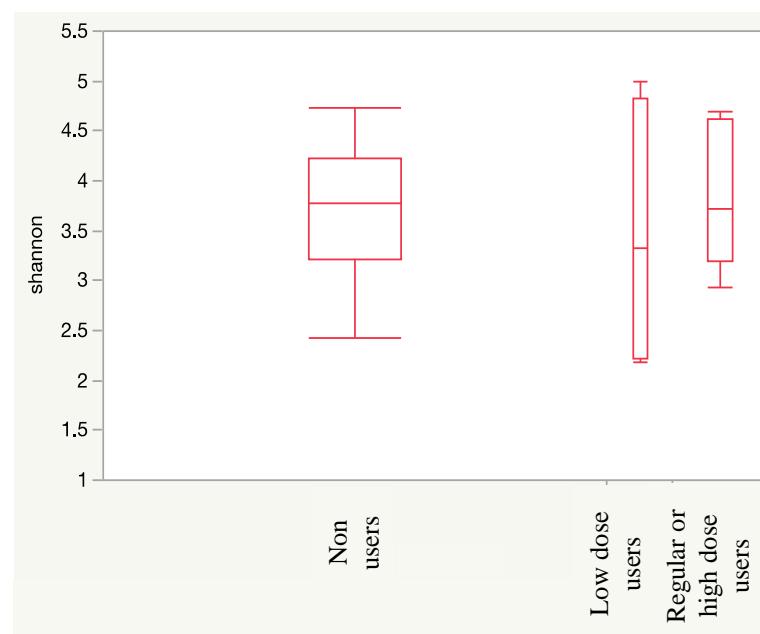
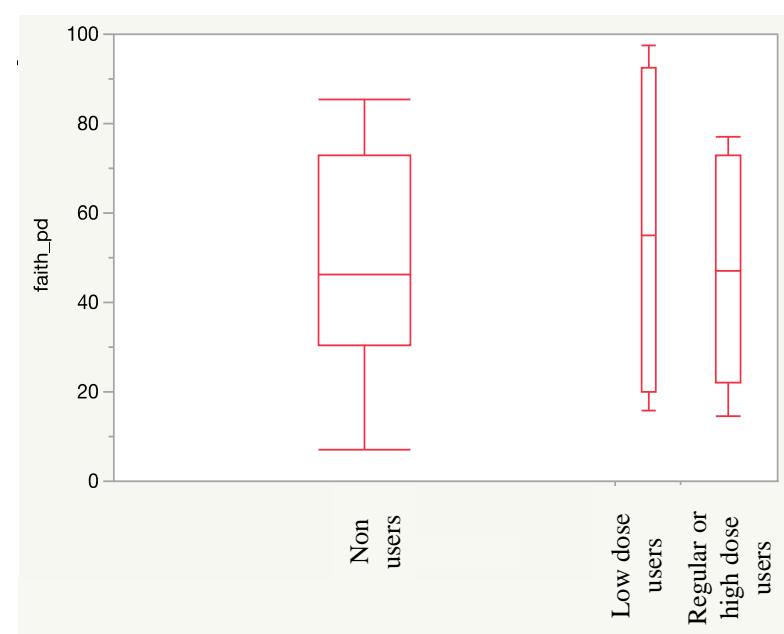
Table S4. Tumor microbiome analysis patient Characteristics

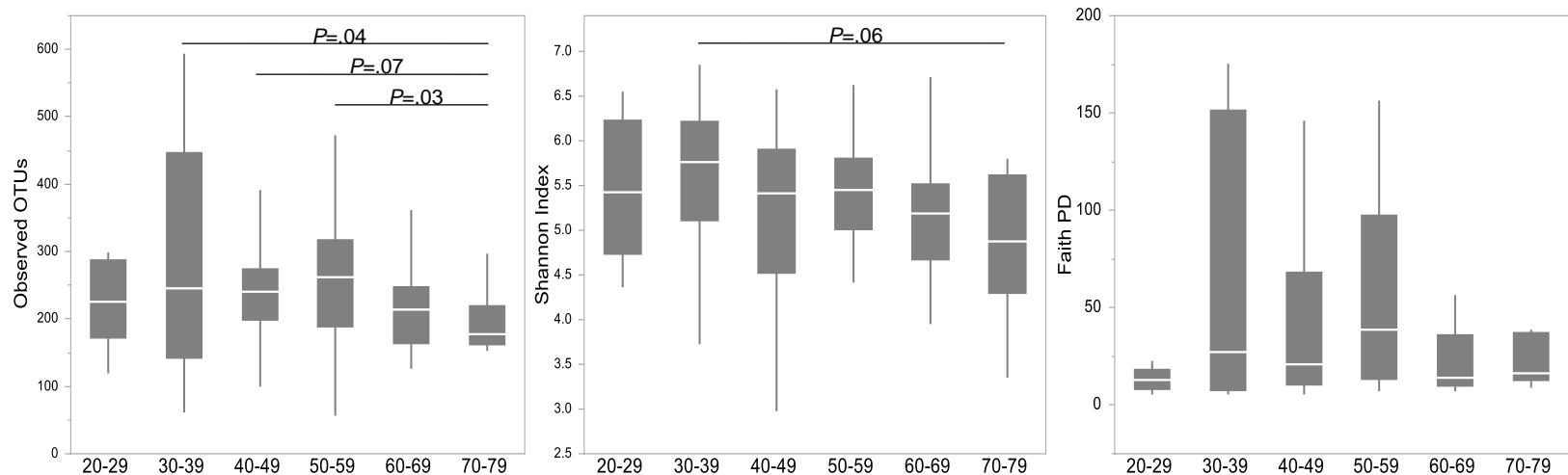
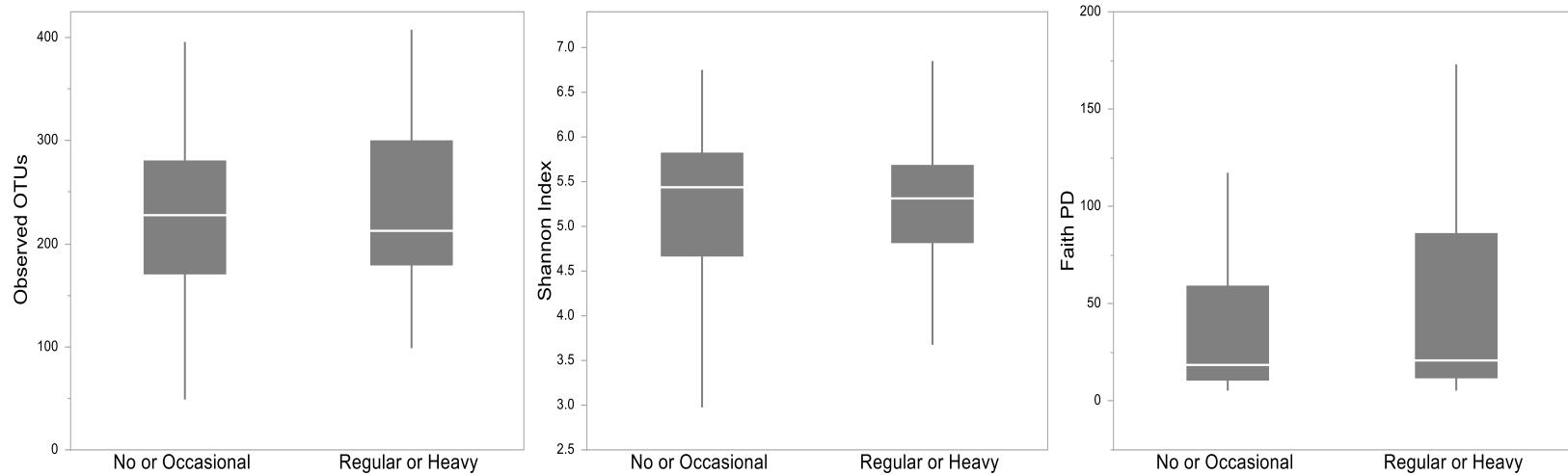
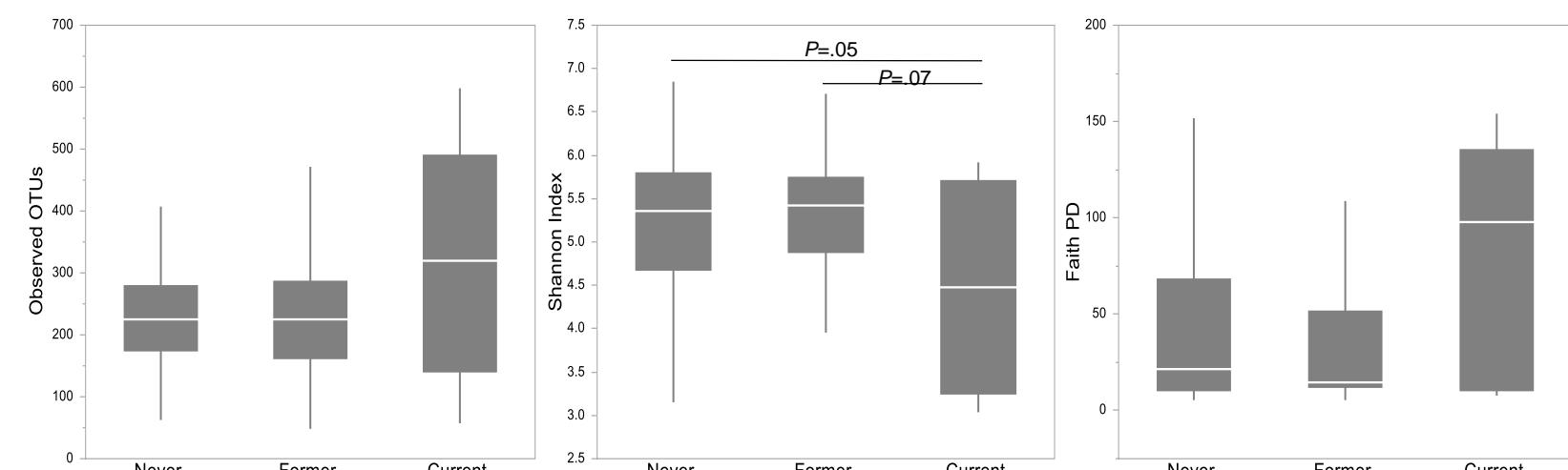
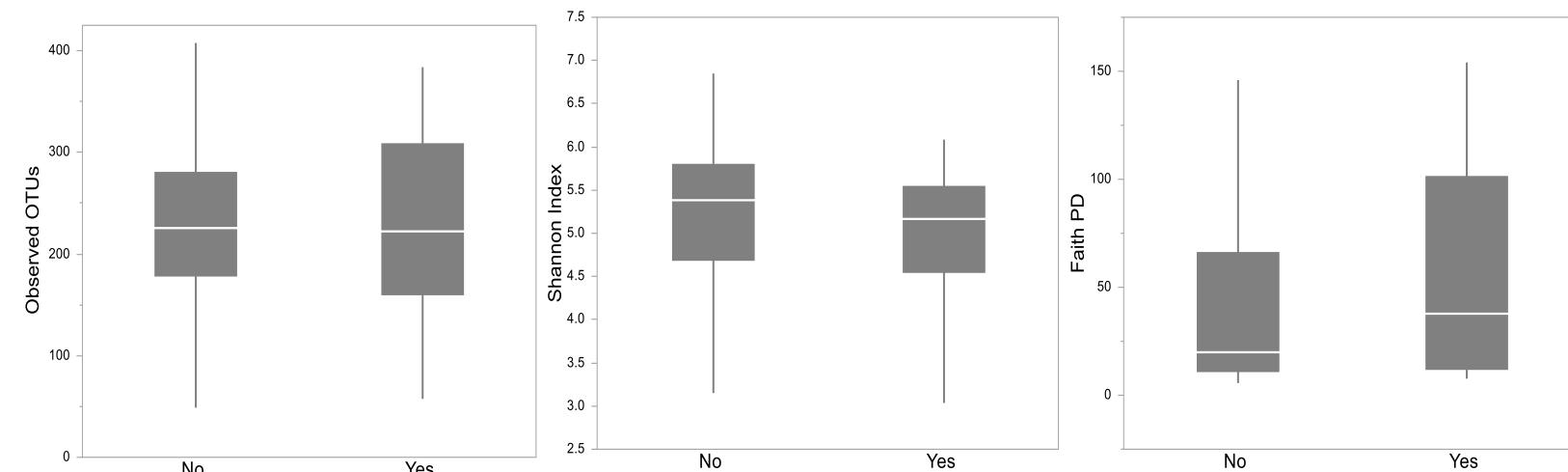
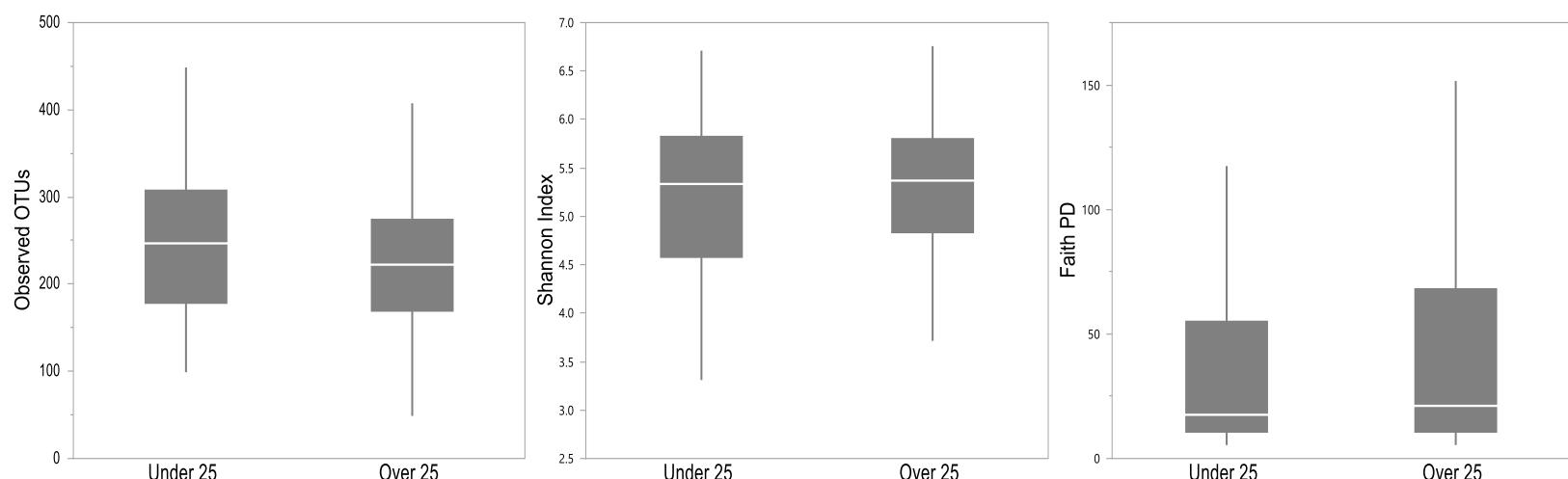
Bacterial and fungal analysis	
PDAC	
Cases	12
Age (years); mean (range)	64.4 (47.5 - 80.1)
Sex	
Male (%)	9 (75%)
Female (%)	3 (25%)
Race	
White (%)	11 (91.7%)
Non-white (%)	1 (8.3%)
Smoking status	
Never smoker (%)	4 (33.3%)
Former smoker (%)	8 (66.7%)
Current smoker (%)	0 (0%)
Alcohol consumption	
Never or occasional (%)	6 (50%)
Regular or heavy (%)	5 (41.7%)
Missing (%)	1 (8.3%)
Diabetes	
Yes (%)	7 (58.3%)
No (%)	5 (41.7%)
PPI use	
Regular (%)	3 (25%)
None (%)	9 (75%)
Probiotics	
Yes (%)	0 (0%)
No (%)	12 (100%)
Antibiotics	
Yes (%)	2 (16.7%)
No (%)	10 (83.3%)
Tumor location	
head (%)	9 (75%)
body (%)	3 (25%)
tail (%)	0 (0%)
Biliary obstruction*	1 (8.3%)
Stage	
IA (%)	0 (0%)
IB (%)	3 (25%)
IIA (%)	2 (16.7%)
IIB (%)	6 (50%)
III (%)	1 (8.3%)
IV (%)	0 (0%)

* at the time of sampling

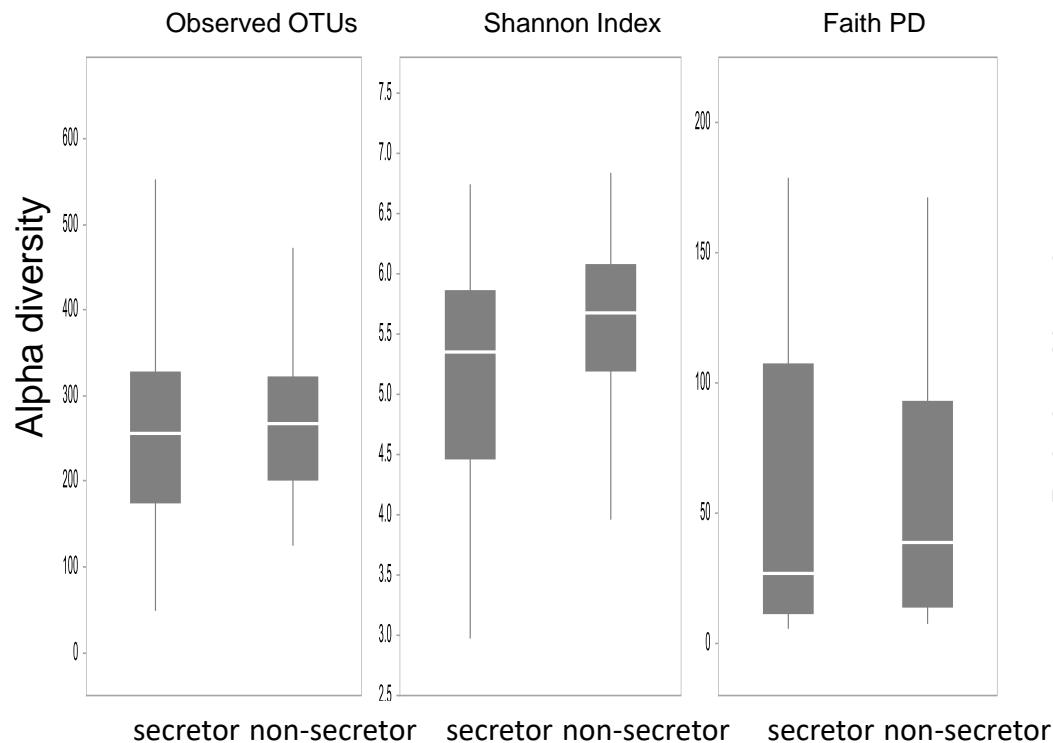


A**B****C****D****E**

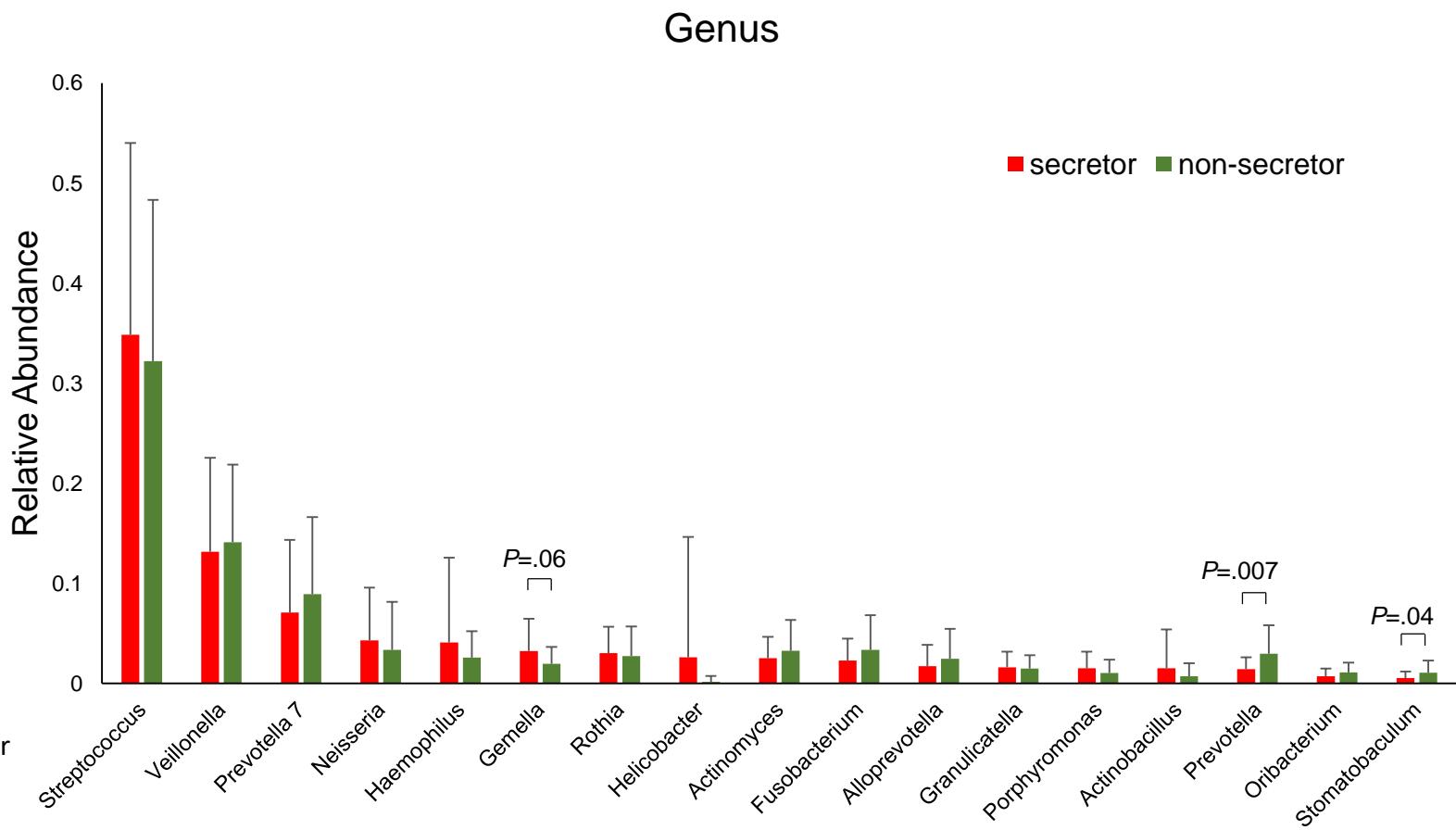
A**Observed OTUs $P = .001^*$** **Shannon Index $P = .001^*$** **Faith PD $P = .06$** **B****Observed OTUs $P = .78$** **Shannon Index $P = .88$** **Faith PD $P = .83$** 

