

Table S1. Characteristics comparison between included and non-included patients in the sub-cohort

Characteristics	Overall (N = 3033)^a	Included in the sub-cohort (n=680)^a	Not included in the sub-cohort (n=2353)^a	P-value^b
Age at baseline (years)	69 [60-76]	68 [61-77]	69 [60-76]	0.77
Men	65.4%	69%	64.3%	0.02
eGFR at baseline (ml/min/1.73 m²)	32 [23-41]	32 [23-41]	32 [23-41]	0.89
Albuminuria categories				0.39
A1 (Normal to mildly increased)	27.8%	30%	27.2%	
A2 (Moderately increased)	31.2%	30%	31.6%	
A3 (Severely increased)	40.9%	40%	41.1%	
NA	275	58	217	
History of acute kidney injury	23.6%	21%	24.4%	0.08
NA	244	51	193	
Smoking status				0.17
Never-smoker	41.3%	38%	42%	
Current smoker	11.9%	13%	12%	
Former smoker	46.8%	49%	46%	
NA	23	5	18	
Hypertension	96.3%	96.6%	96.2%	0.64
NA	7	2	5	
Diabetes	43.2%	40%	44%	0.08
NA	7	2	5	
Dyslipidemia	73.6%	73%	73.9%	0.46
NA	14	3	11	
History of cardiovascular disease	53.3%	52%	53.6%	0.52
NA	42	4	38	
Serum albumin (g/l)	40.3 [38.0-43.0]	40.5 [37.8-43]	40.2 [38.0-43.0]	0.91
NA	489	94	395	
Hemoglobin (g/dl)	13 (1.65)	13.1 (1.64)	12.9 (1.65)	0.07
NA	23	4	19	
High-sensitivity C-reactive protein (mg/l)	2 [1-6]	2 [1-6]	3 (1, 6)	0.92
NA	356	0	356	
Body mass index (kg/m²)	27.8 [24.6-31.8]	28 [25.2-31.4]	27.8 [24.5-31.9]	0.56
NA	65	8	57	
Proton pump inhibitor	32.8%	31%	33.3%	0.25
NA	7	0	7	

Total number of medications	8 [5-10]	8 [5-10]	8 (5, 10)	0.36
NA	9	2	7	

^a Median [interquartile range] or mean (standard deviation); %

^b Wilcoxon rank sum test; Pearson's Chi-squared test

Table S2. Different types of PPI and their affinity to OAT1/3

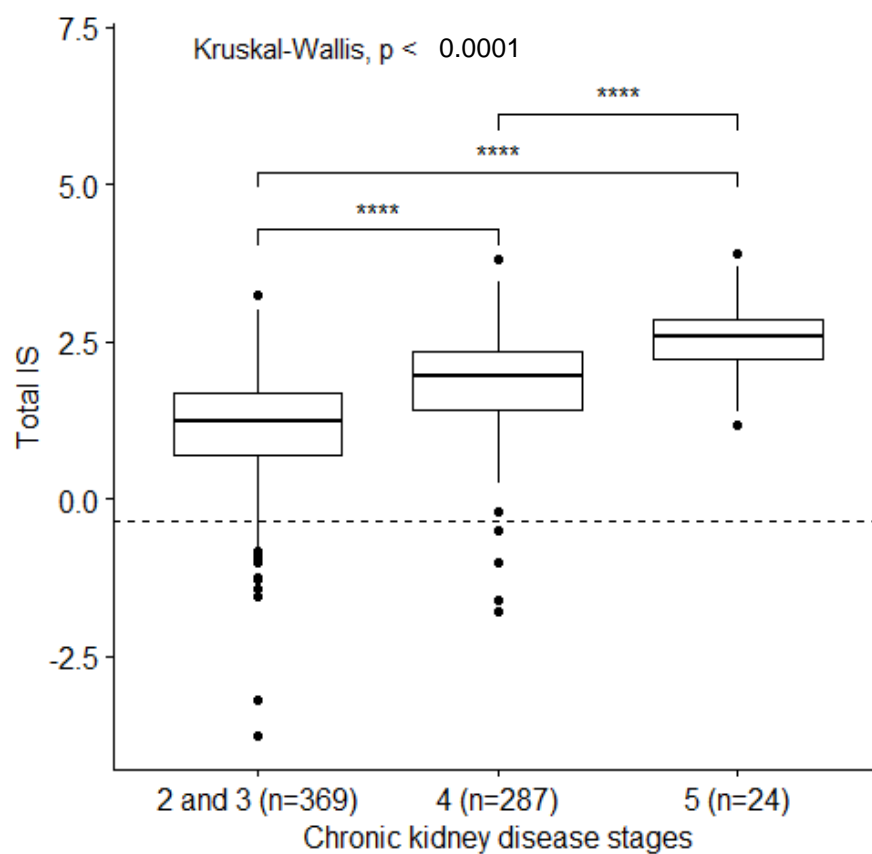
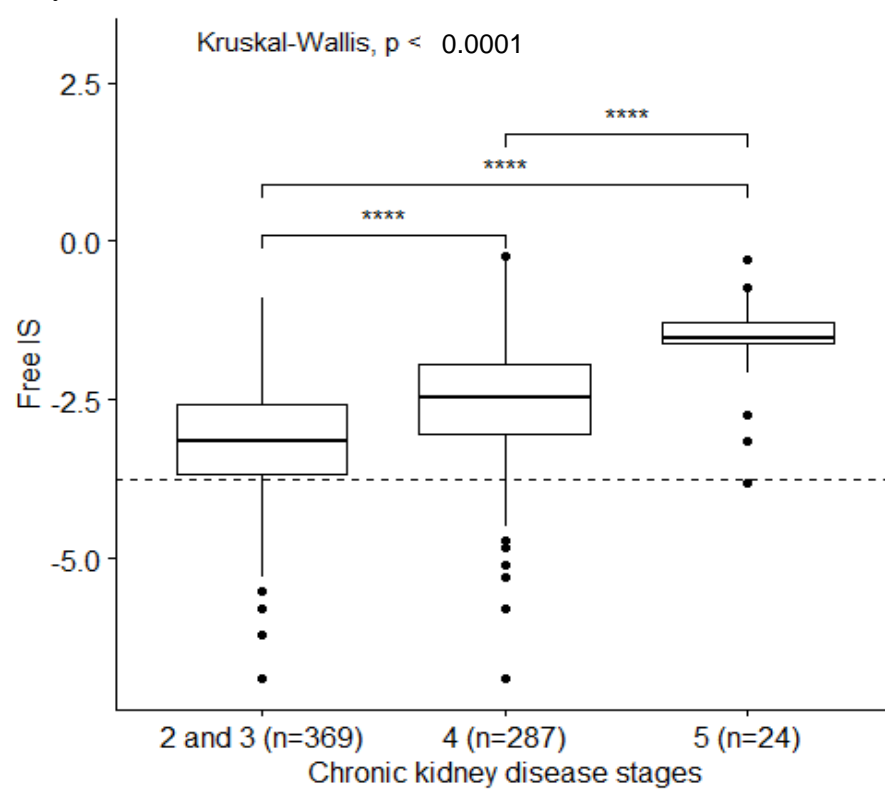
Types of PPI	Plasma Protein Binding [22]	Affinity to OAT1	Affinity to OAT3
Omeprazole	95-96%	Strongly high affinity [21, 23]	High affinity [21-24]
Esomeprazole	97%	Limited data [23]	High affinity [22-24]
Pantoprazole	92%	Moderate affinity [21]	High affinity [21,22,24]
Lansoprazole	97%	Strongly high affinity [21]	High affinity [21-26]
Rabeprazole	97%	Limited data [23]	High affinity [22,23]