A
Age**B**
Alcohol**C**
Smoking**D**
DM**E**
BMI

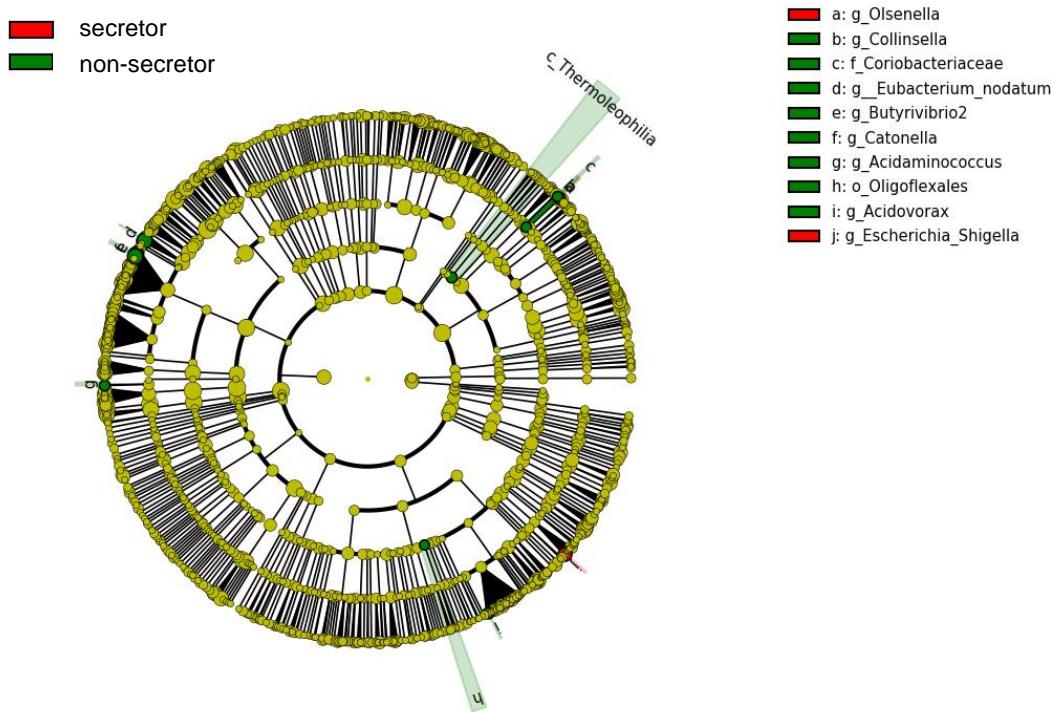
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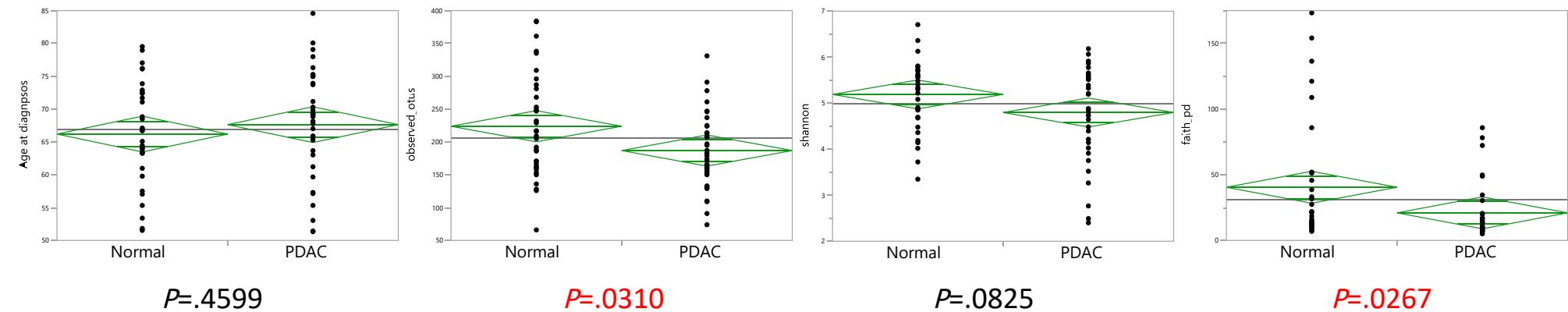
B



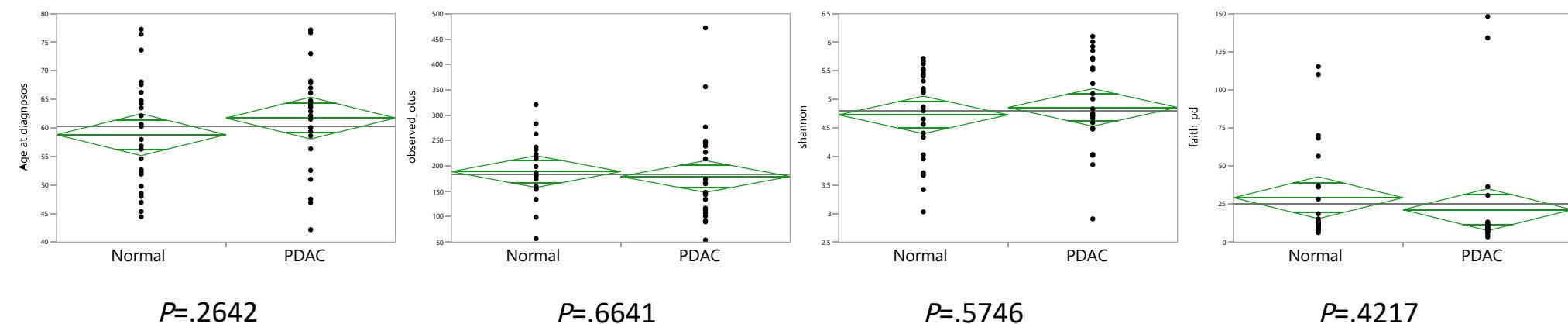
C



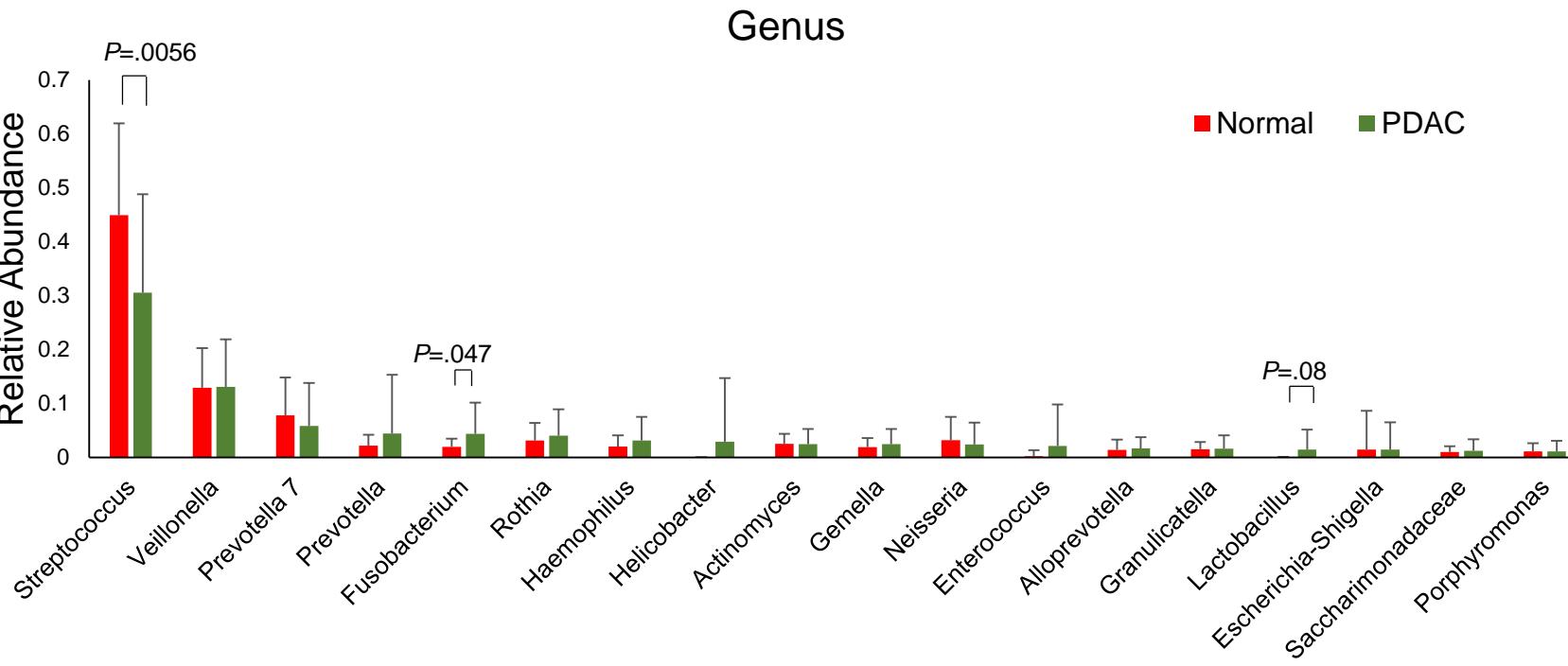
PPI Non-users: PDAC vs age-matched normal pancreas (n=34 per group)



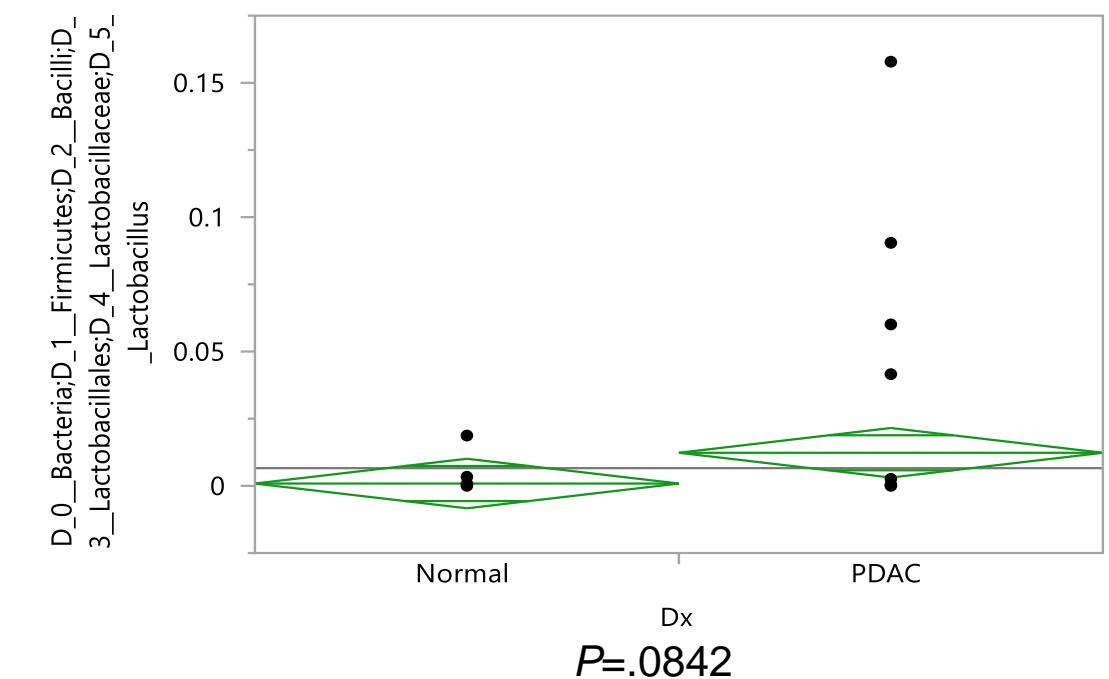
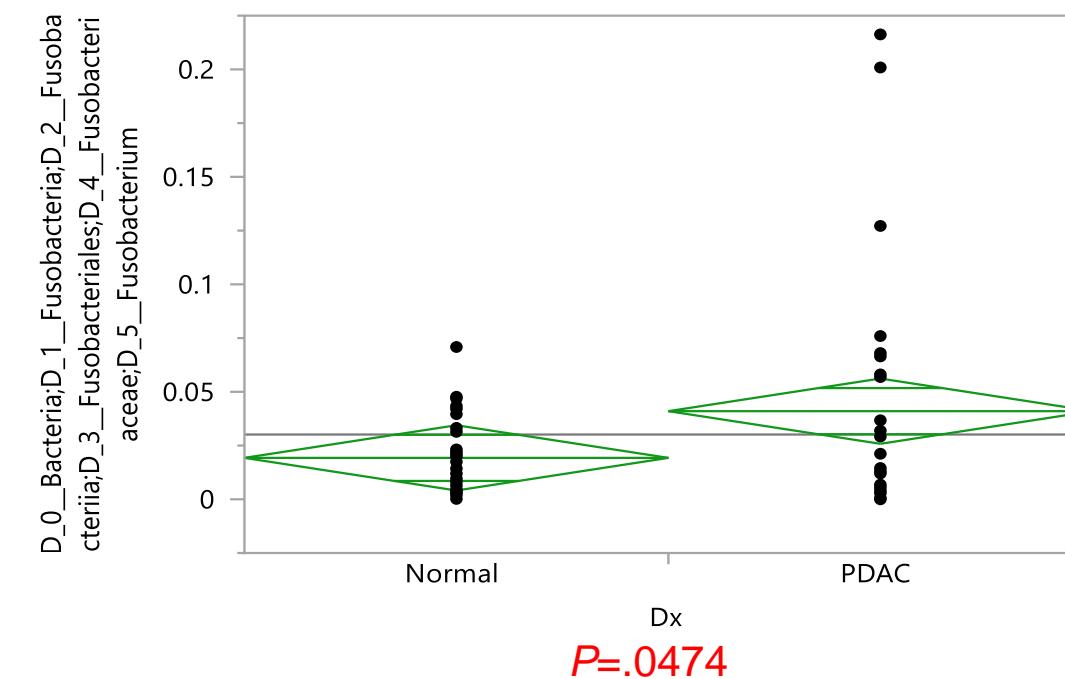
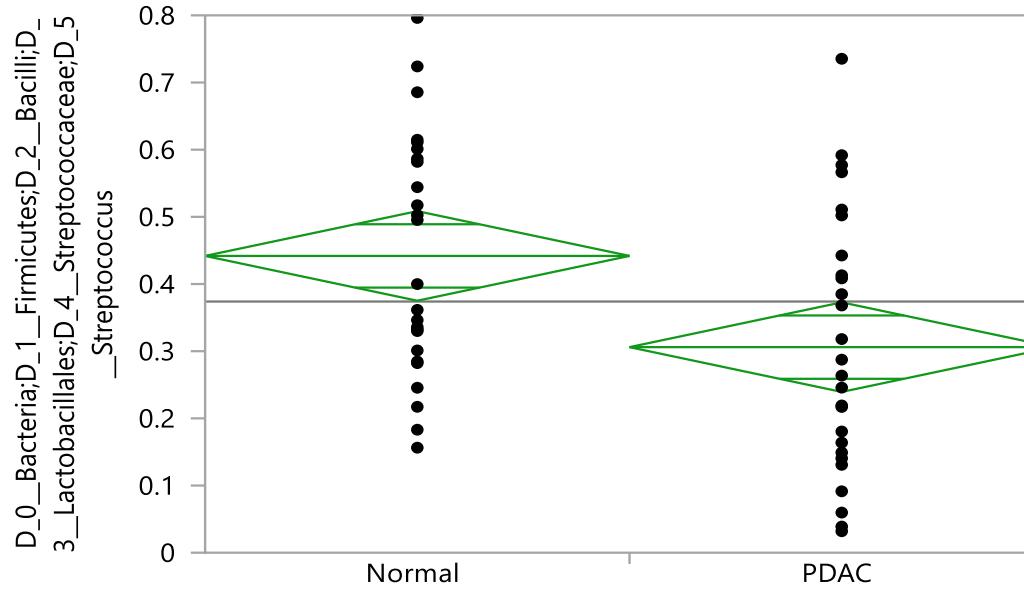
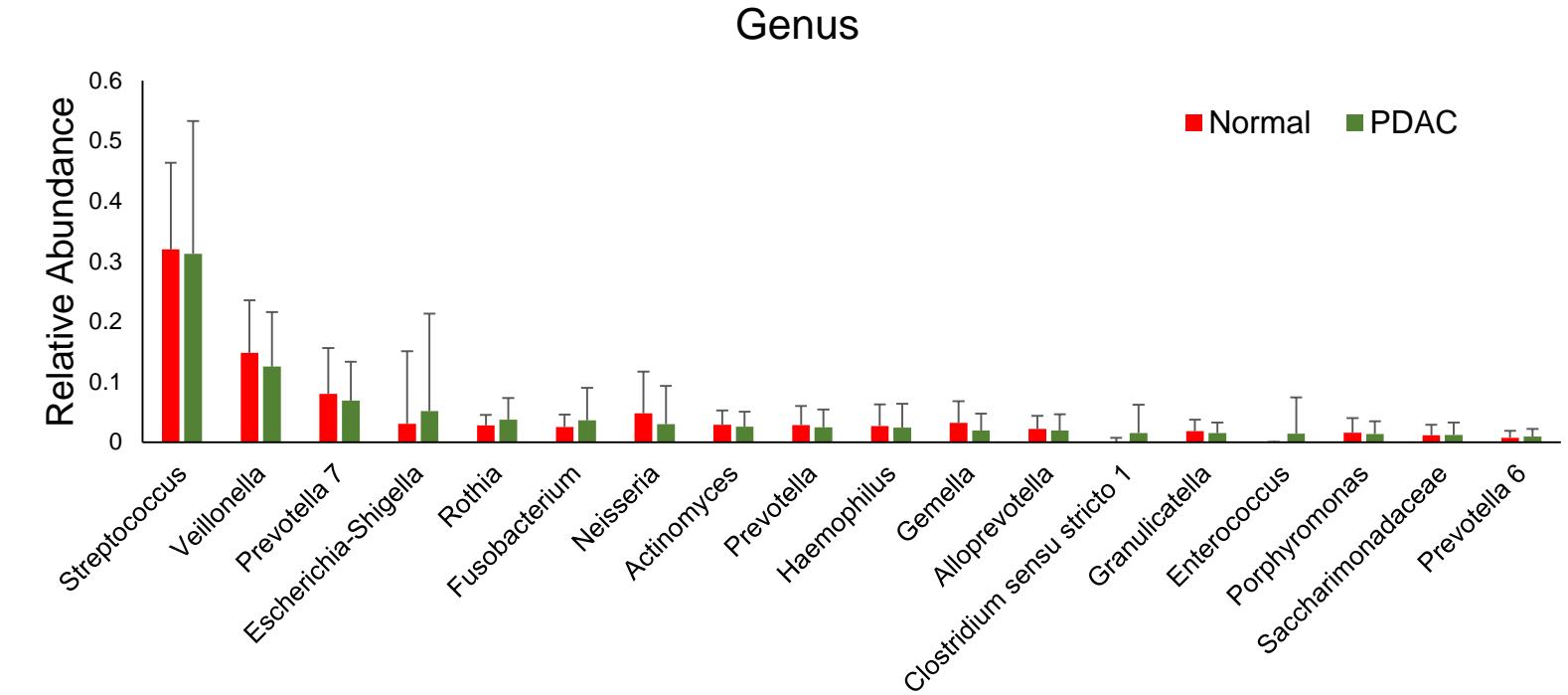
PPI users: PDAC vs age-matched normal pancreas (n=25 per group)



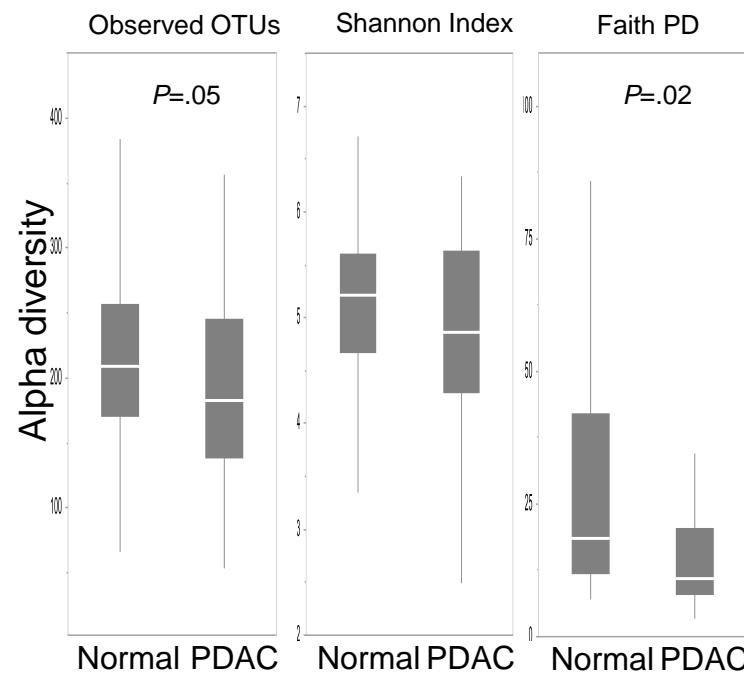
PPI users



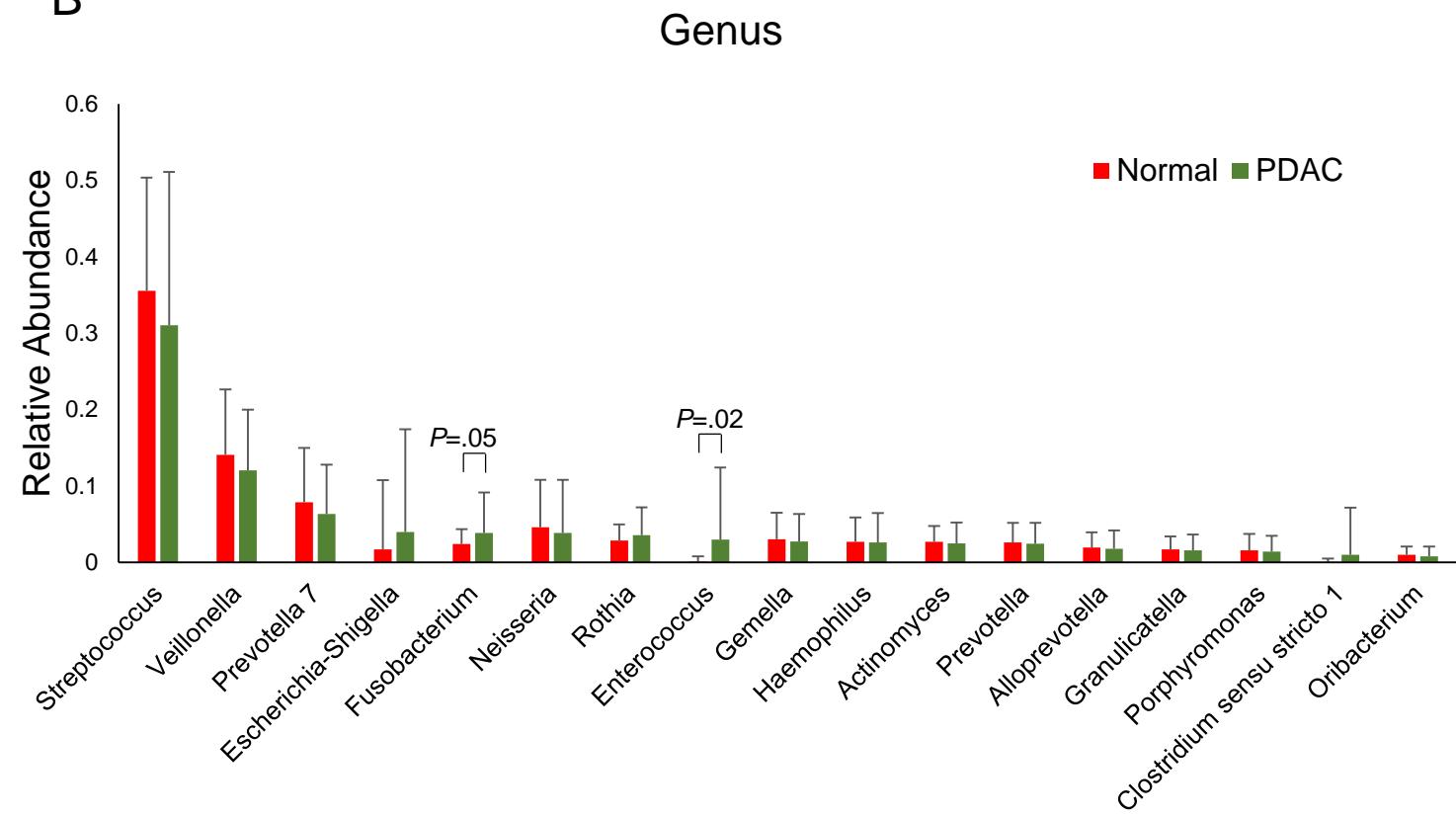
PPI non users



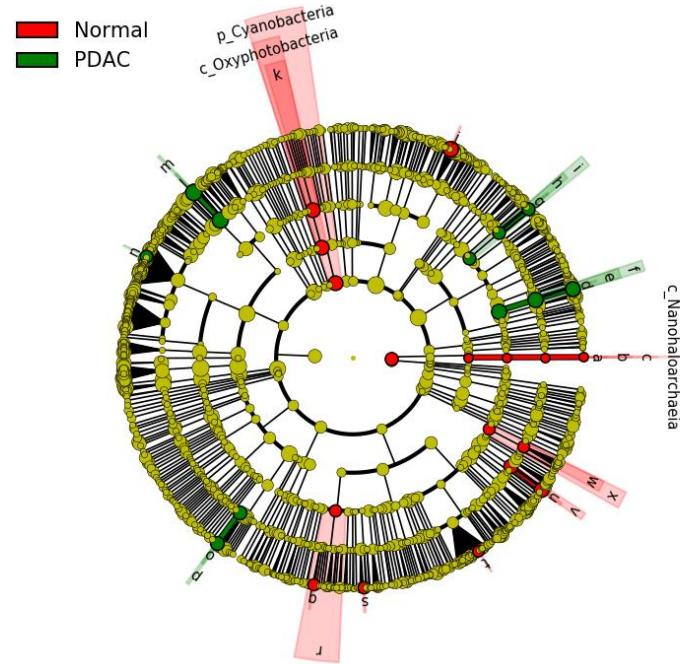
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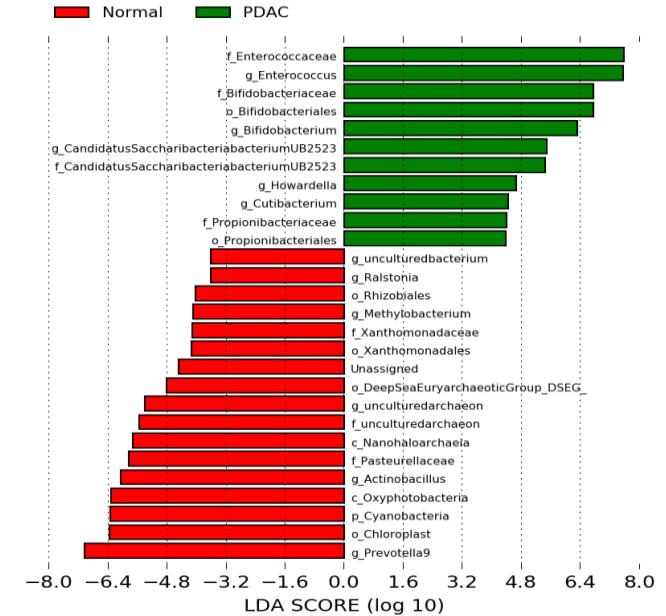
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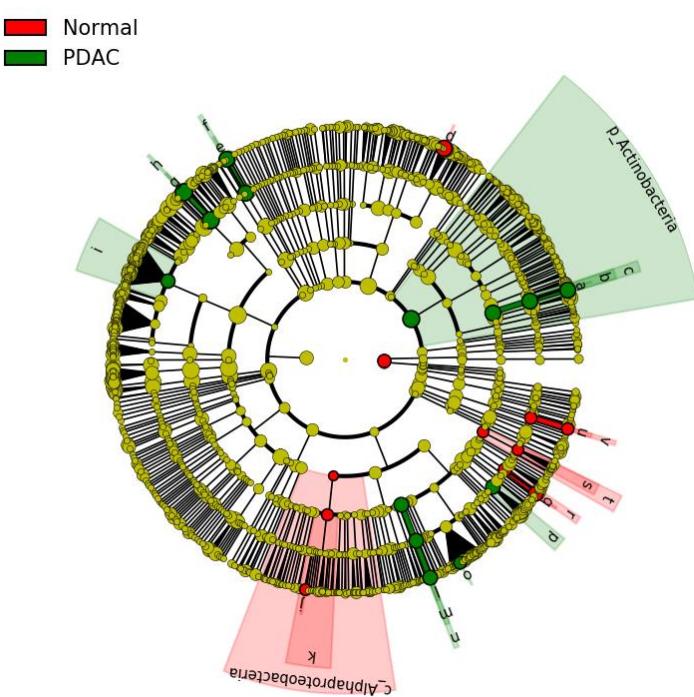
C



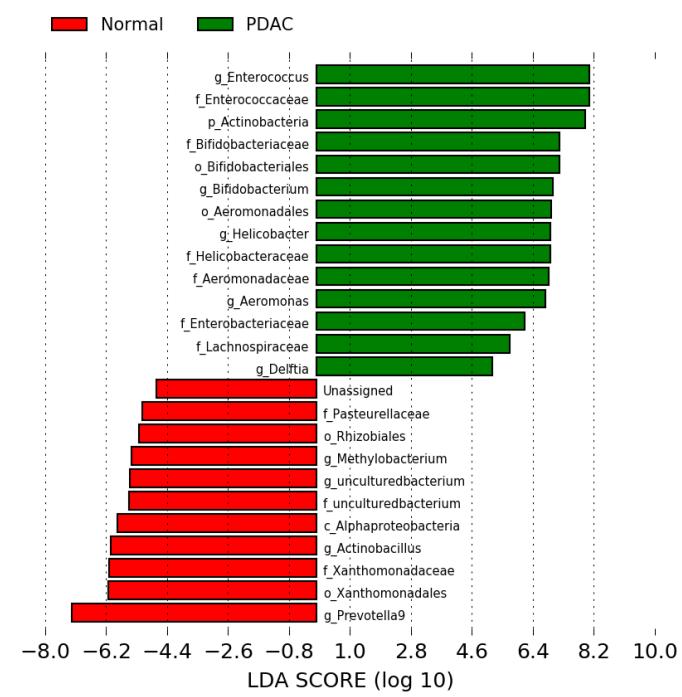
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- c: o_DeepSeaEuryarchaeotic
- d: g_Bifidobacterium
- e: f_Bifidobacteriaceae
- f: o_Bifidobacteriales
- g: g_Cutibacterium
- h: f_Propionibacteriaceae
- i: o_Propionibacteriales
- j: g_Prevotella9
- k: o_Chloroplast
- l: g_Enterococcus
- m: f_Enterococcaceae
- n: g_Howardella
- o: g_CandidatusSaccharibact
- p: f_CandidatusSaccharibact
- q: g_Methylobacterium
- r: o_Rhizobiales
- s: g_unculturedbacterium
- t: g_Ralstonia
- u: g_Actinobacillus
- v: f_Pasteurellaceae
- w: f_Xanthomonadaceae
- x: o_Xanthomonadales
- y: g_Xanthomonadaceae
- z: o_Xanthomonadales



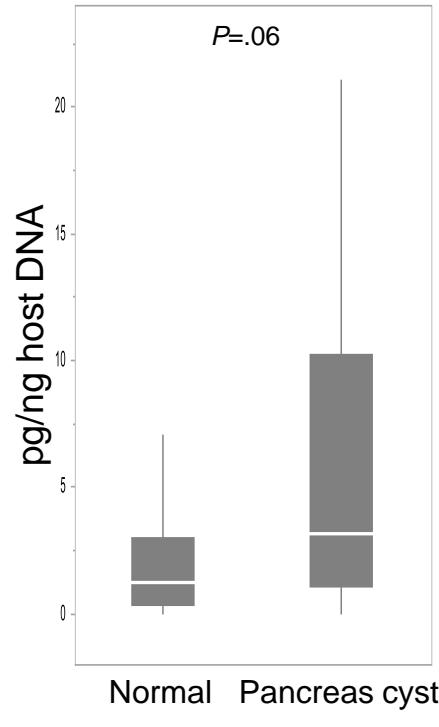
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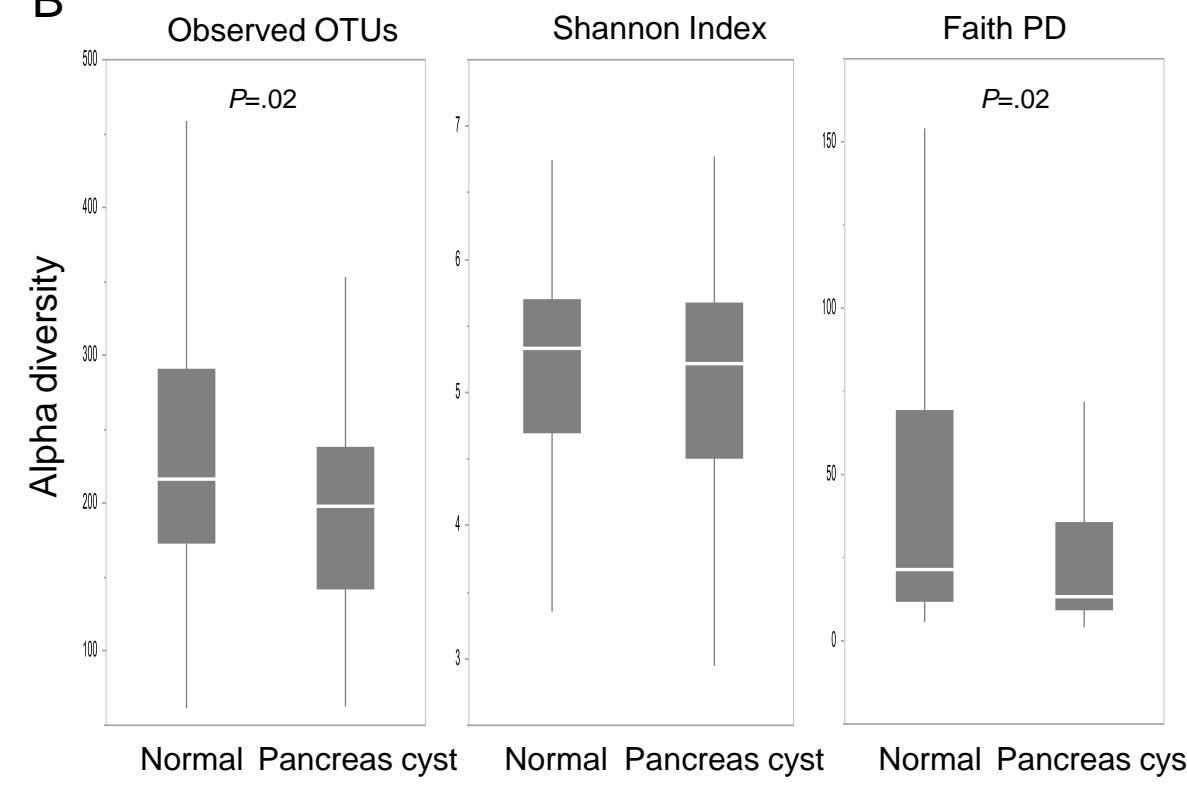
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- b: f_Bifidobacteriaceae
- c: o_Bifidobacteriales
- d: g_Prevotellag
- e: g_Helicobacter
- f: f_Helicobacteraceae
- g: g_Enterococcus
- h: f_Enterococcaceae
- i: f_Lachnospiraceae
- j: g_Methylobacterium
- k: o_Rhizobiales
- l: g_Aeromonas
- m: f_Aeromonadaceae
- n: o_Aeromonadales
- o: g_Delftia
- p: f_Enterobacteriaceae
- q: g_Actinobacillus
- r: f_Pasteurellaceae
- s: f_Xanthomonadaceae
- t: o_Xanthomonadales
- u: g_unculturedbacterium
- v: f_unculturedbacterium