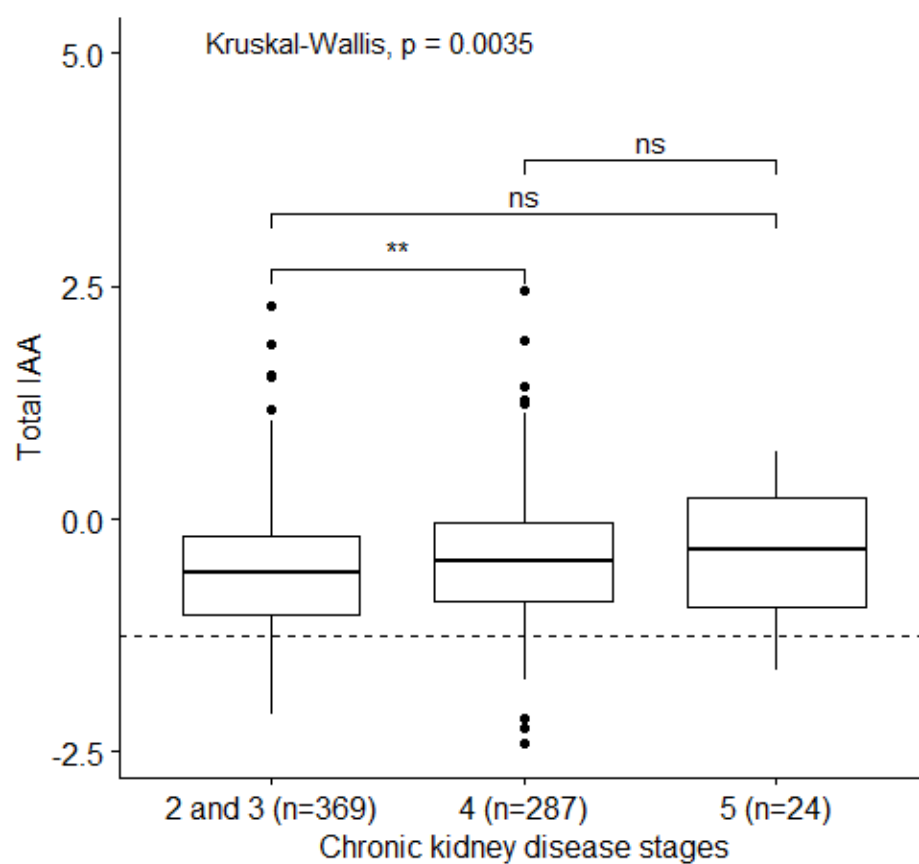
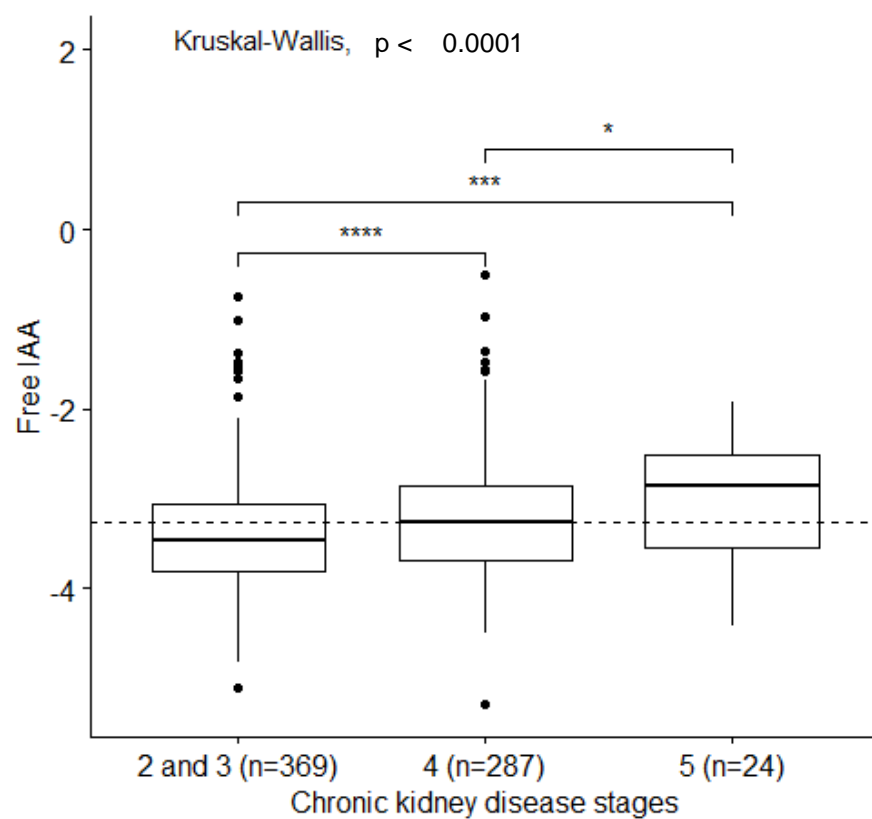
^a n (%)