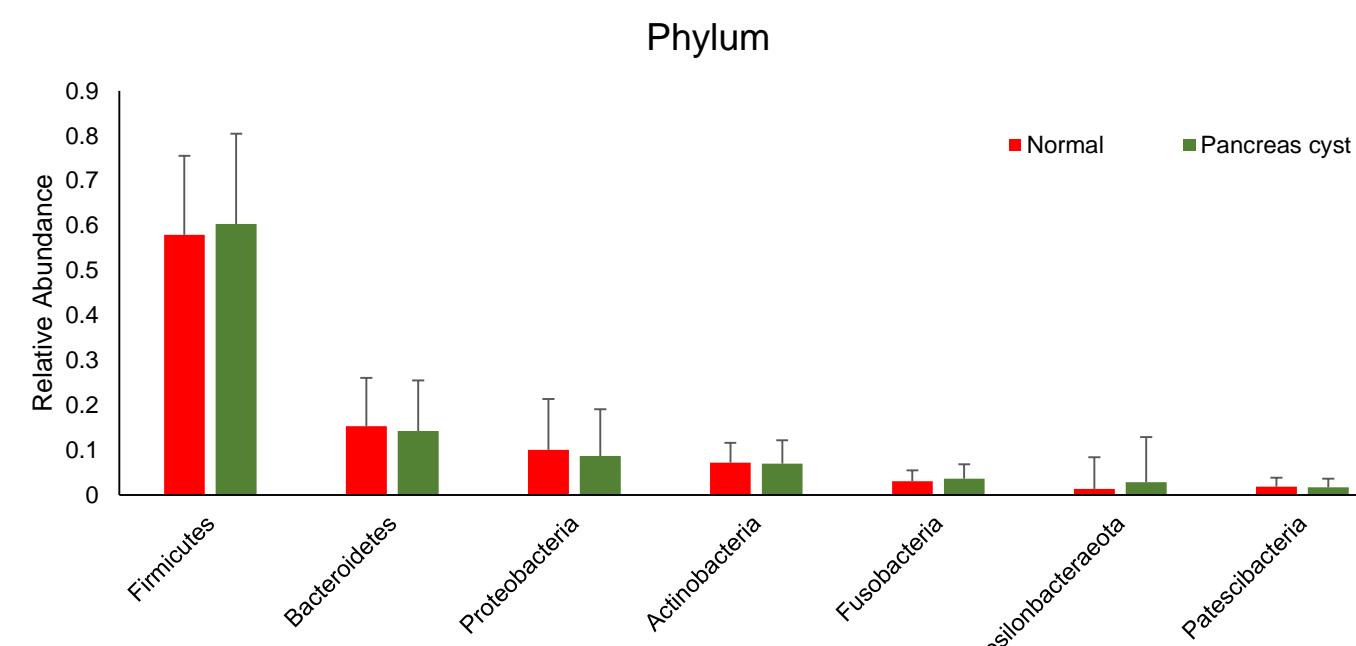
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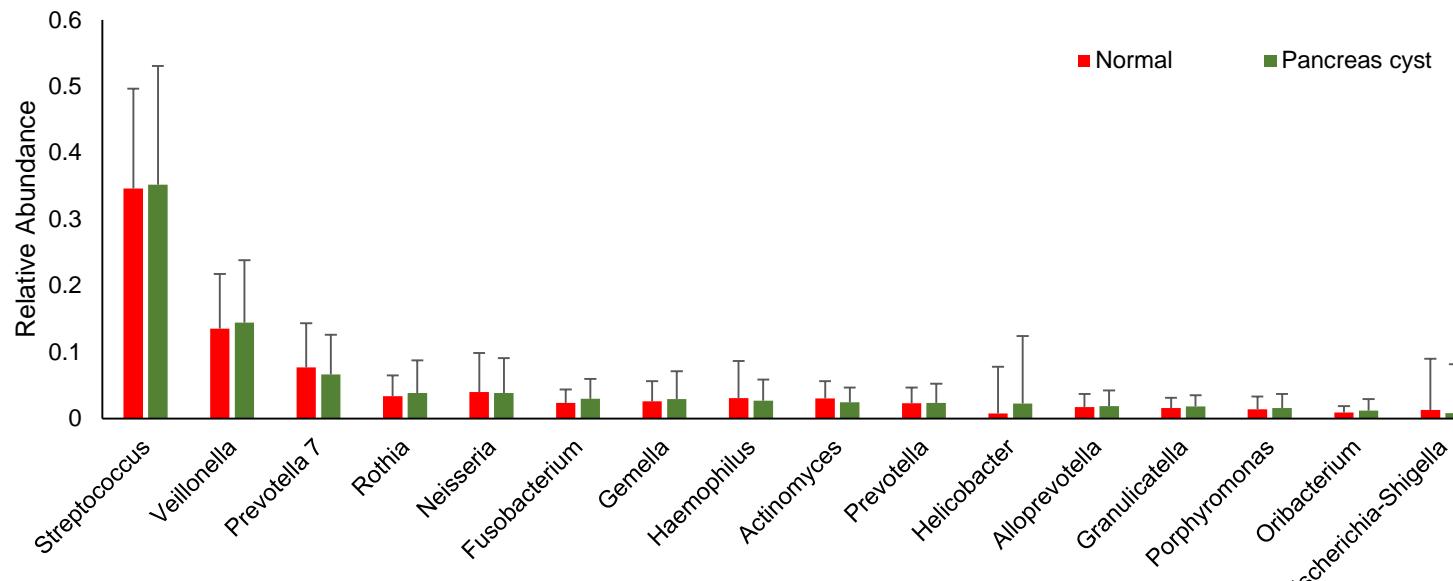
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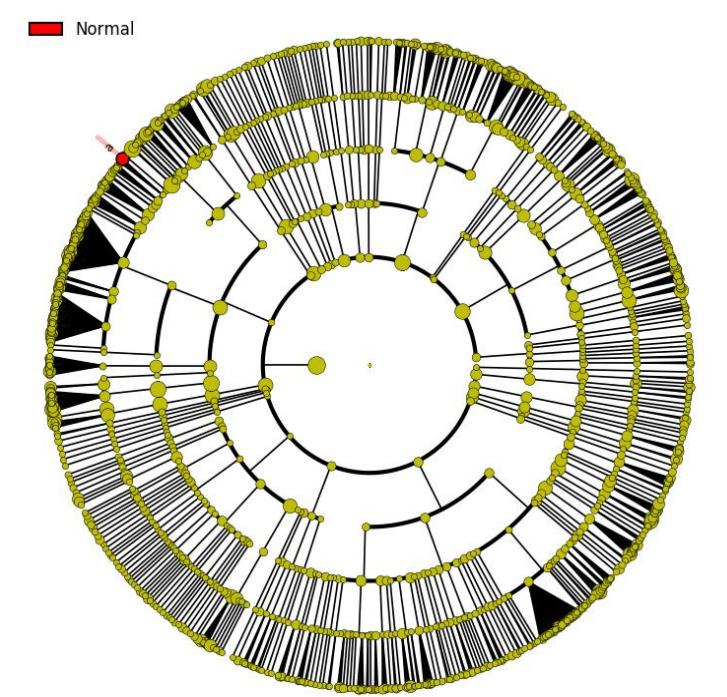
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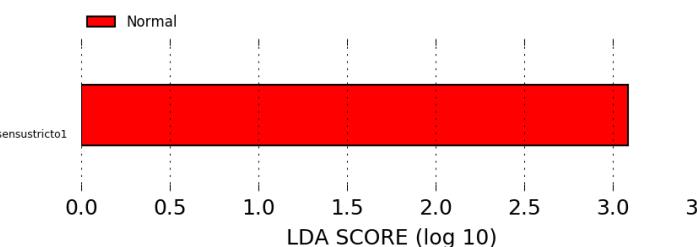
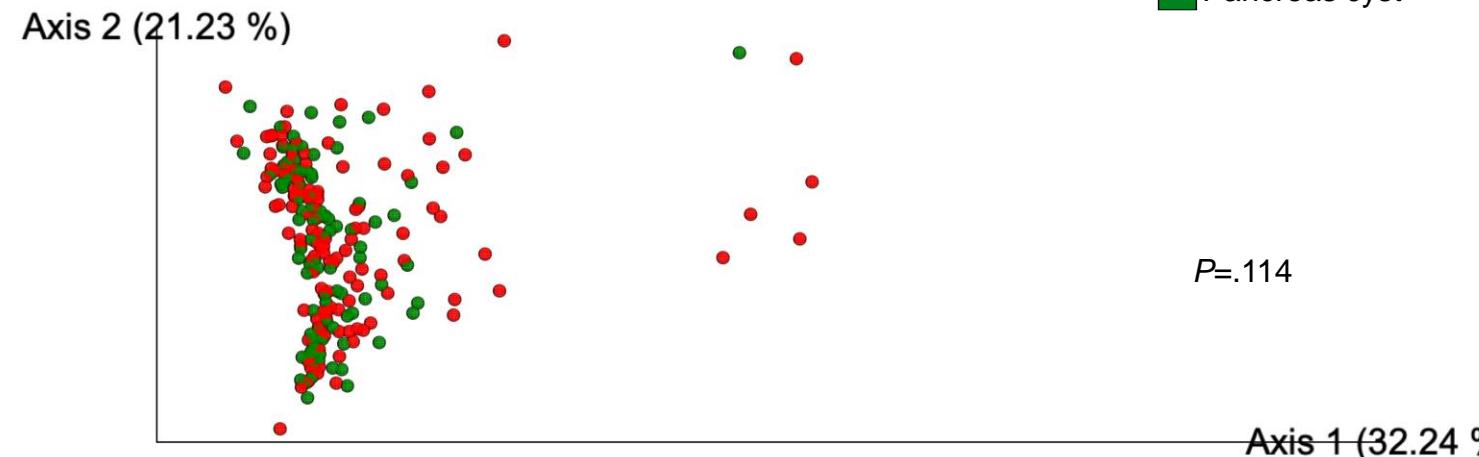
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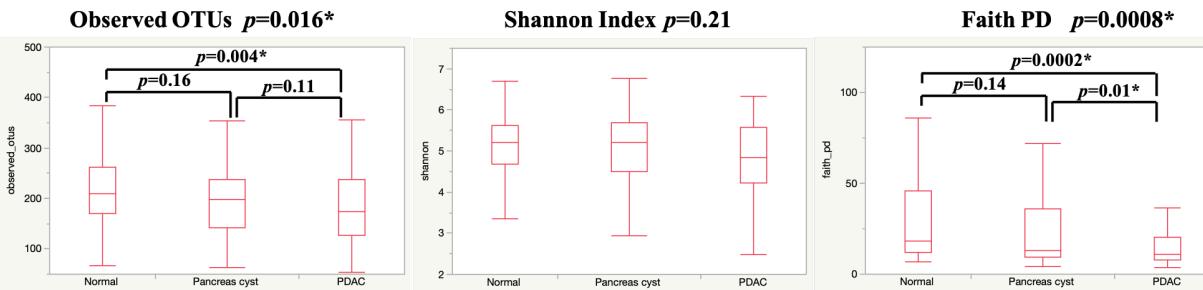
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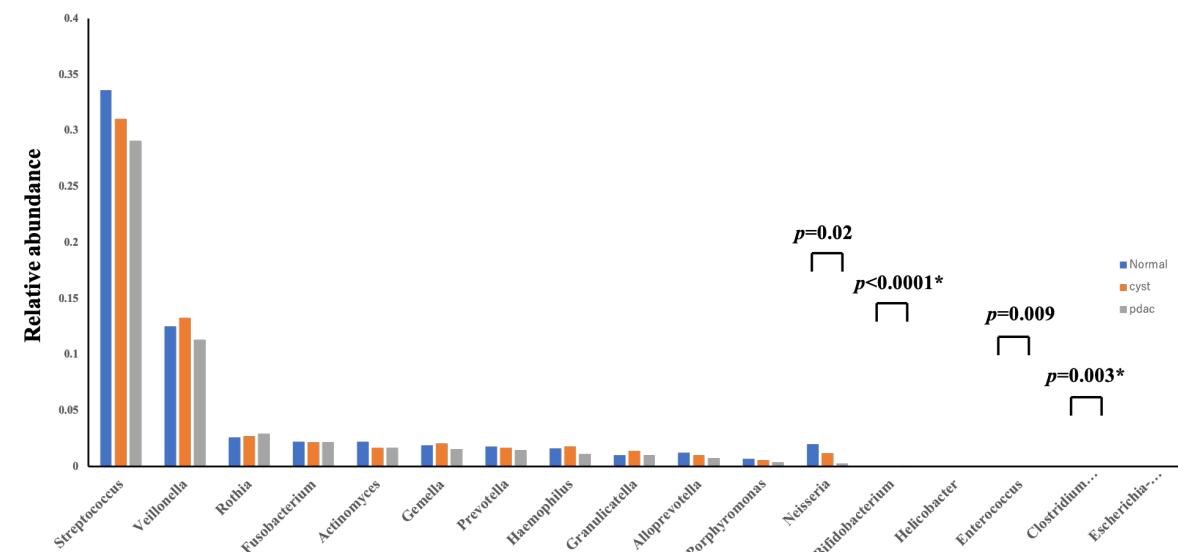
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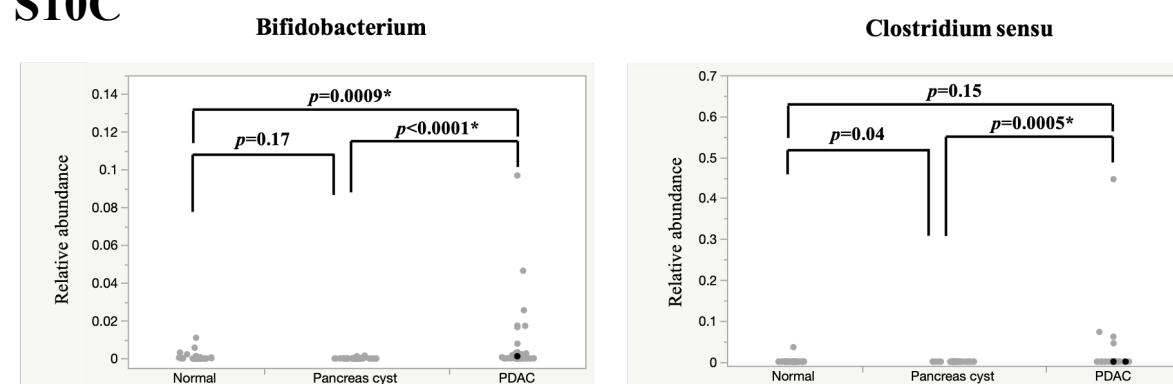
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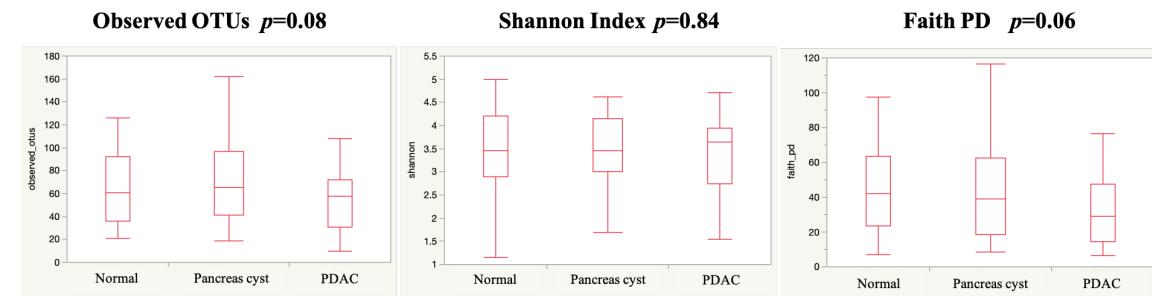
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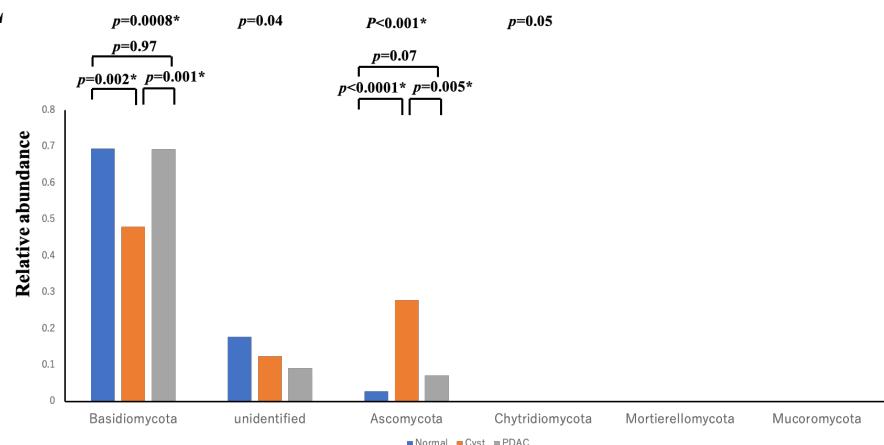
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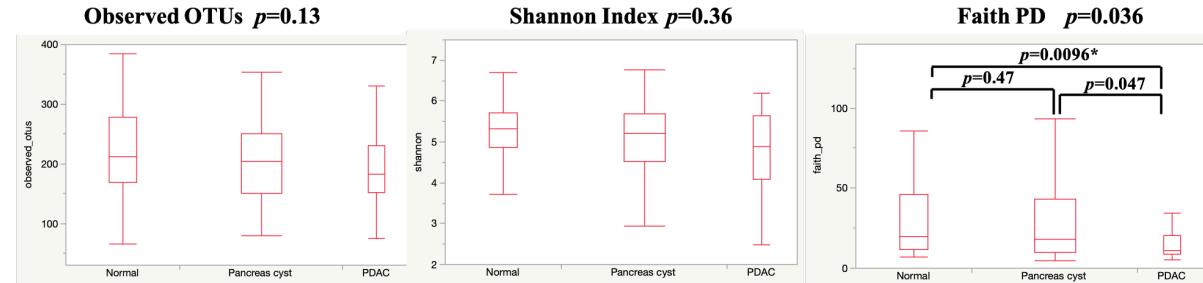
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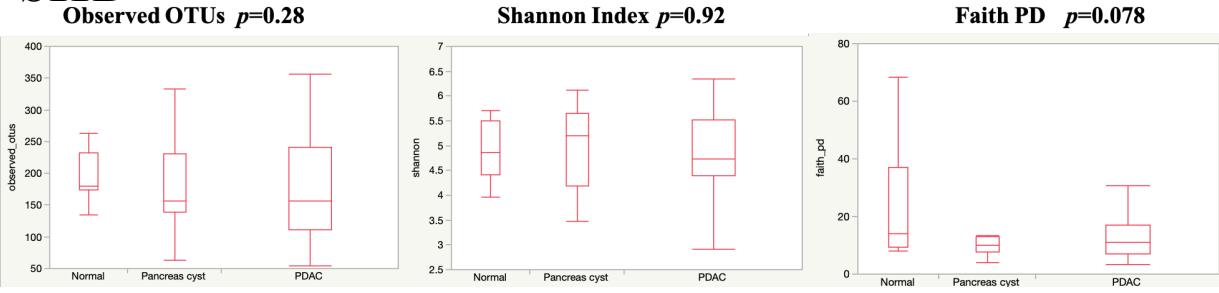
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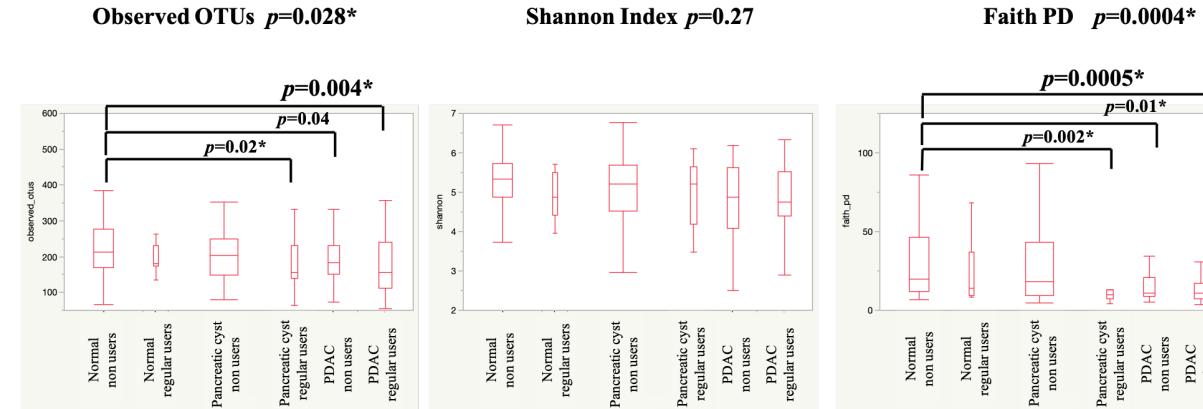
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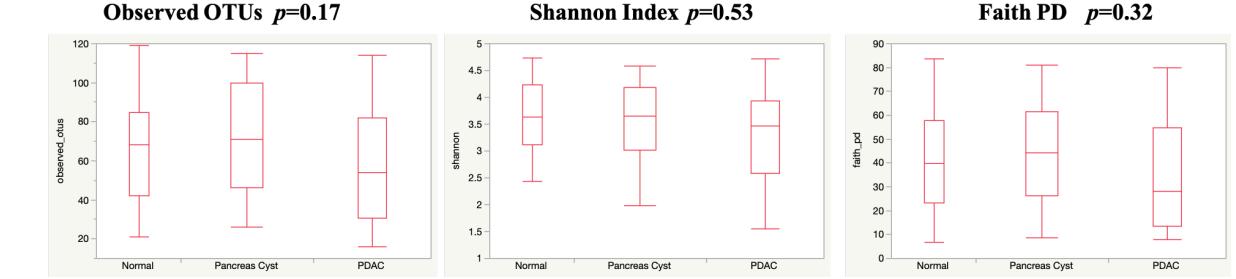
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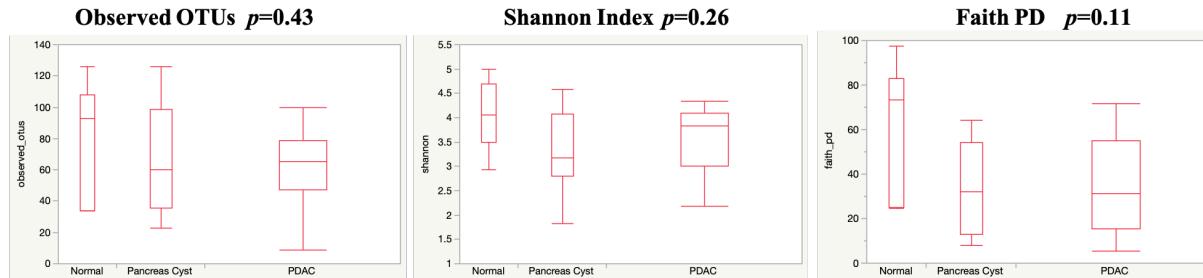
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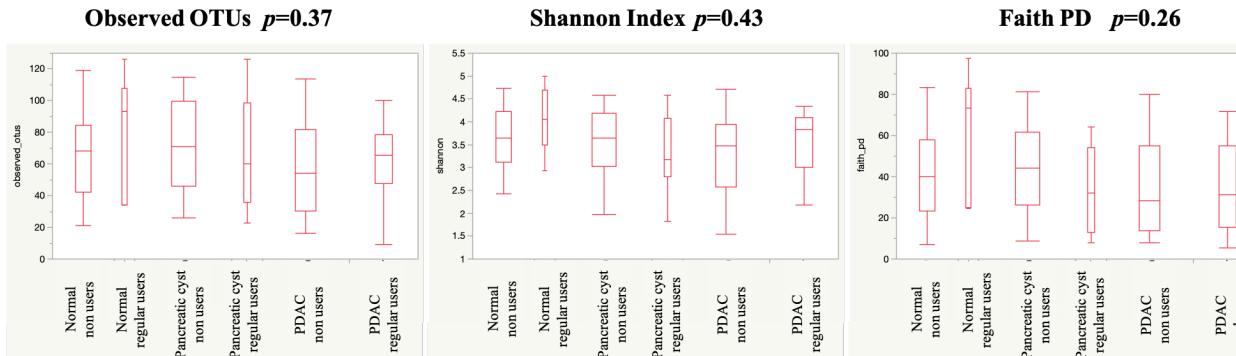
S11D