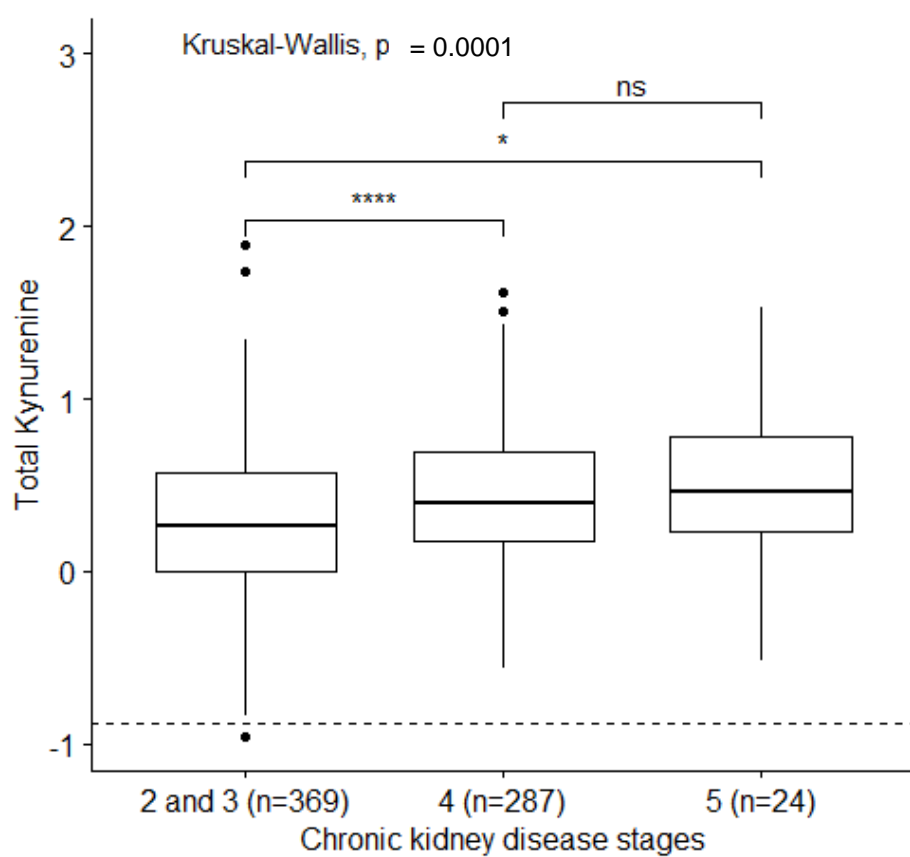
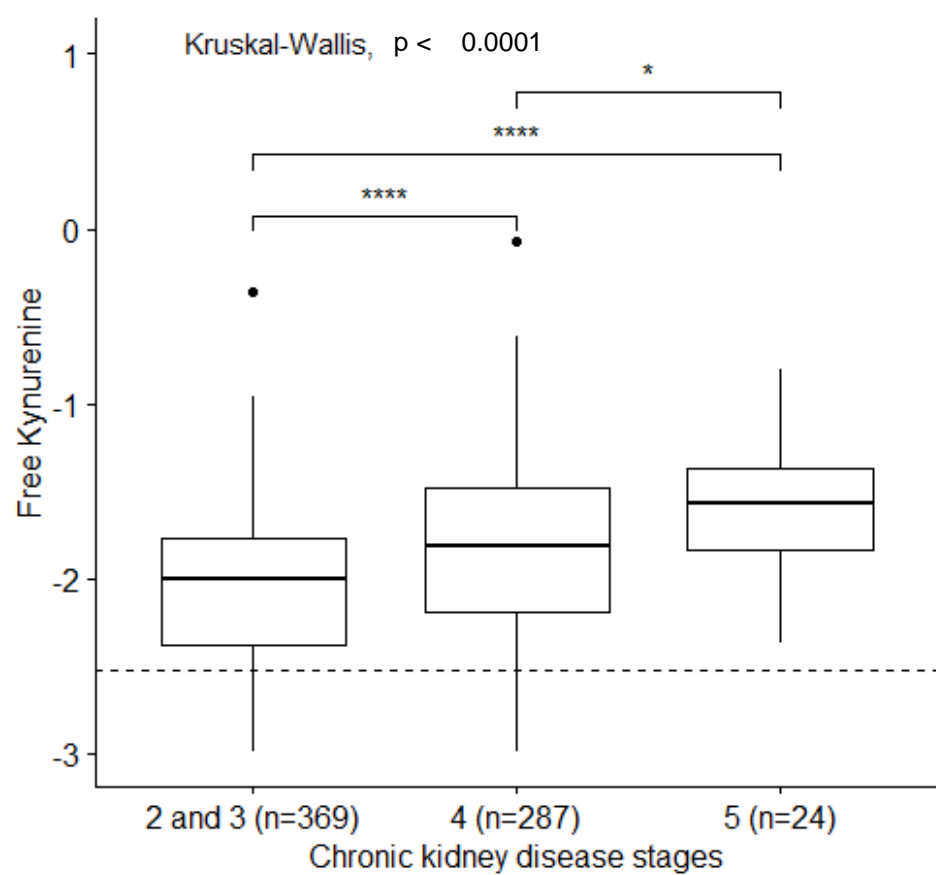
Table S3. Affinity of uremic toxins to OAT1/3