S11E

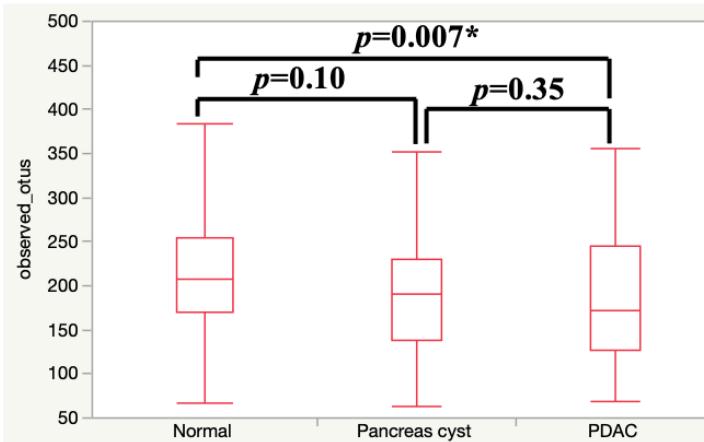


S11F

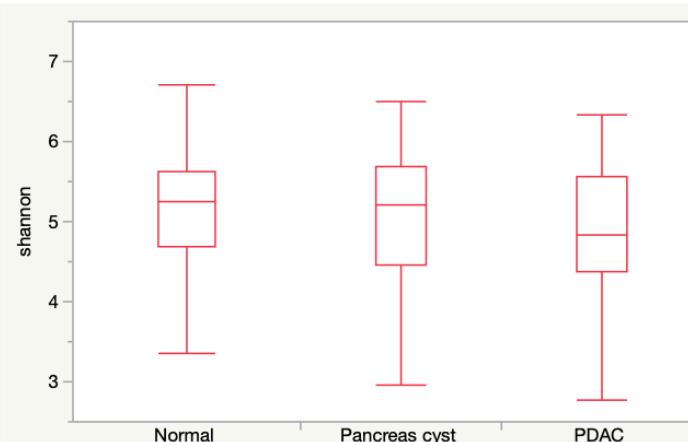


S12A

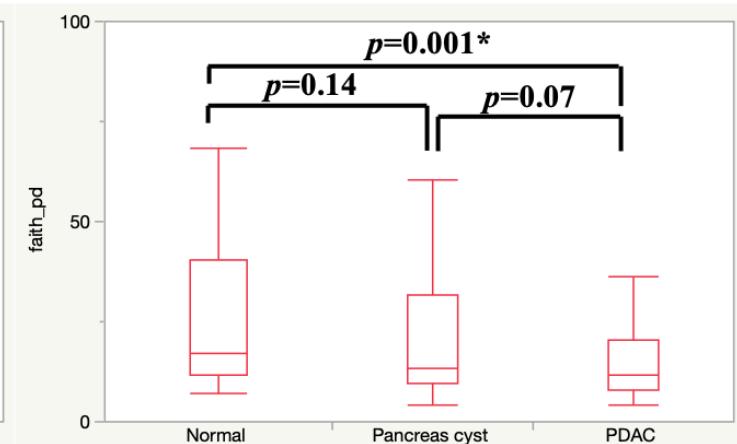
Observed OTUs $p=0.025^*$



Shannon Index $p=0.23$

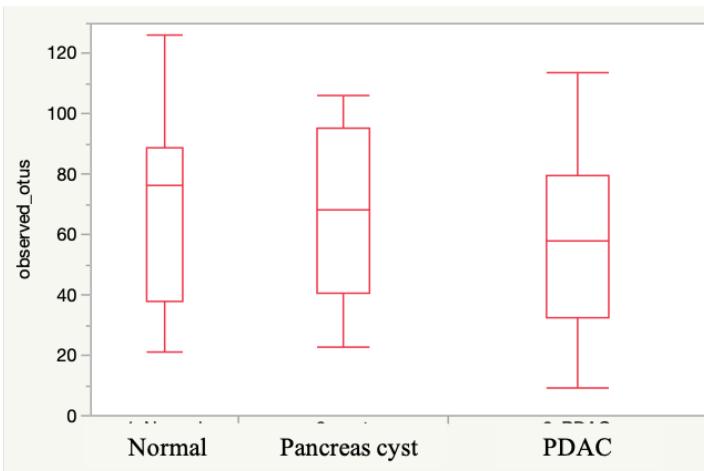


Faith PD $p=0.004^*$

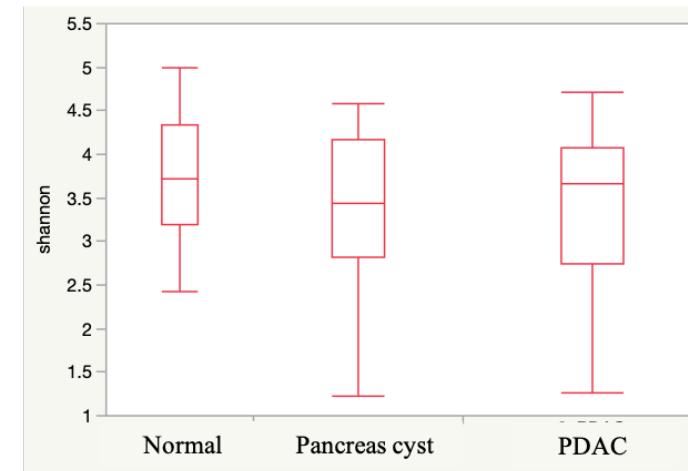


S12B

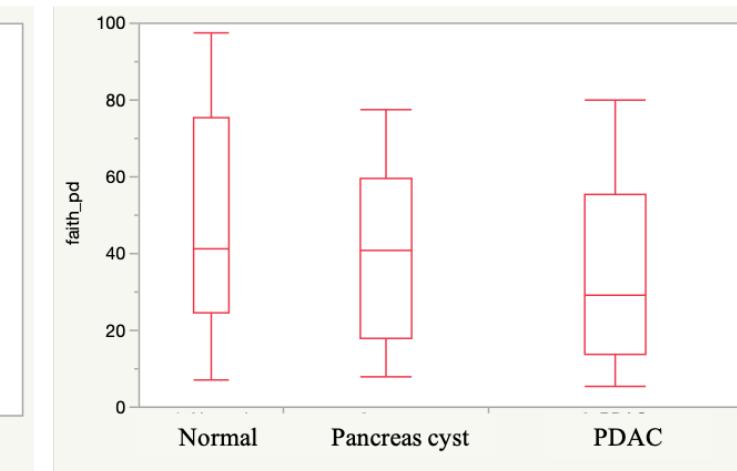
Observed OTUs $p=0.21$

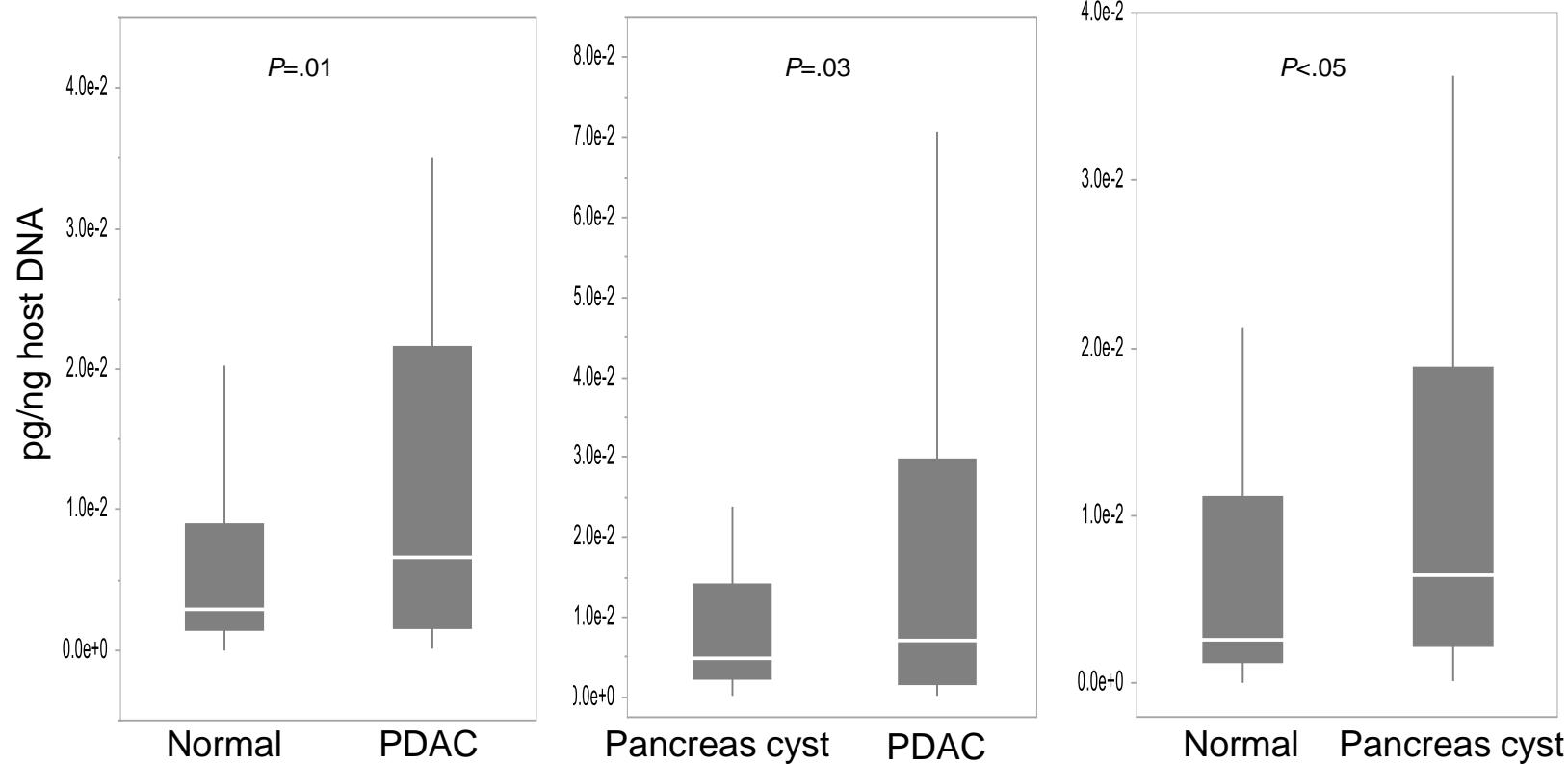


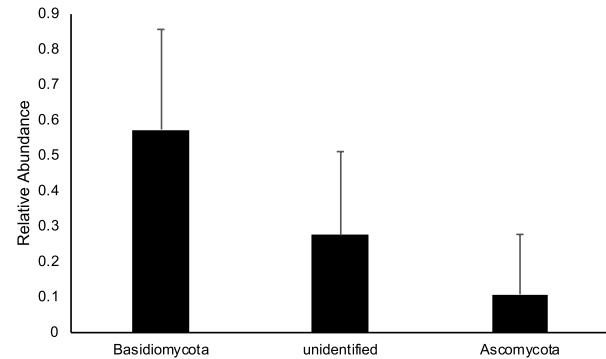
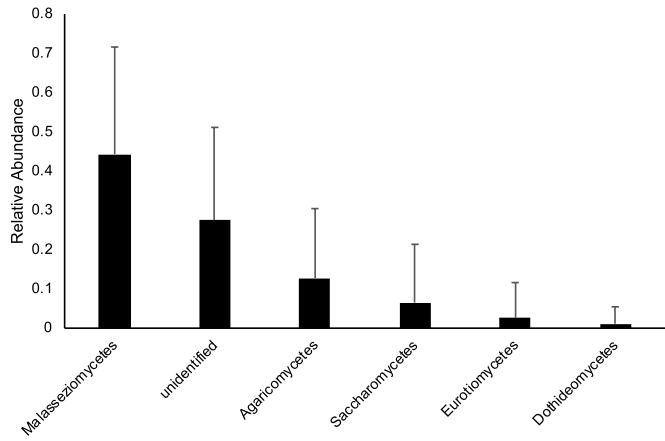
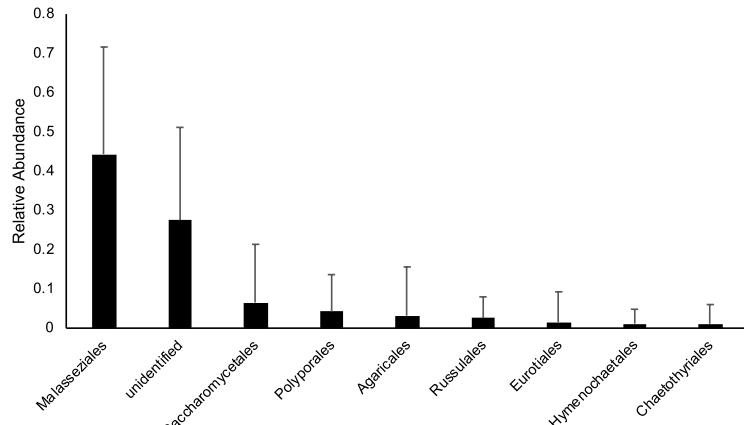
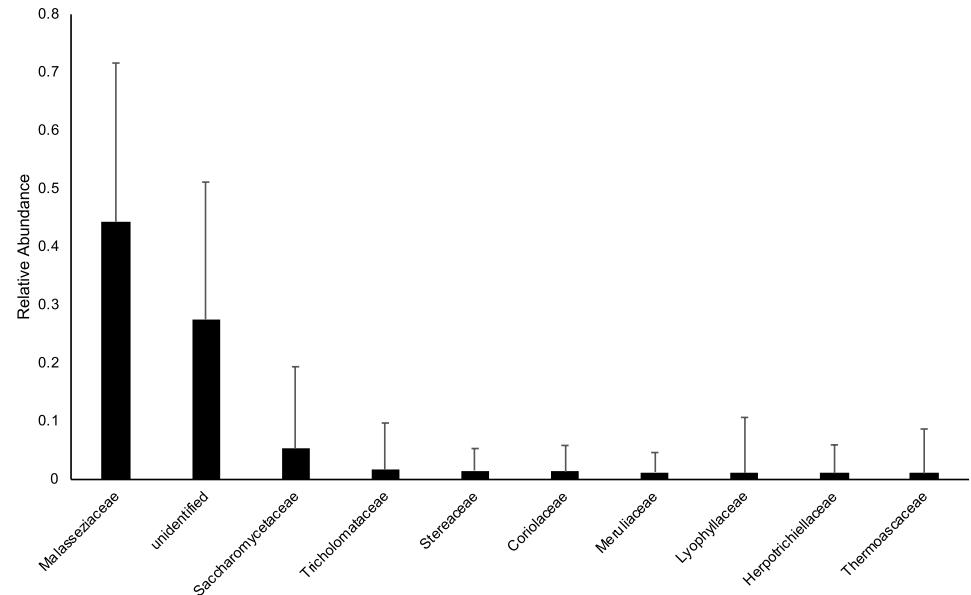
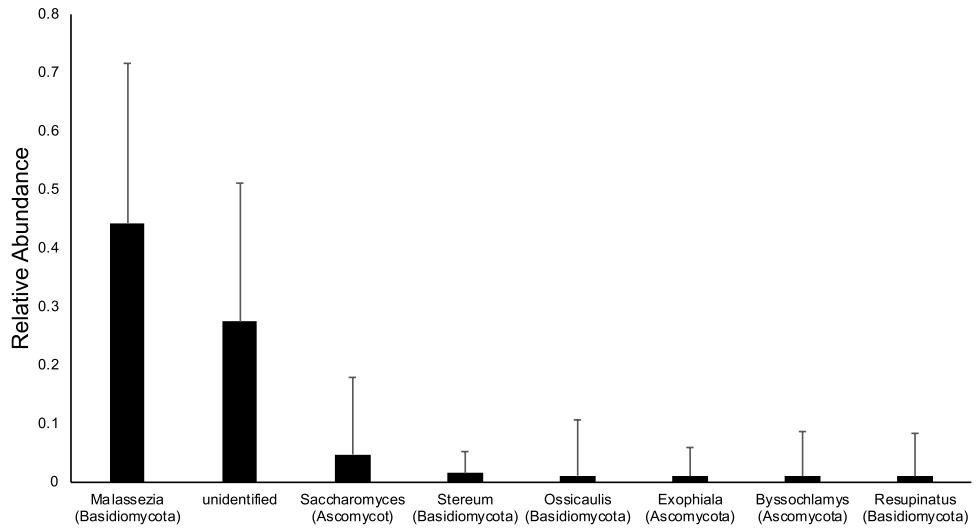
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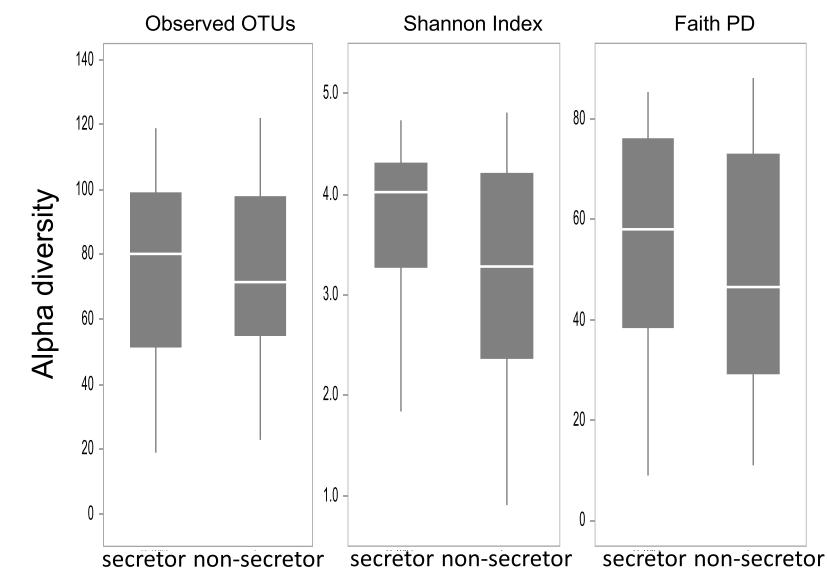
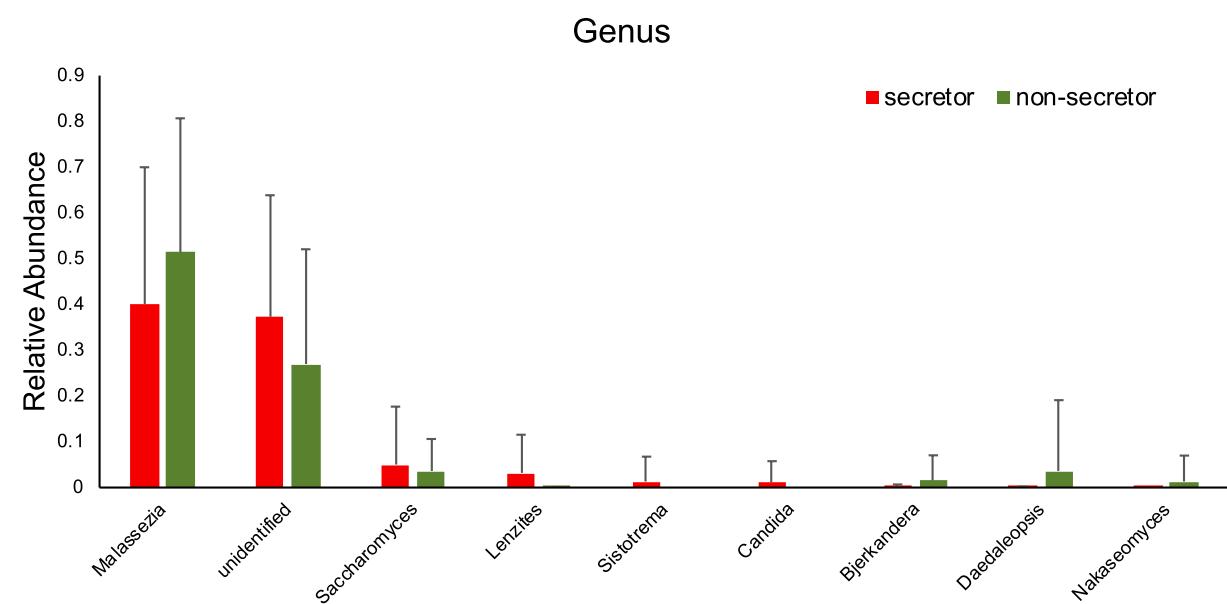
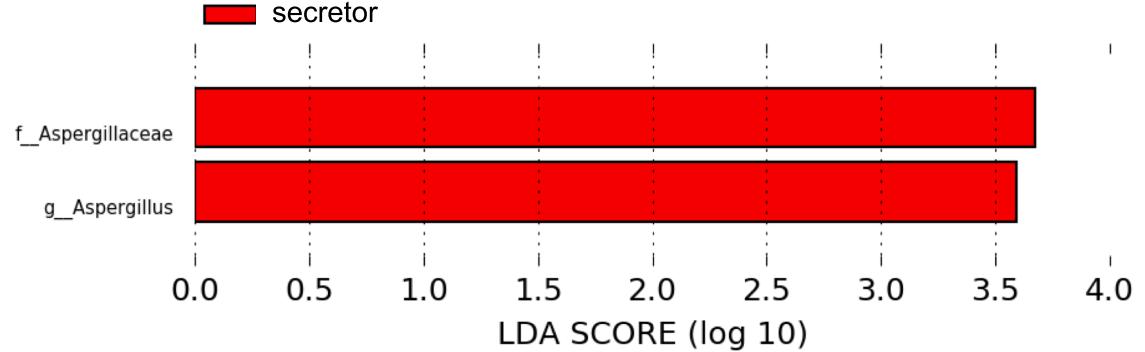
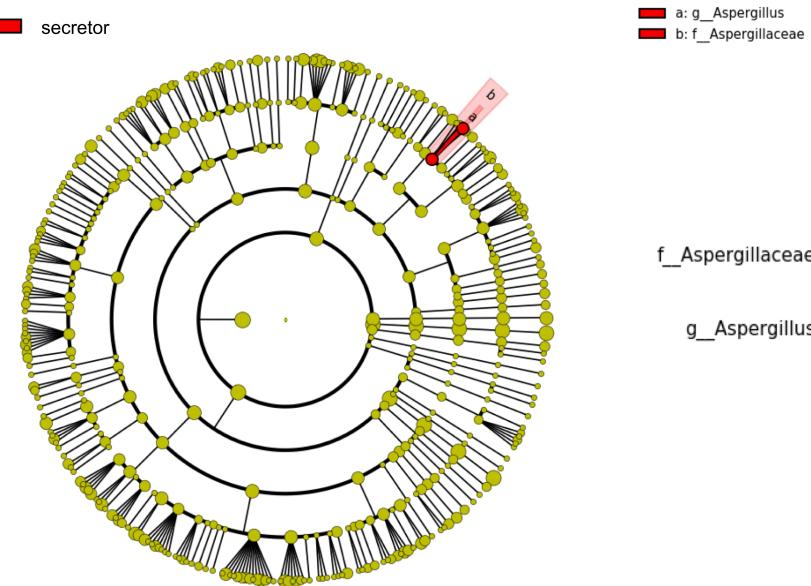


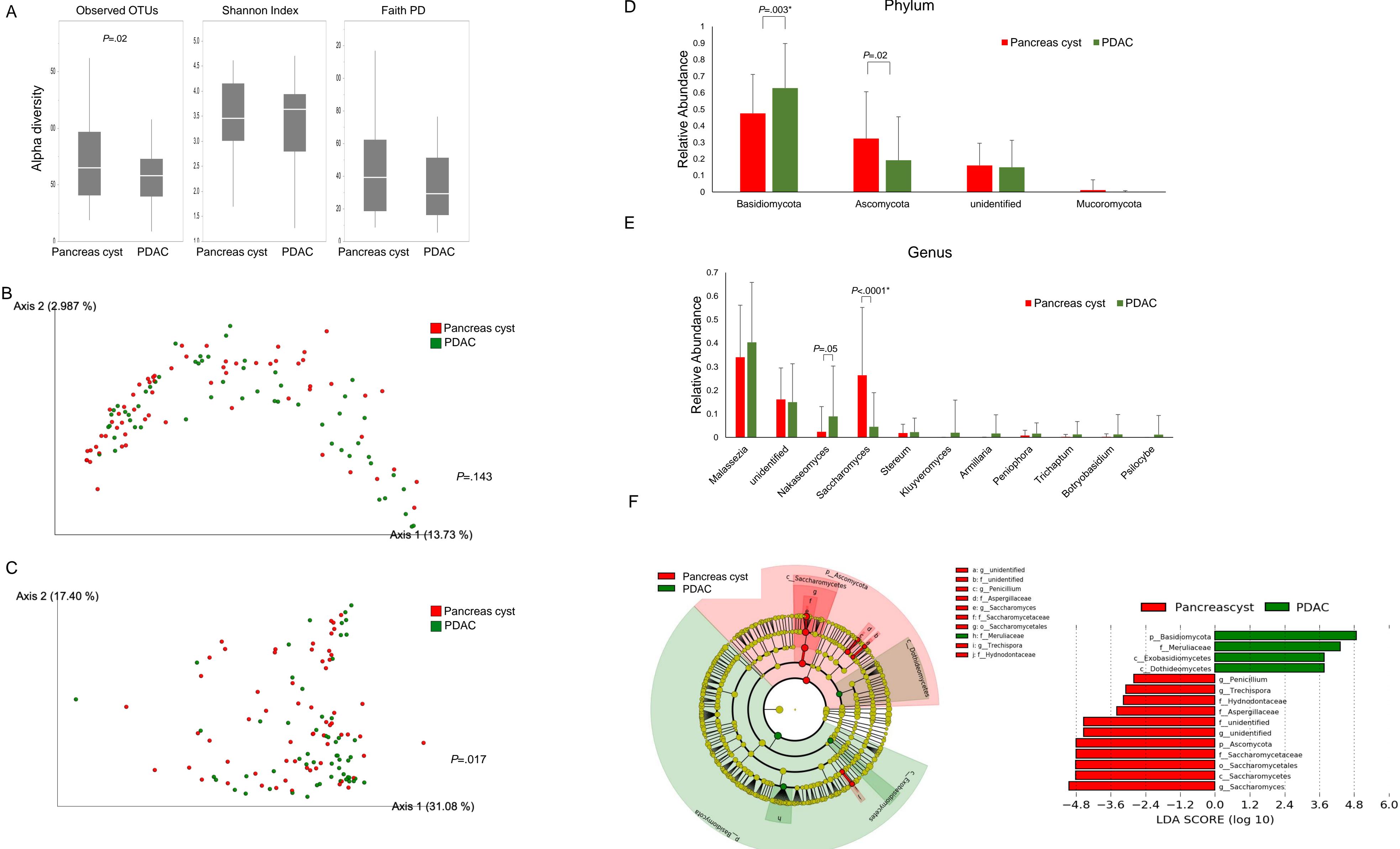
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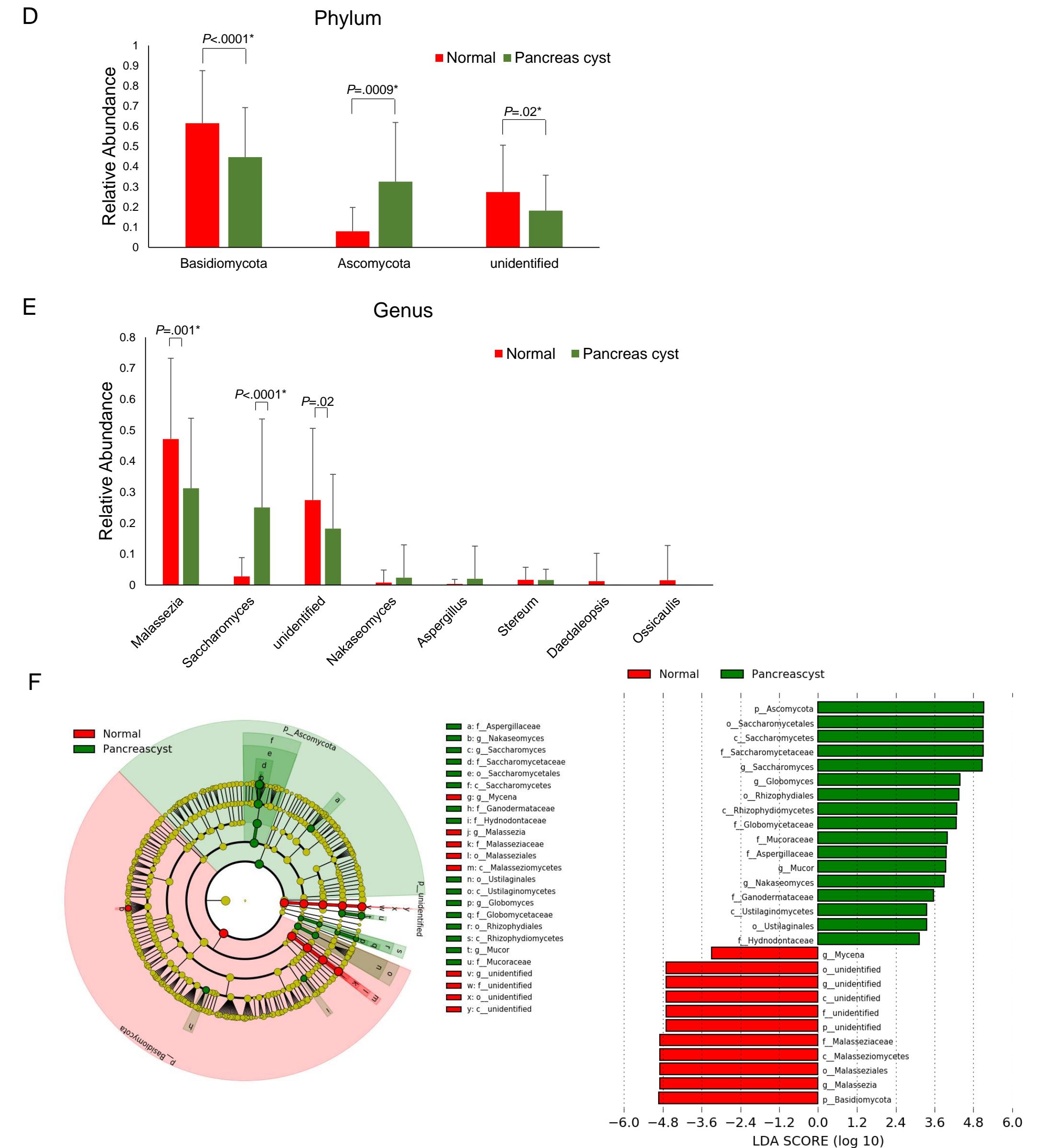
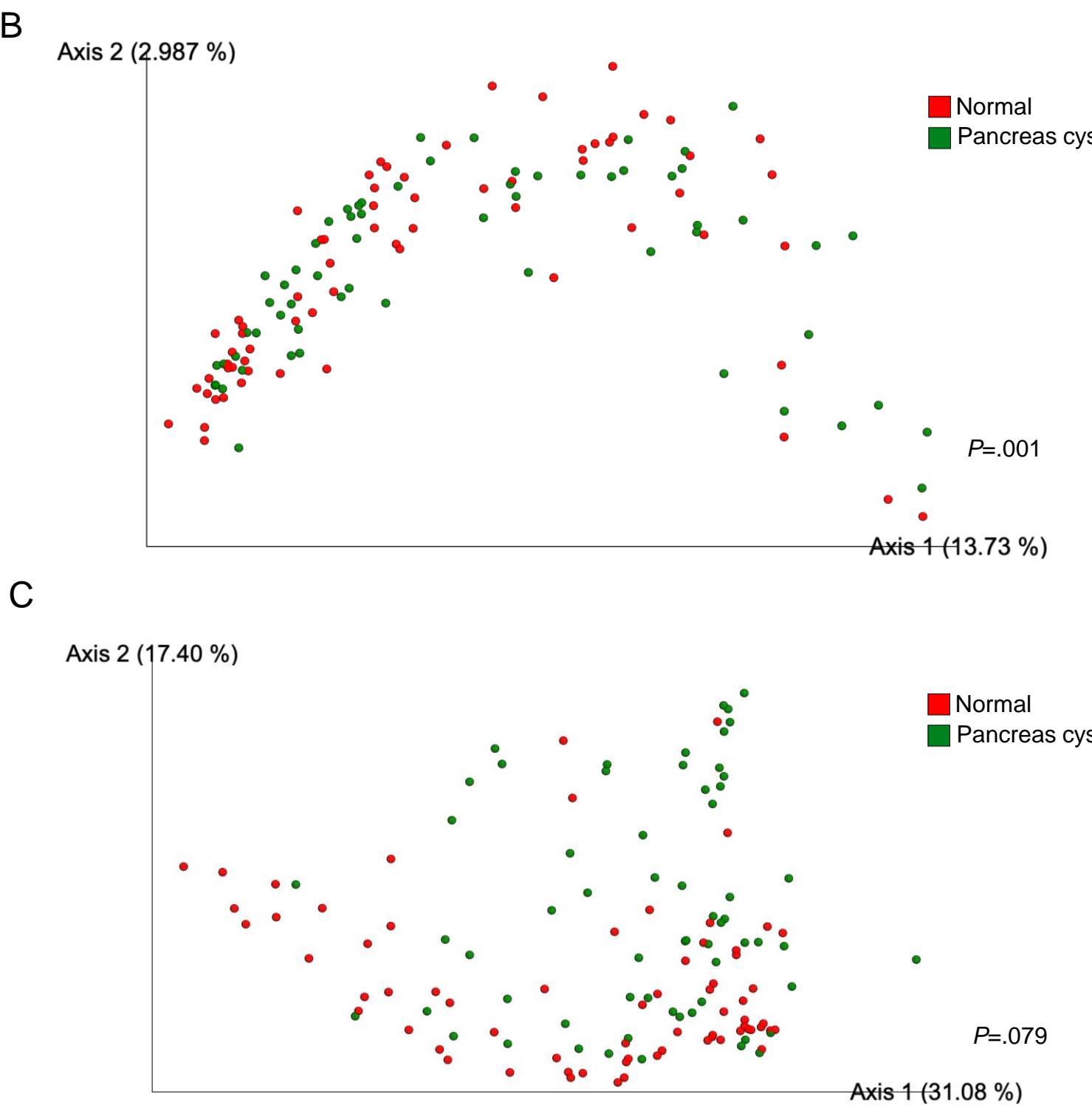
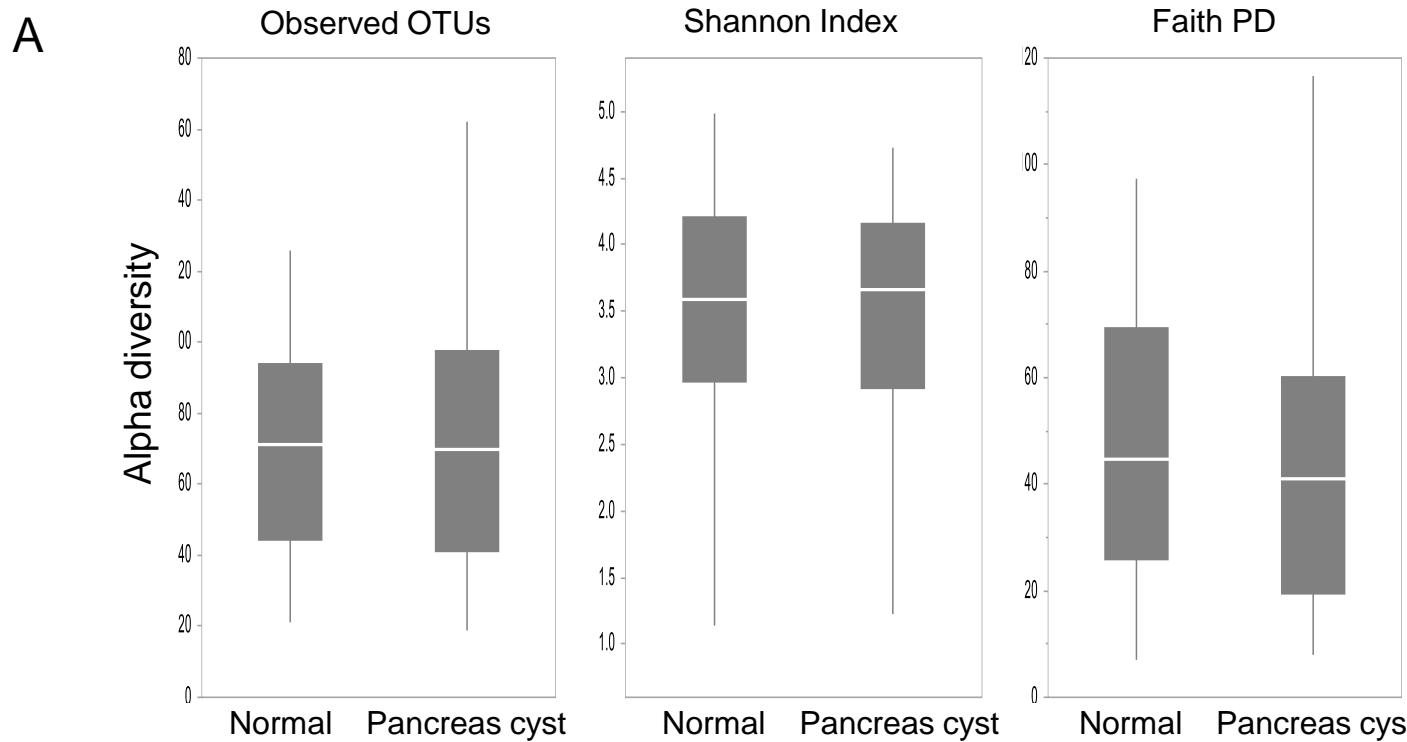


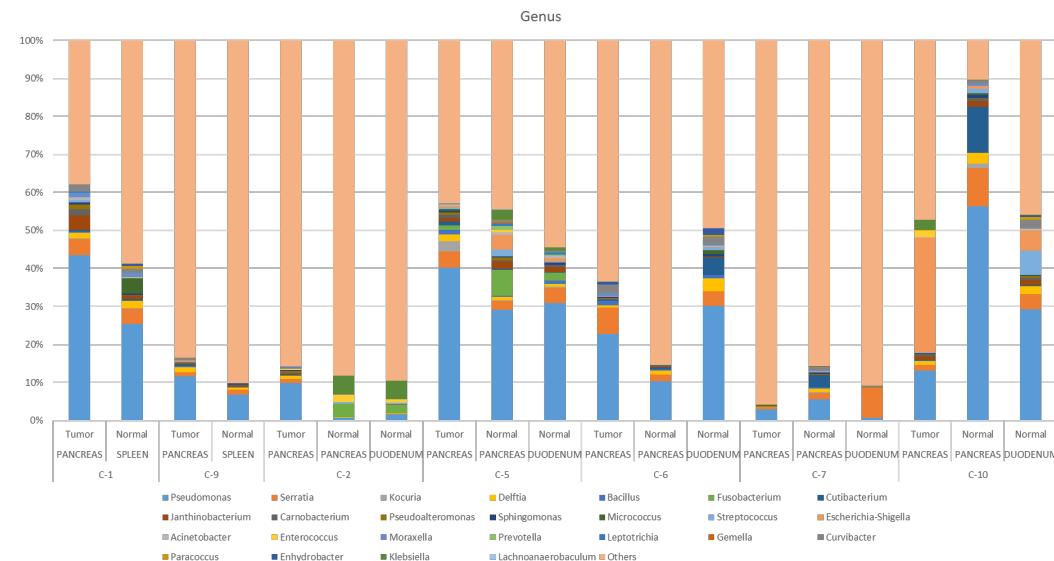
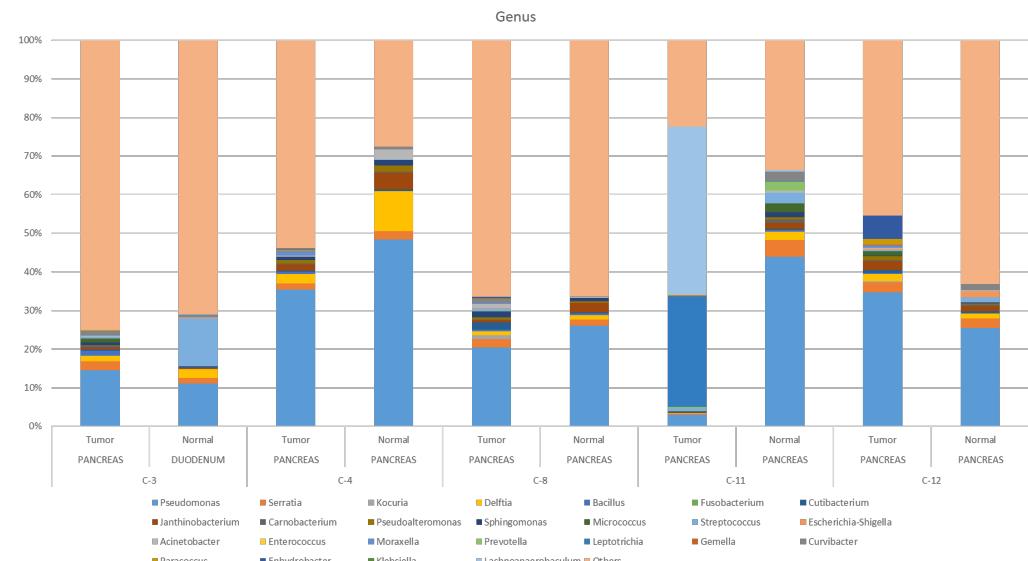


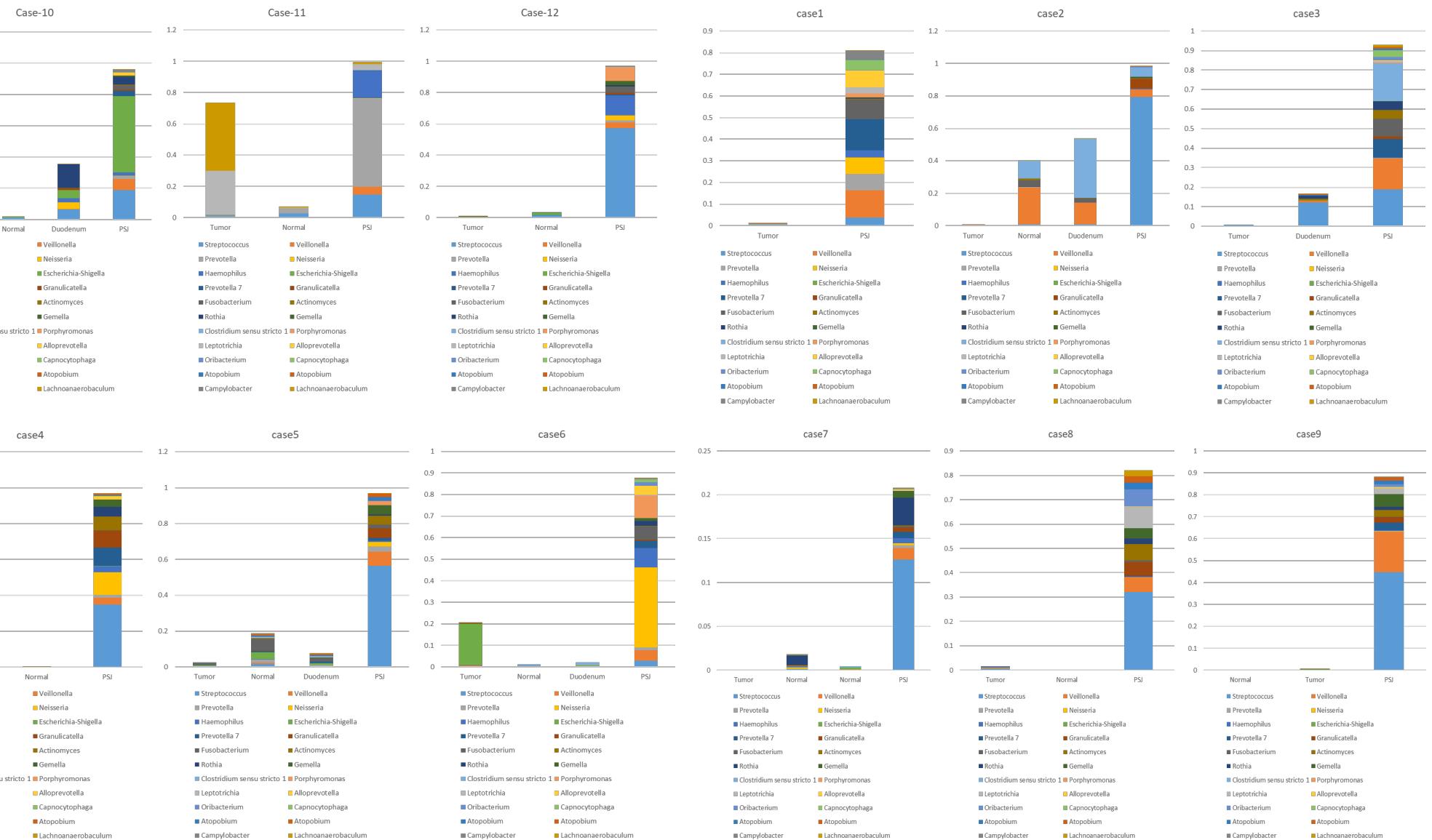
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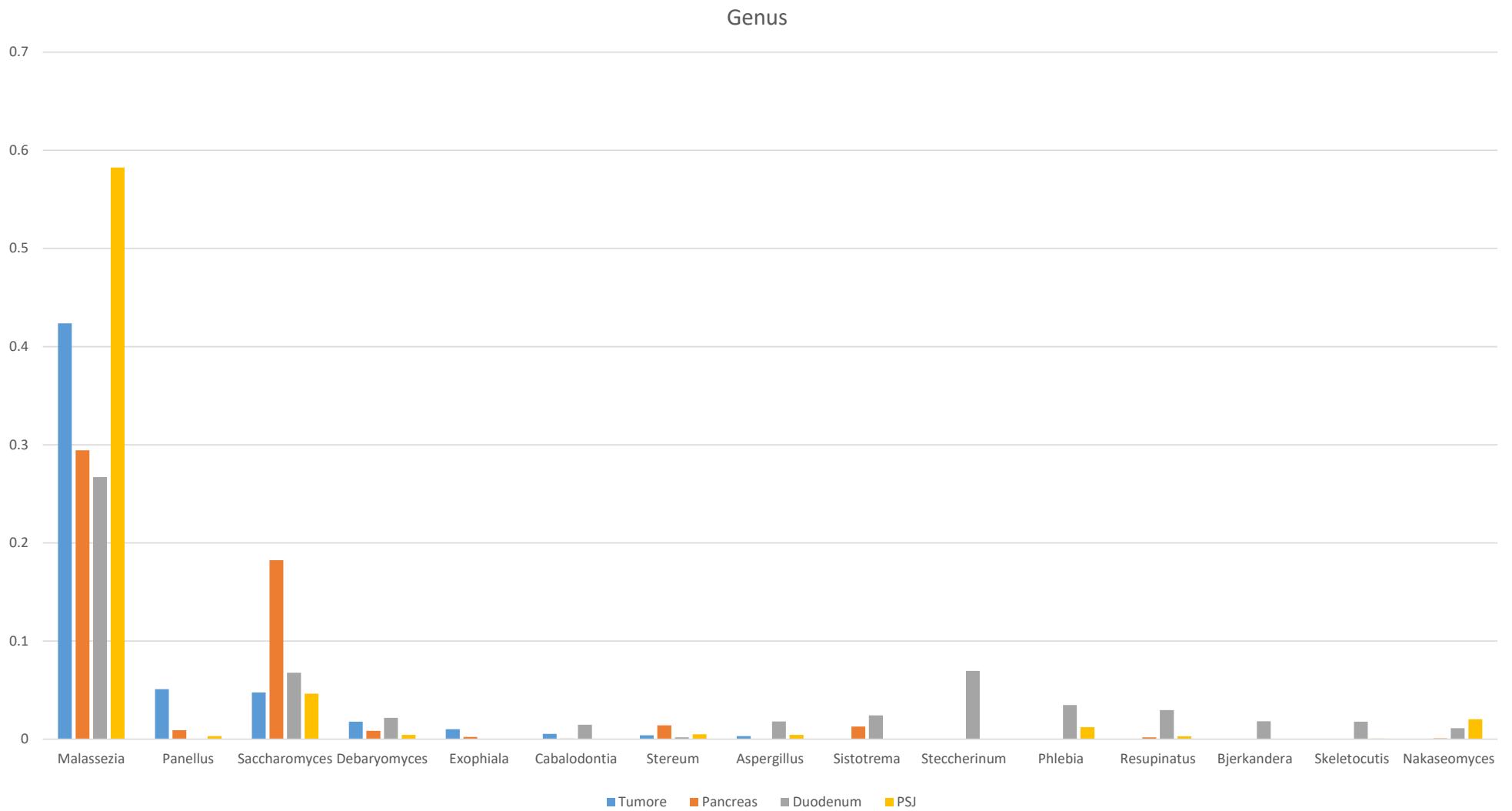
A**B****C**