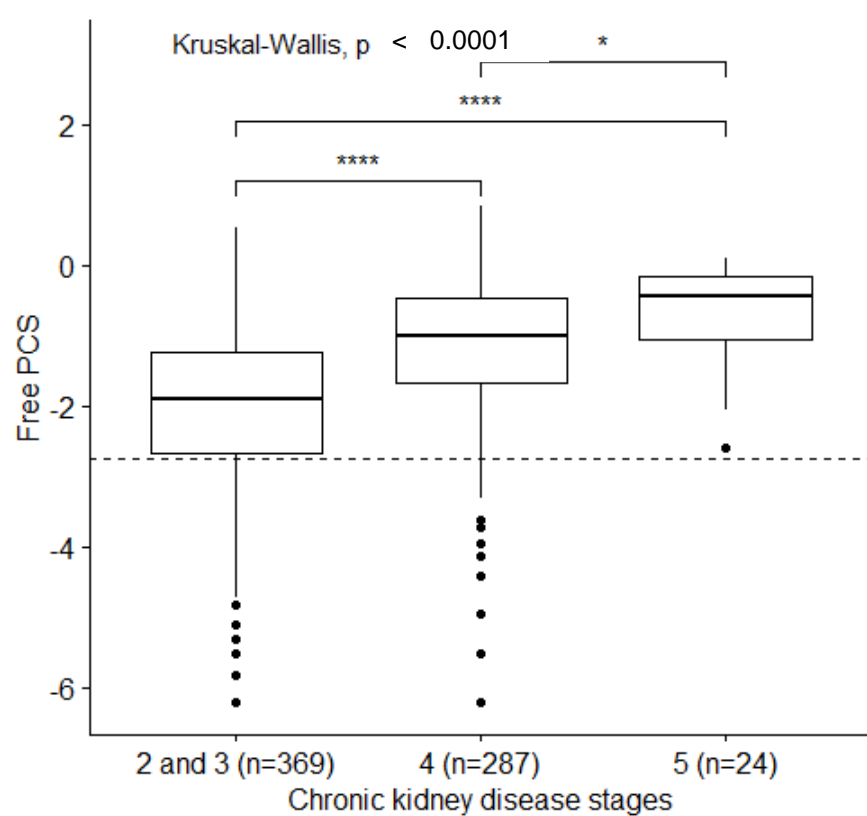
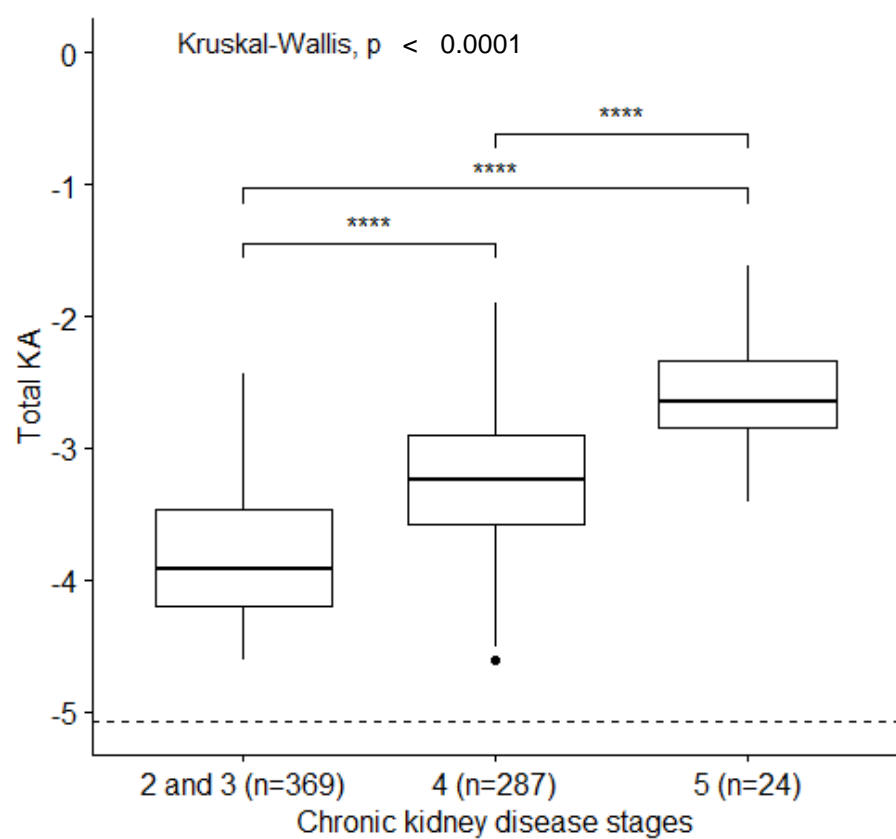
Uremic toxin	Affinity to OAT1/3 [10]	Gut-derived [2]
Indoxyl sulfate	High affinity for both	yes
Indole-3-acetic acid	Moderate affinity for both	yes
Kynurenine	High affinity for both	yes
Kynurenic acid	Moderate affinity for both	yes
p-cresyl sulfate	High affinity for both	yes
p-cresyl glucuronide	No affinity	yes
Hippuric acid	High affinity for both	yes
Phenylacetylglutamine	No affinity	yes
CMPF	More studies are needed to confirm, affinity rather for OAT3)	no
TMAO	Not confirmed yet	yes
Urée	No affinity	no