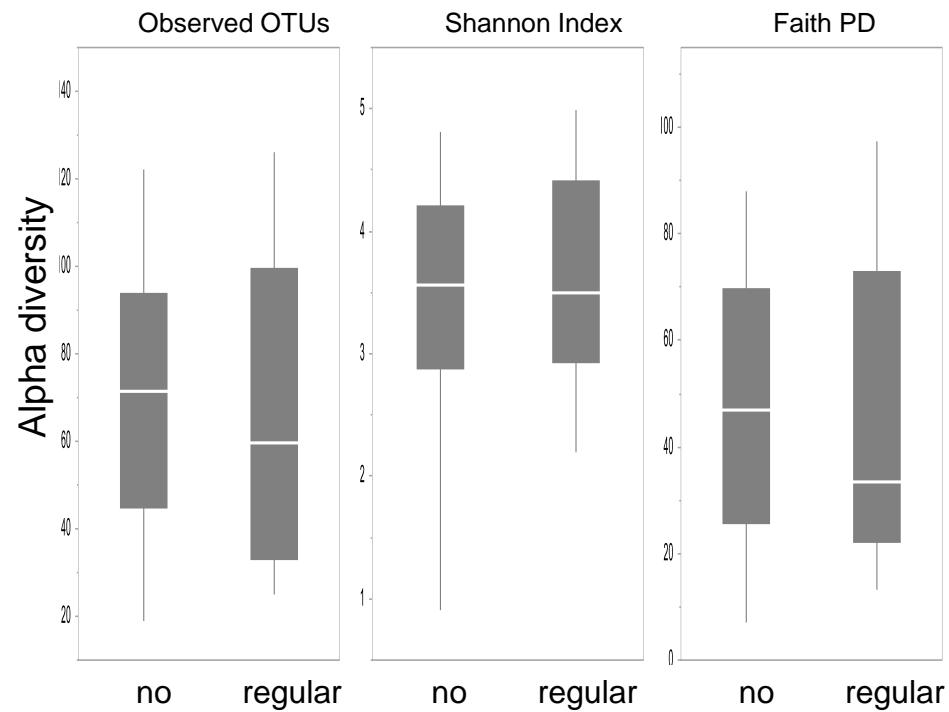




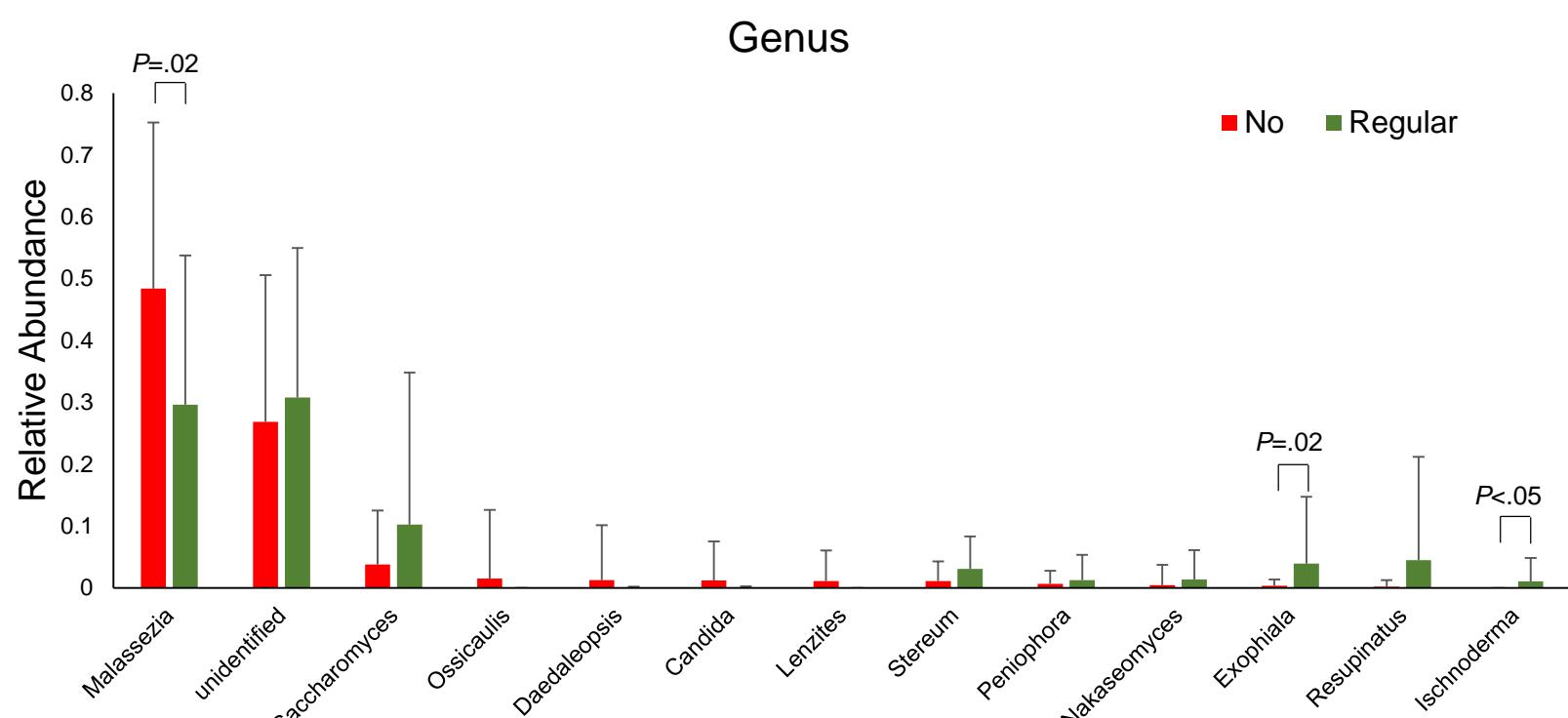




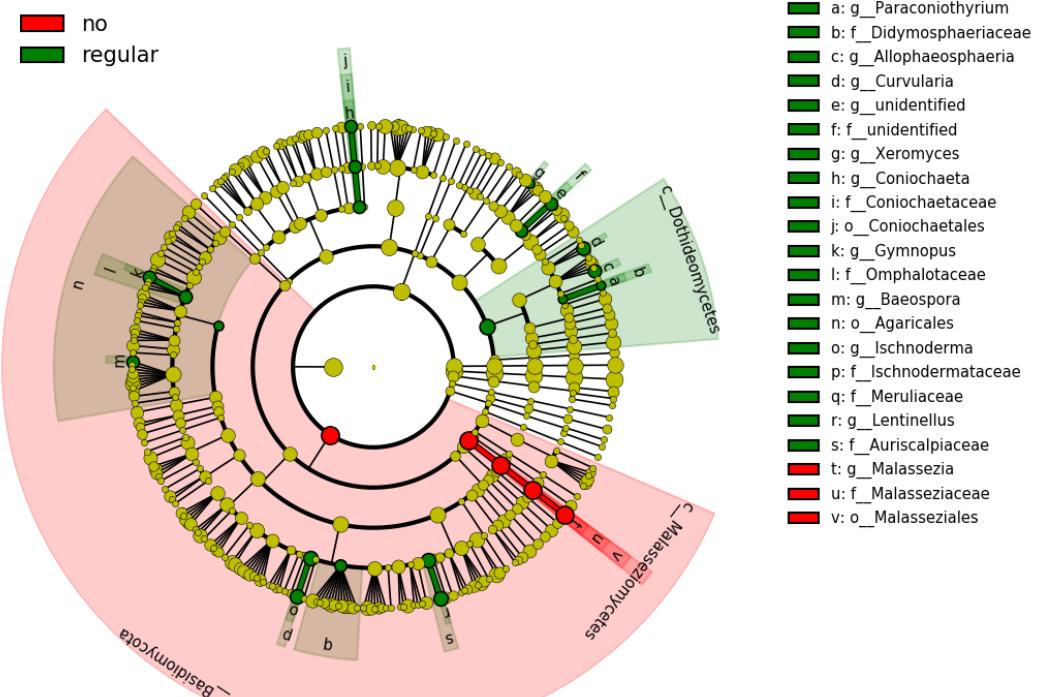
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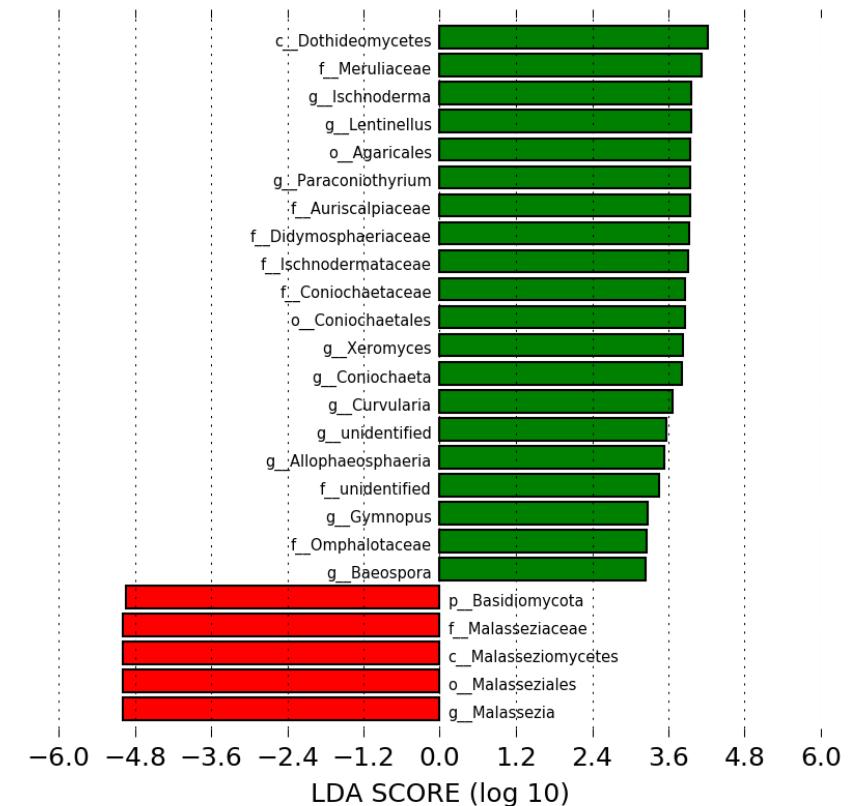
B



C

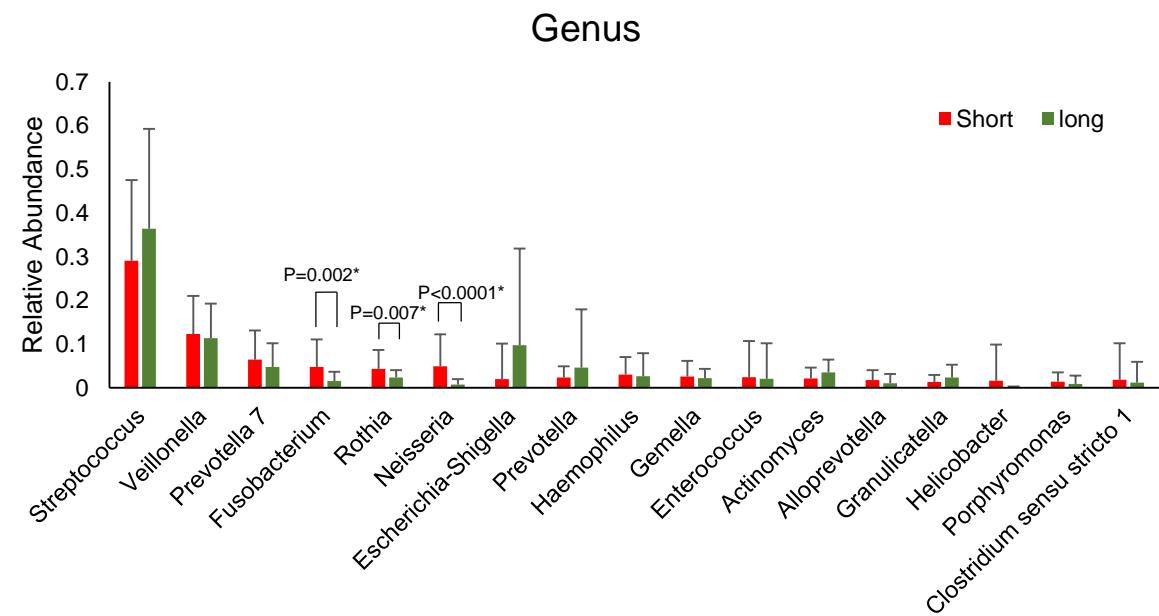
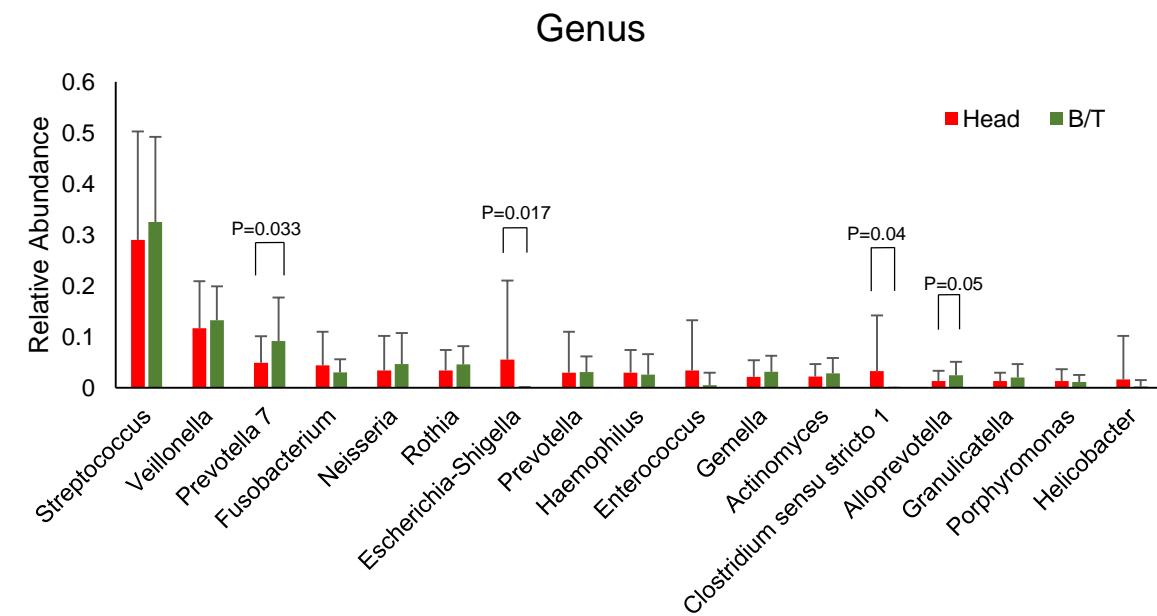
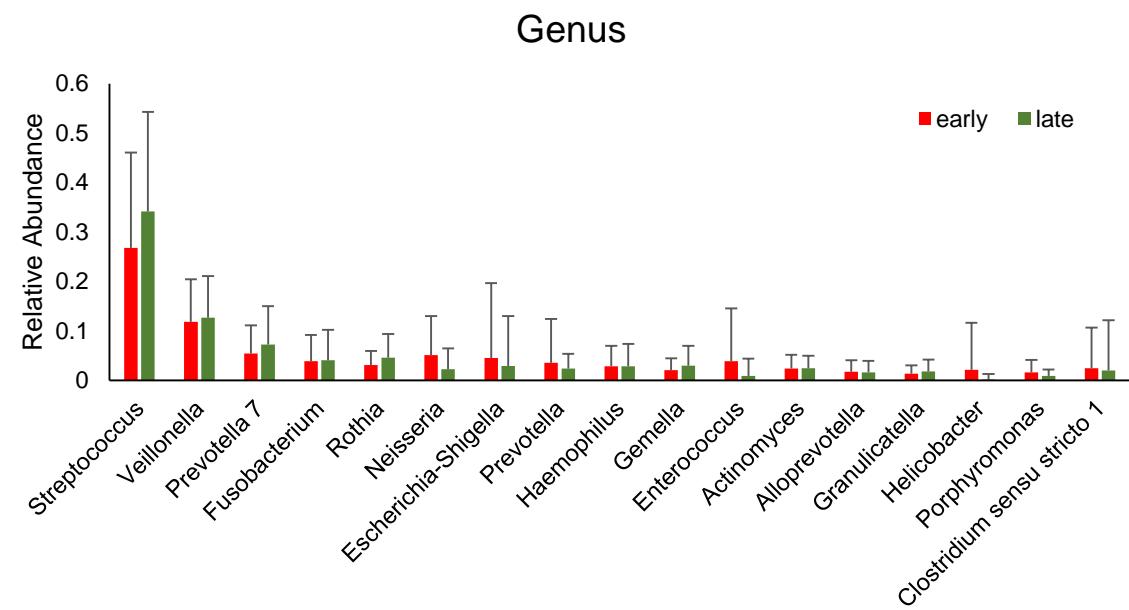
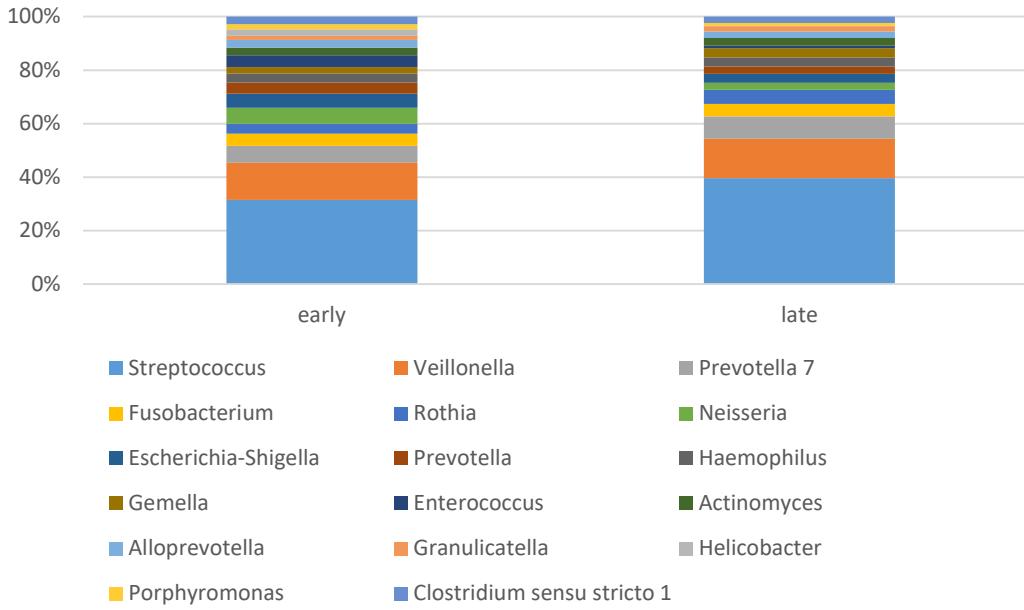


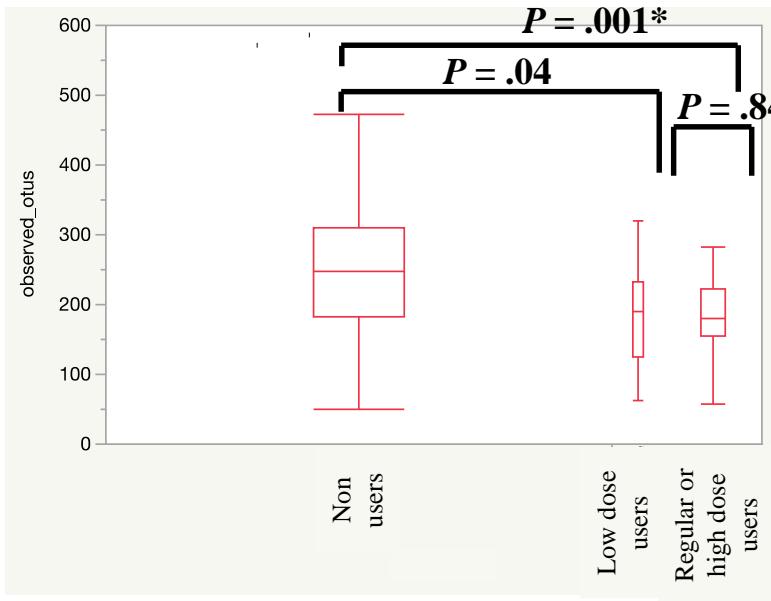
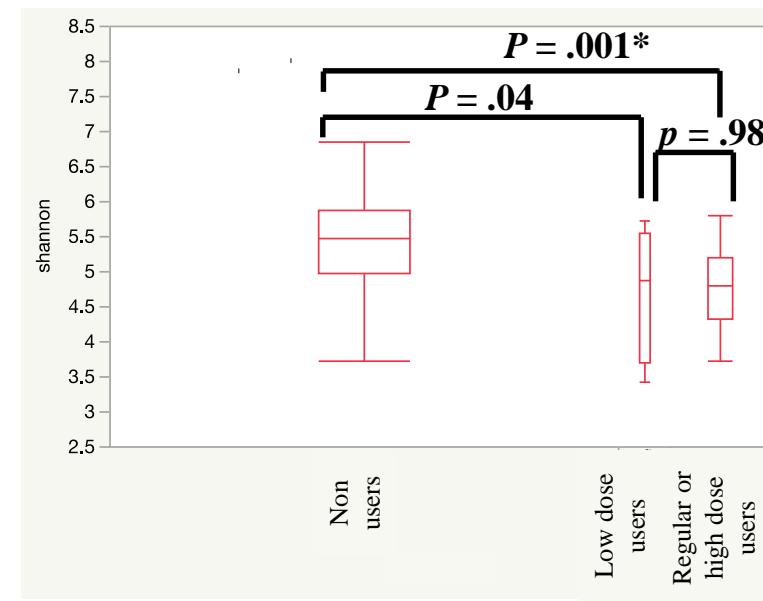
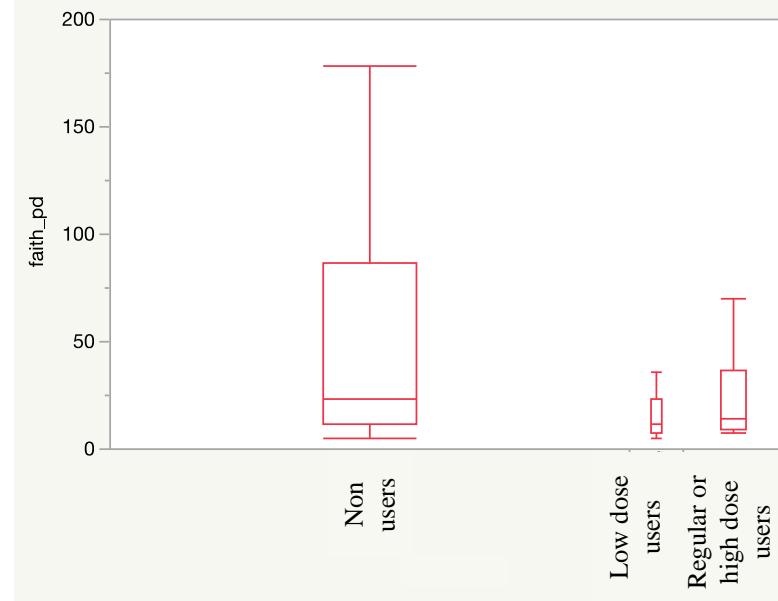
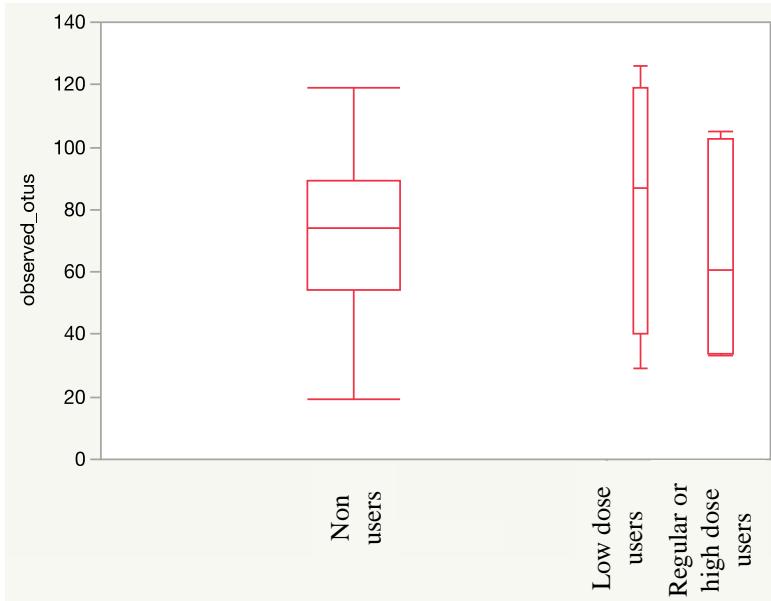
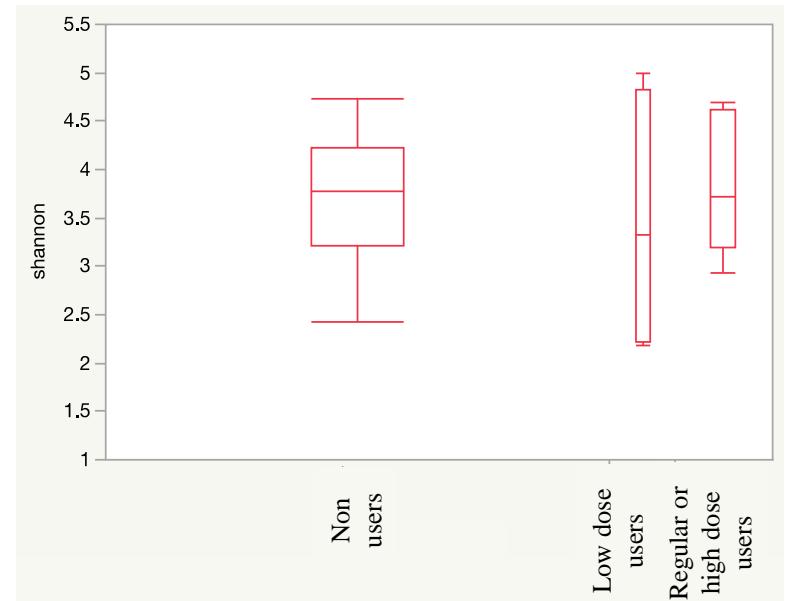
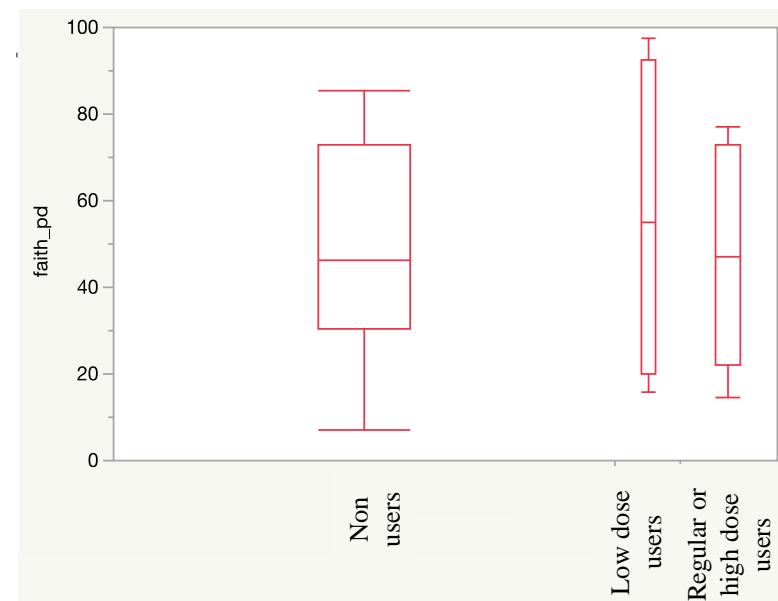
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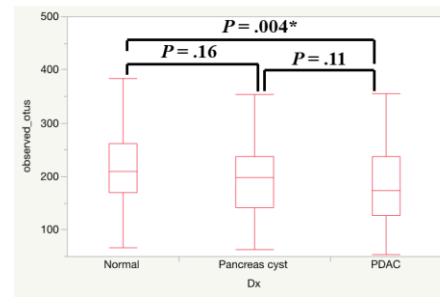
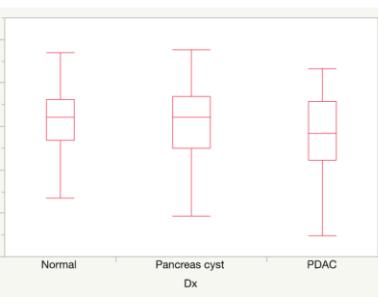
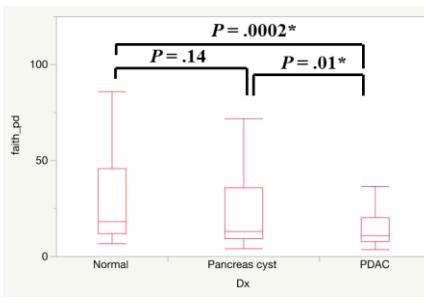
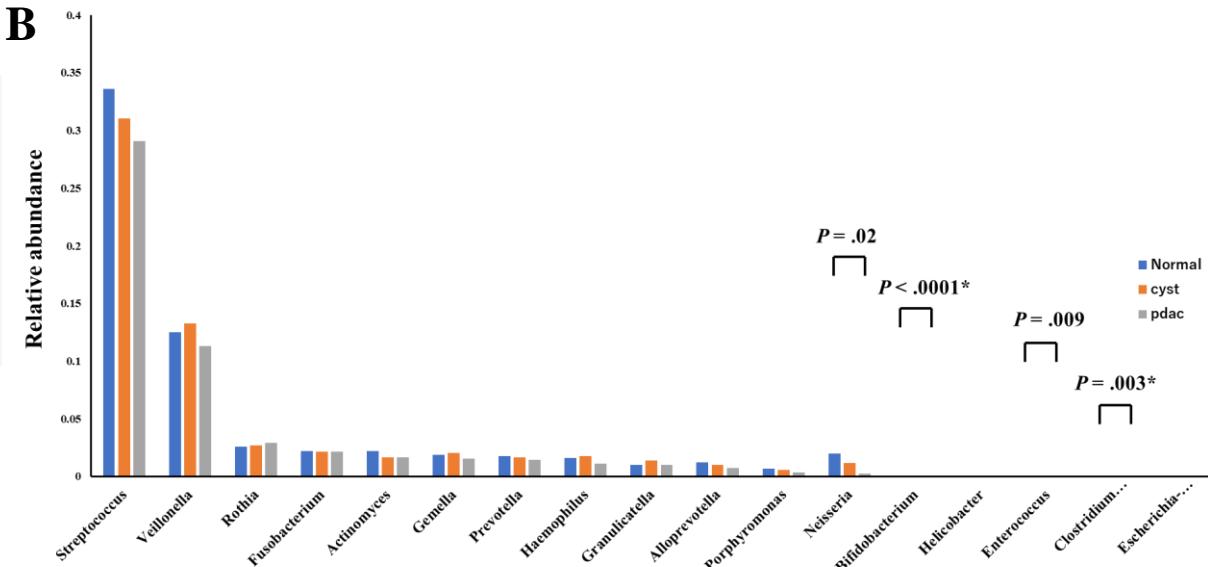
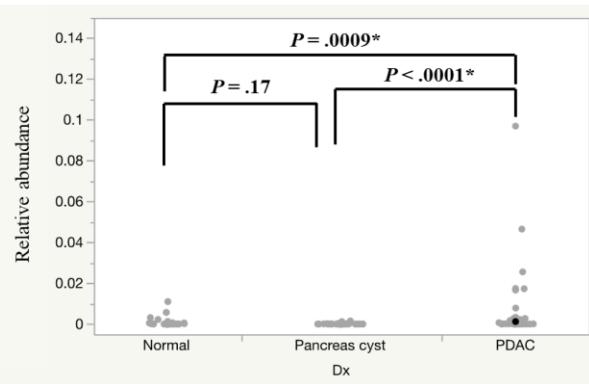
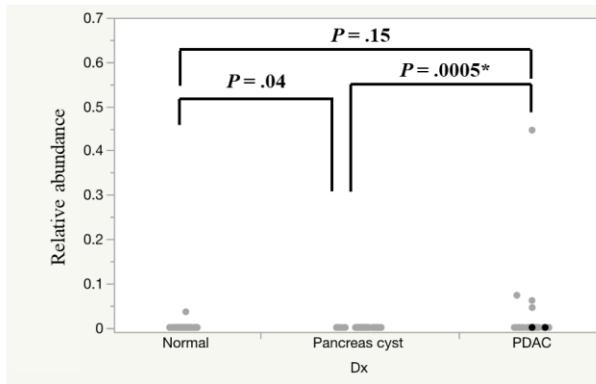
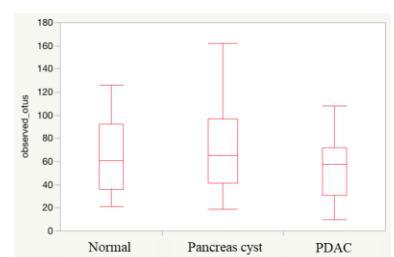
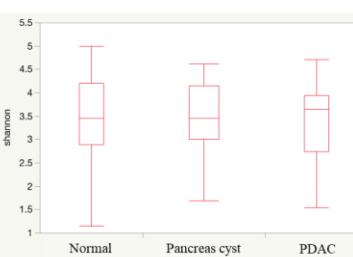
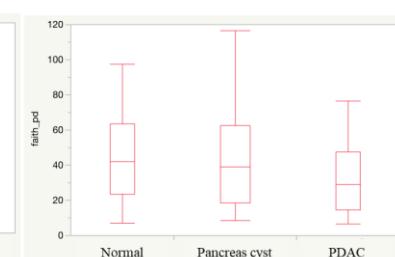
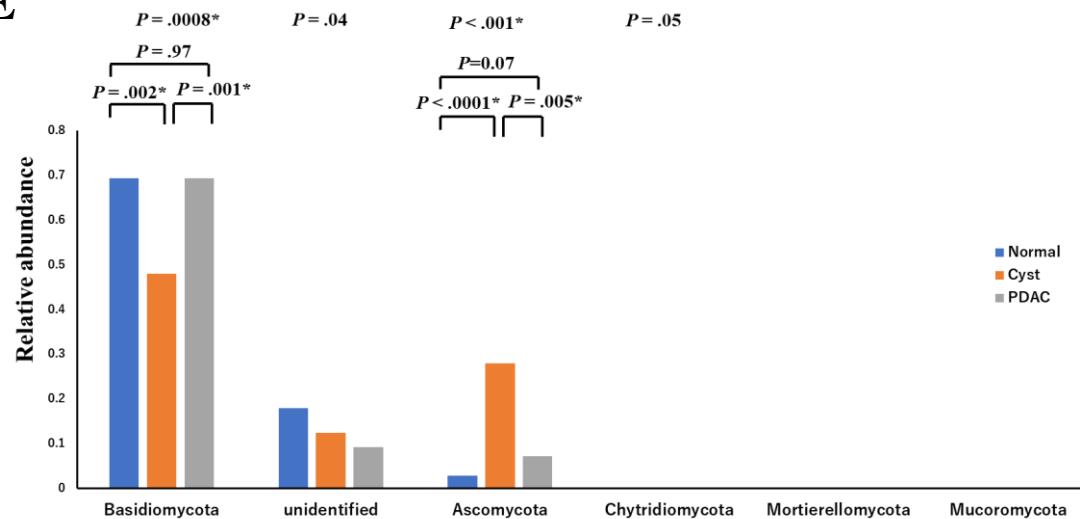