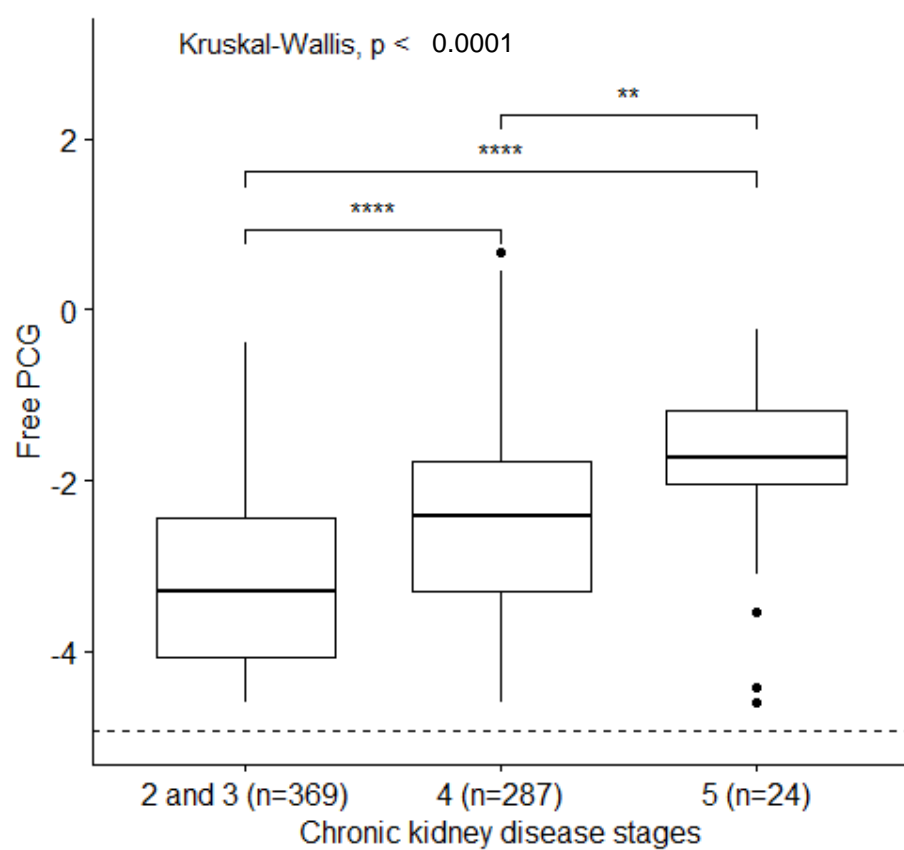
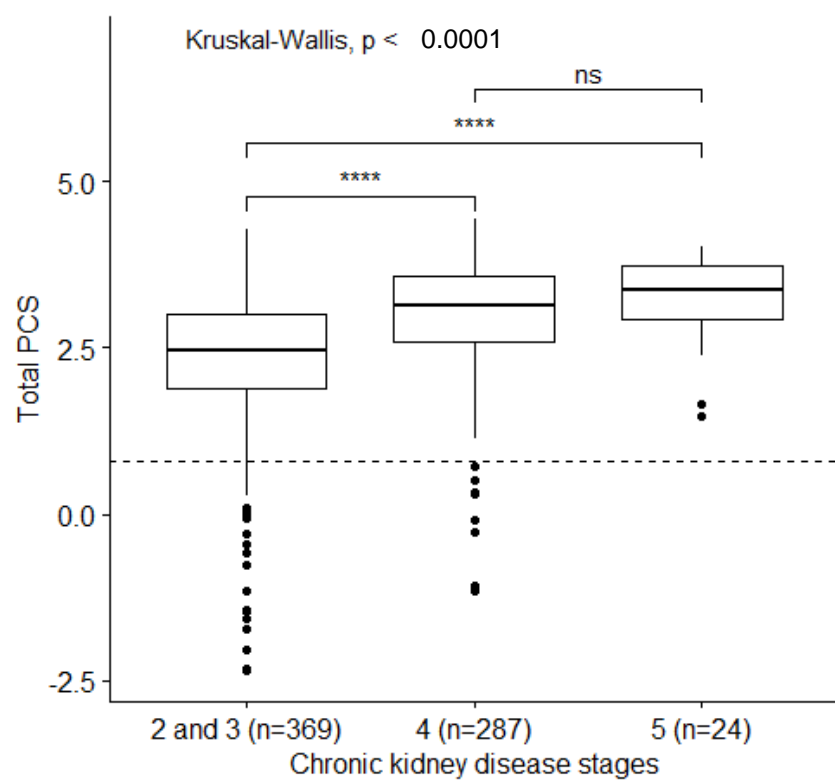
Figure S1. Distribution of log normalized uremic toxins according to the stages of chronic kidney disease.

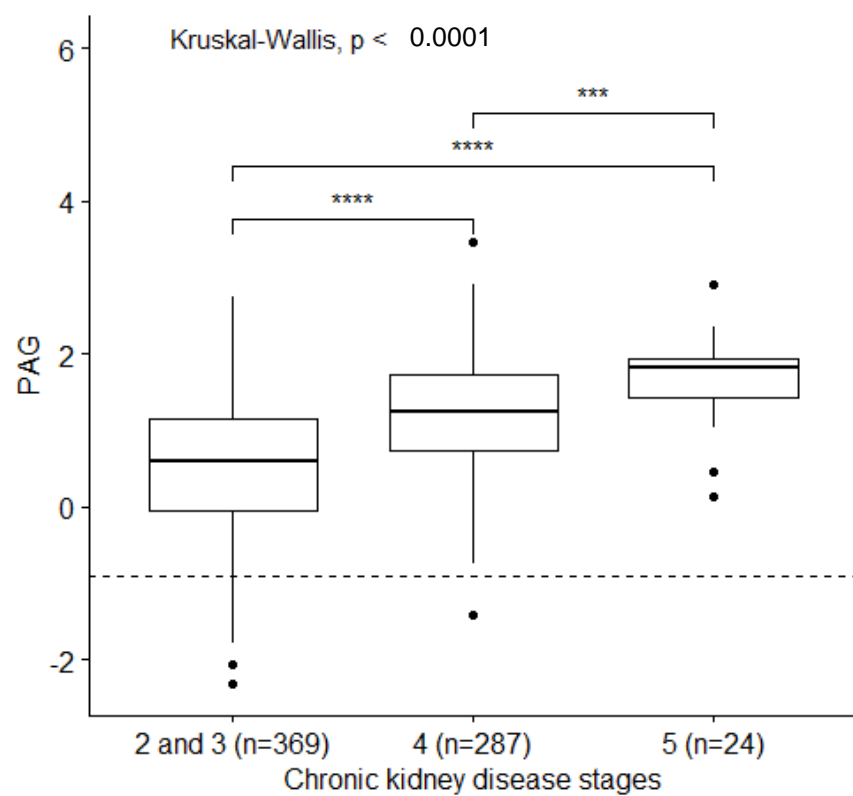
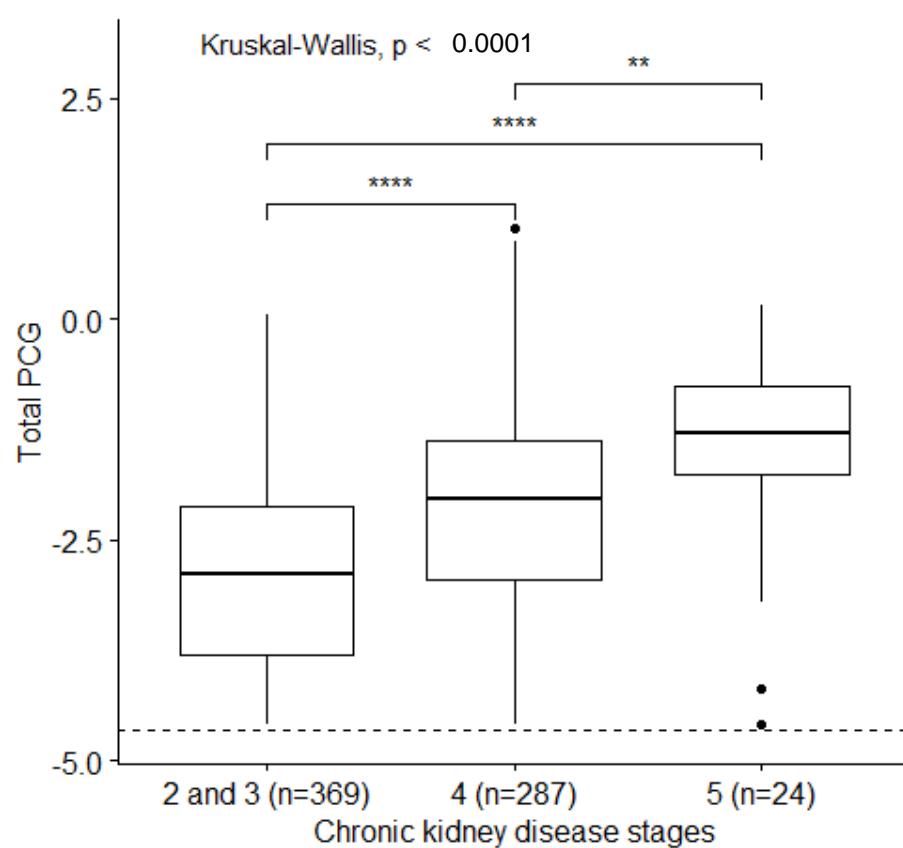


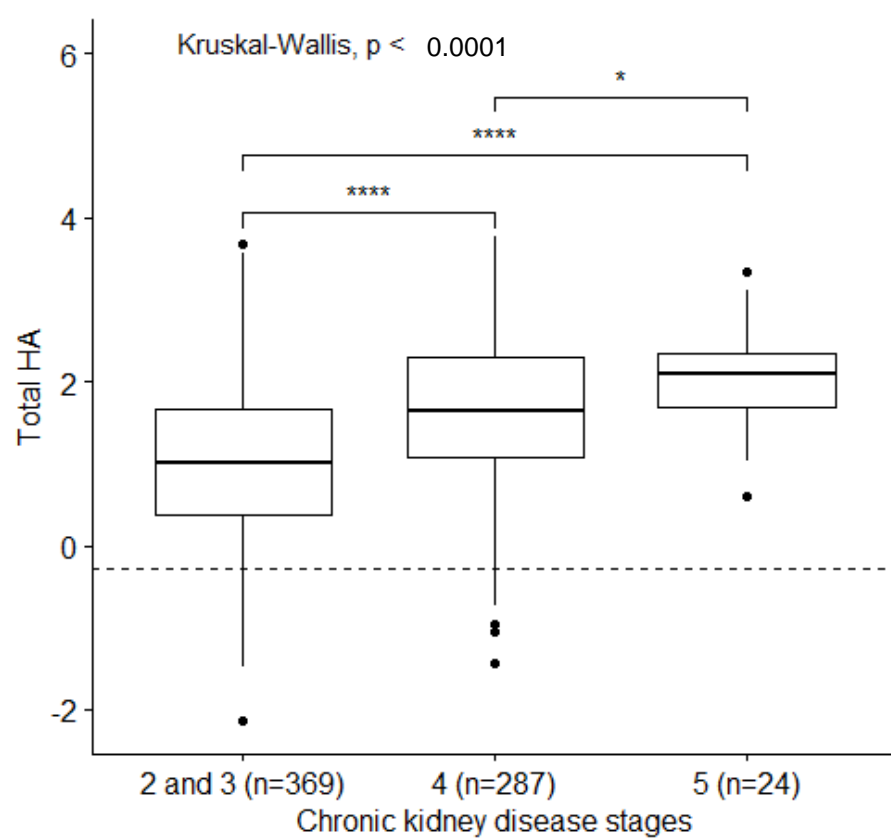
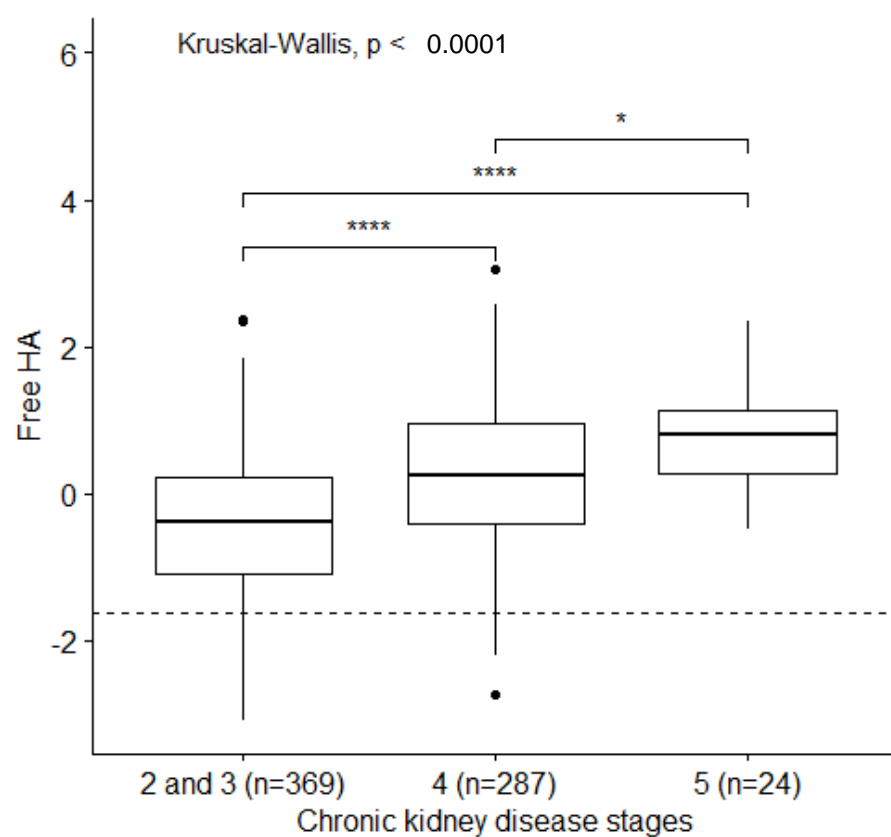