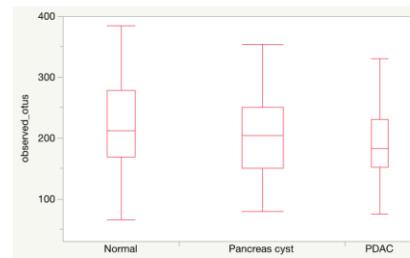
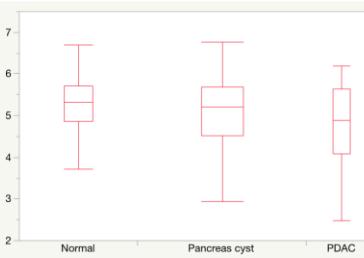
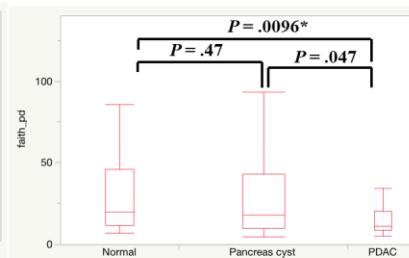
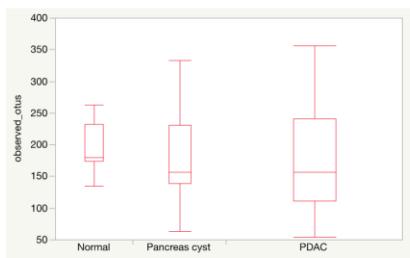
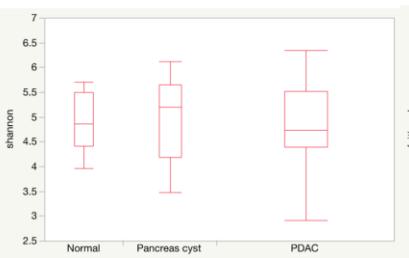
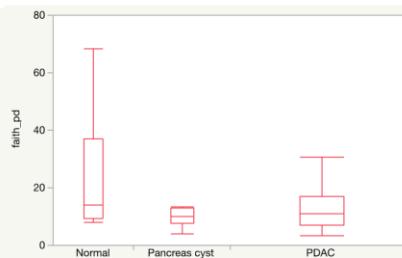
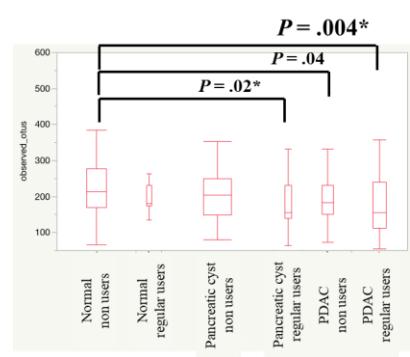
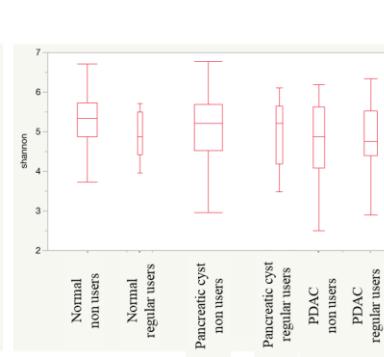
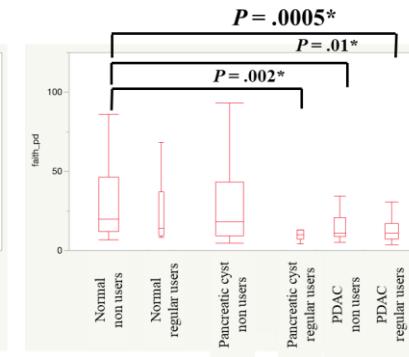
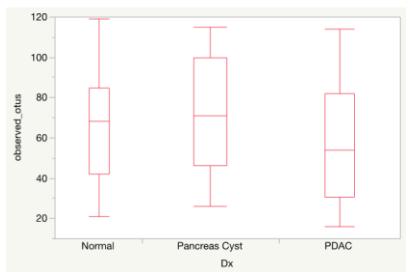
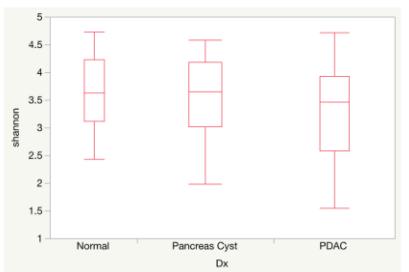
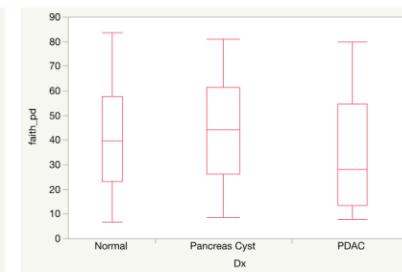
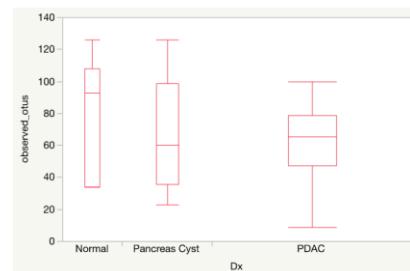
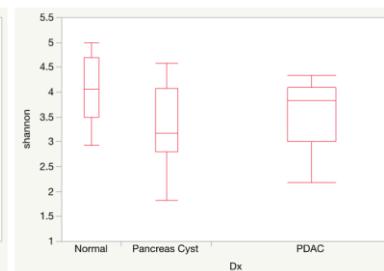
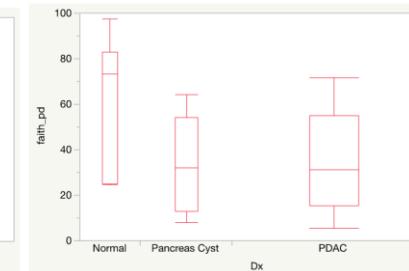
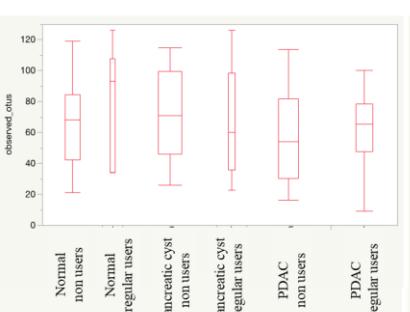
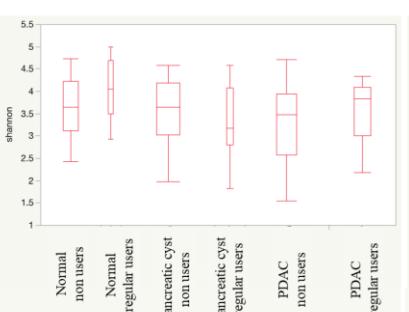
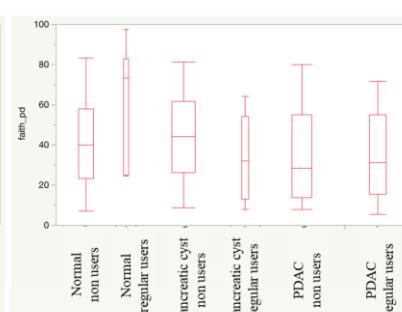
Genus

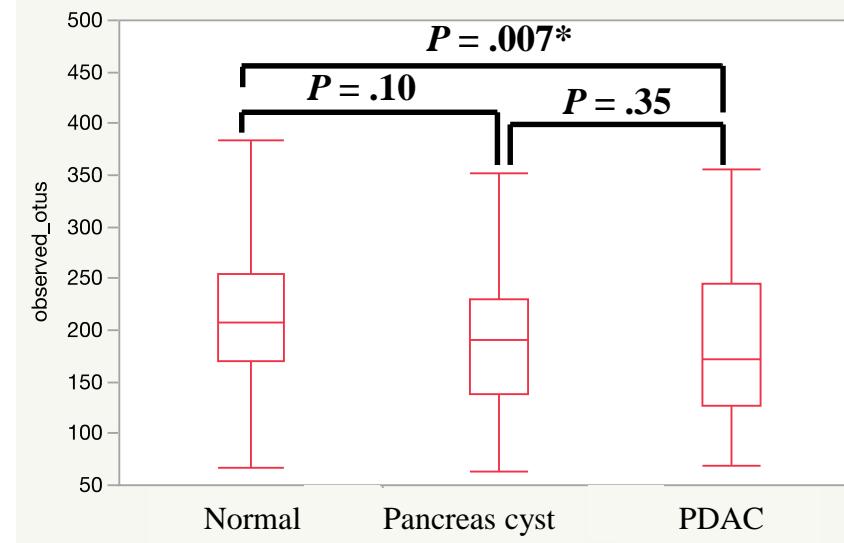
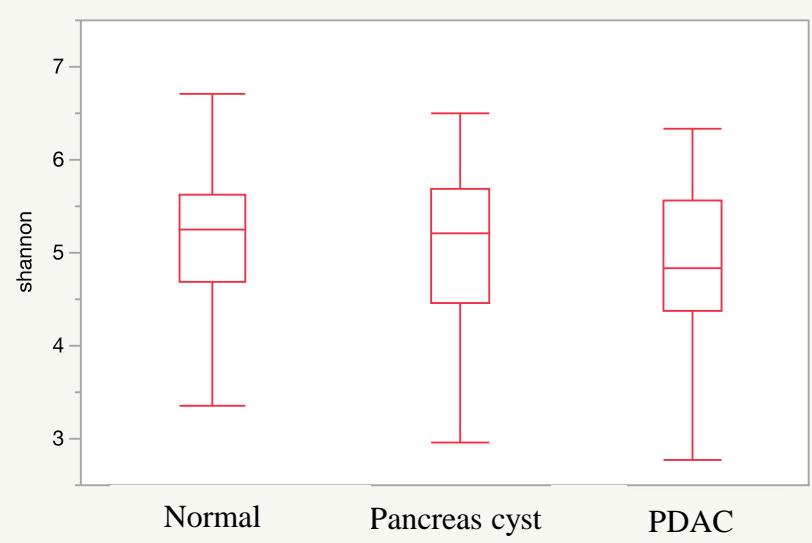
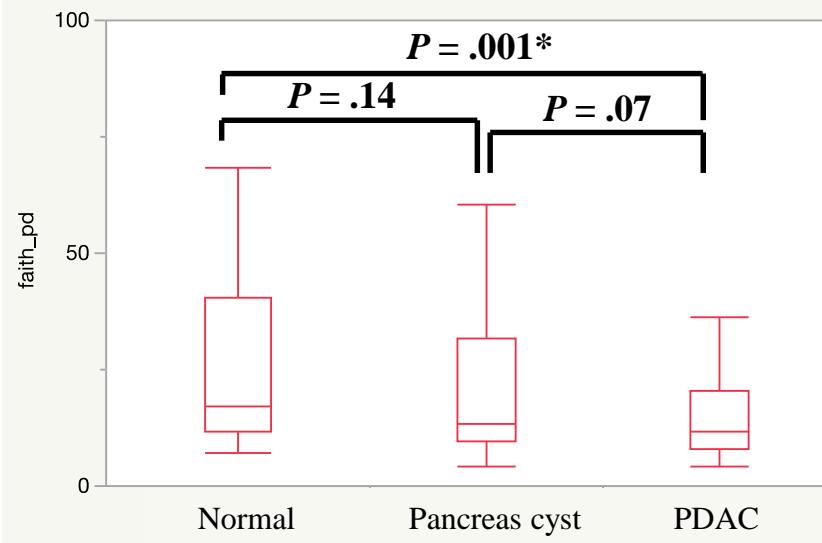
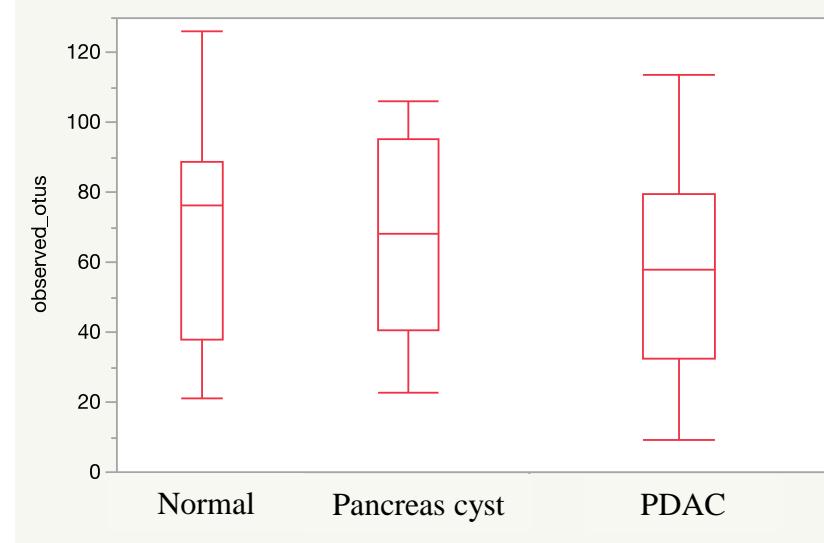
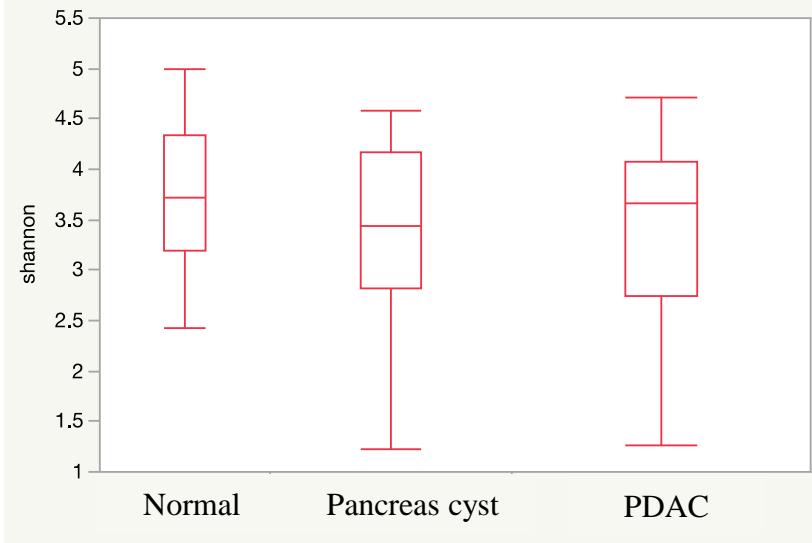




A**Observed OTUs $P = .001^*$** **Shannon Index $P = .001^*$** **Faith PD $P = .06$** **B****Observed OTUs $P = .78$** **Shannon Index $P = .88$** **Faith PD $P = .83$** 

A**Observed OTUs $P = .016^*$** **Shannon Index $P = .21$** **Faith PD $P = .0008^*$** **B****C****Bifidobacterium****Clostridium sensu****D****Observed OTUs $P = .08$** **Shannon Index $P = .84$** **Faith PD $P = .06$** **E**

A**Observed OTUs** $P = .13$ **Shannon Index** $P = .36$ **Faith PD** $P = .036$ **B****Observed OTUs** $P = .28$ **Shannon Index** $P = .92$ **Faith PD** $P = .078$ **C****Observed OTUs** $P = .028^*$ **Shannon Index** $P = .27$ **Faith PD** $P = .0004^*$ **D****Observed OTUs** $P = .17$ **Shannon Index** $P = .53$ **Faith PD** $P = .32$ **E****Observed OTUs** $P = .43$ **Shannon Index** $P = .26$ **Faith PD** $P = .11$ **F****Observed OTUs** $P = .37$ **Shannon Index** $P = .43$ **Faith PD** $P = .26$ 

A**Observed OTUs $P = .025^*$** **Shannon Index $P = .23$** **Faith PD $P = .004^*$** **B****Observed OTUs $P = .21$** **Shannon Index $P = .41$** **Faith PD $P = .21$** 