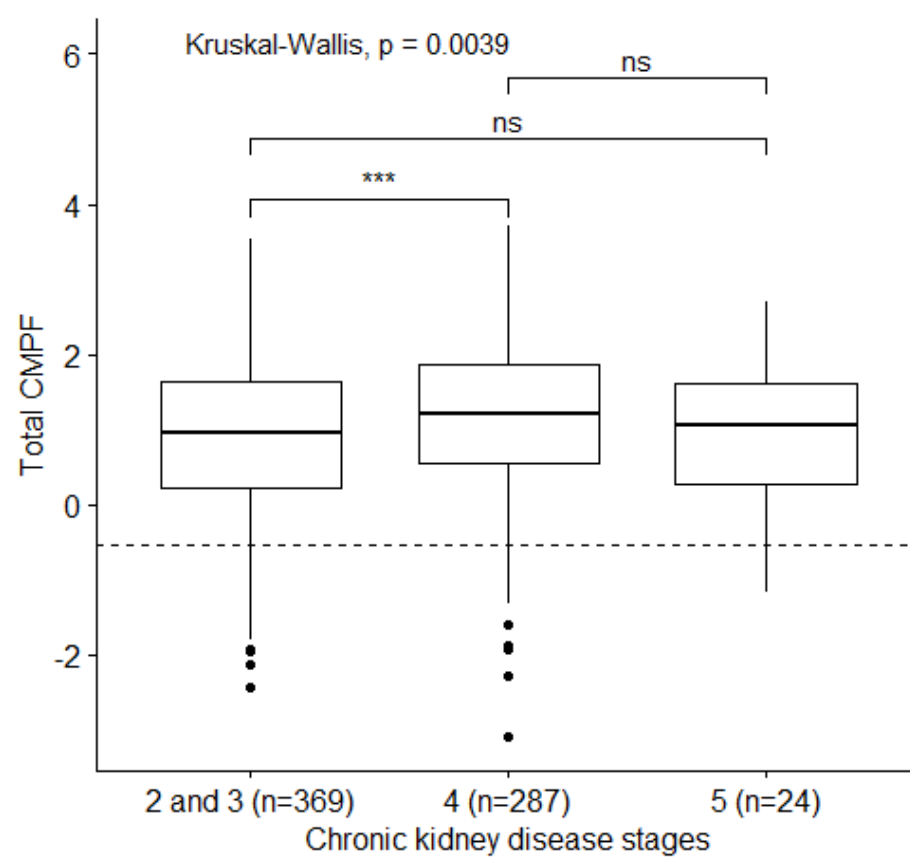
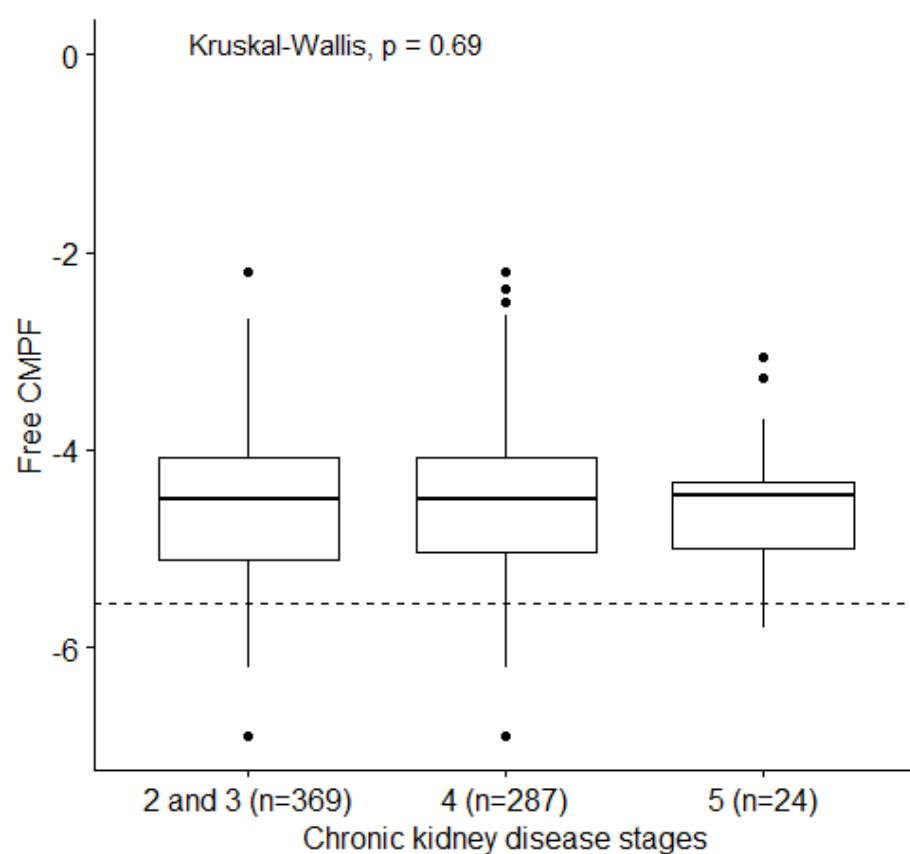


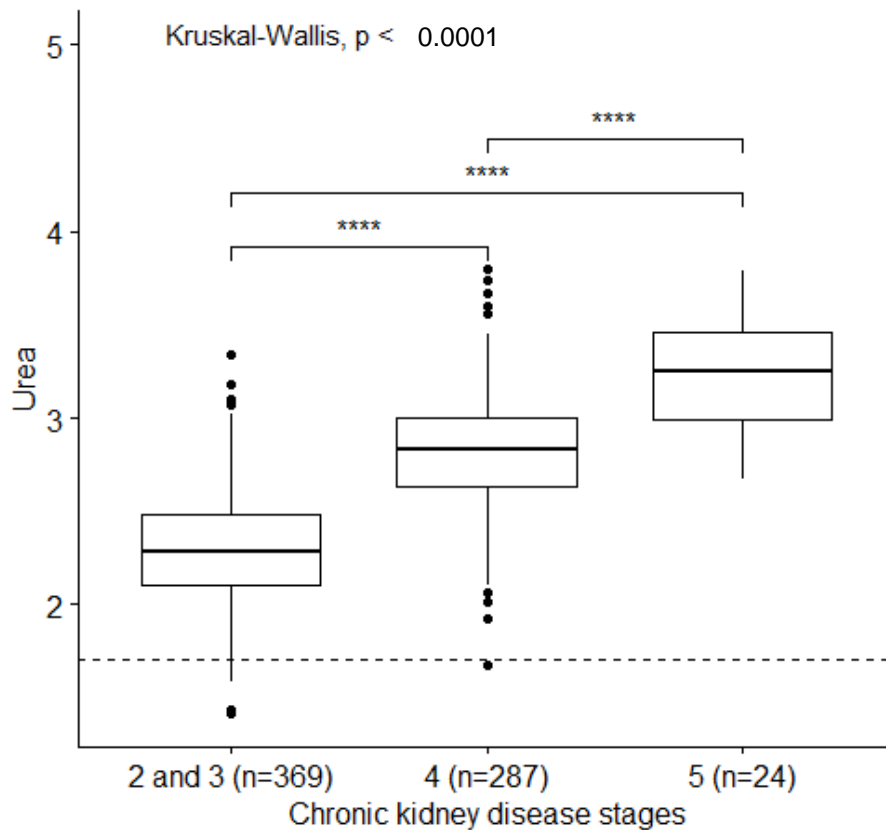
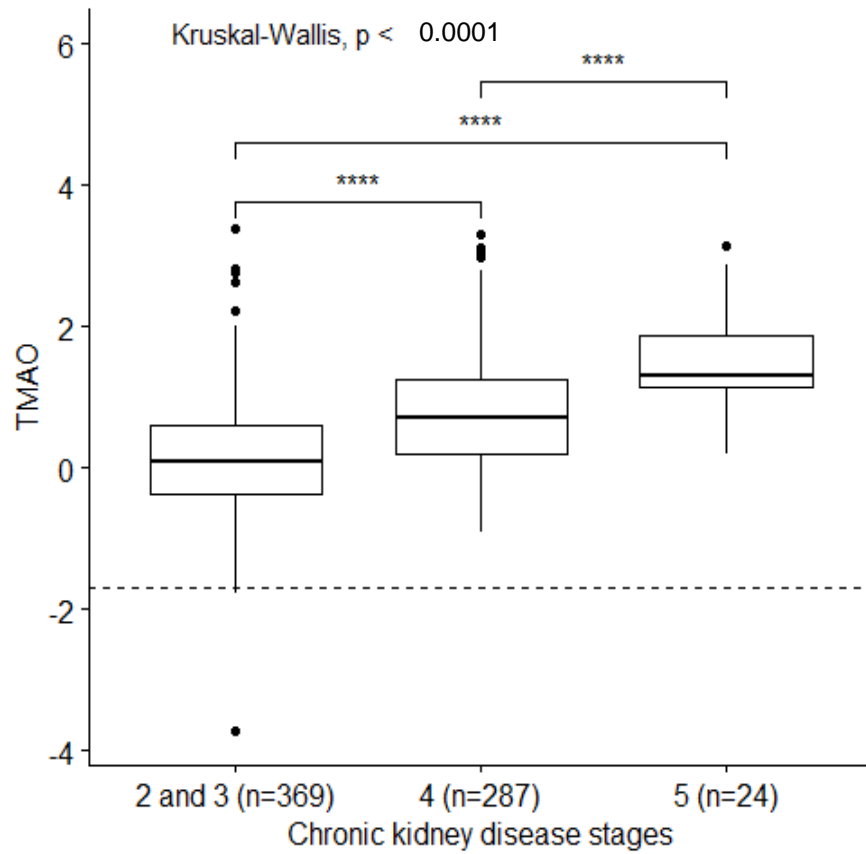










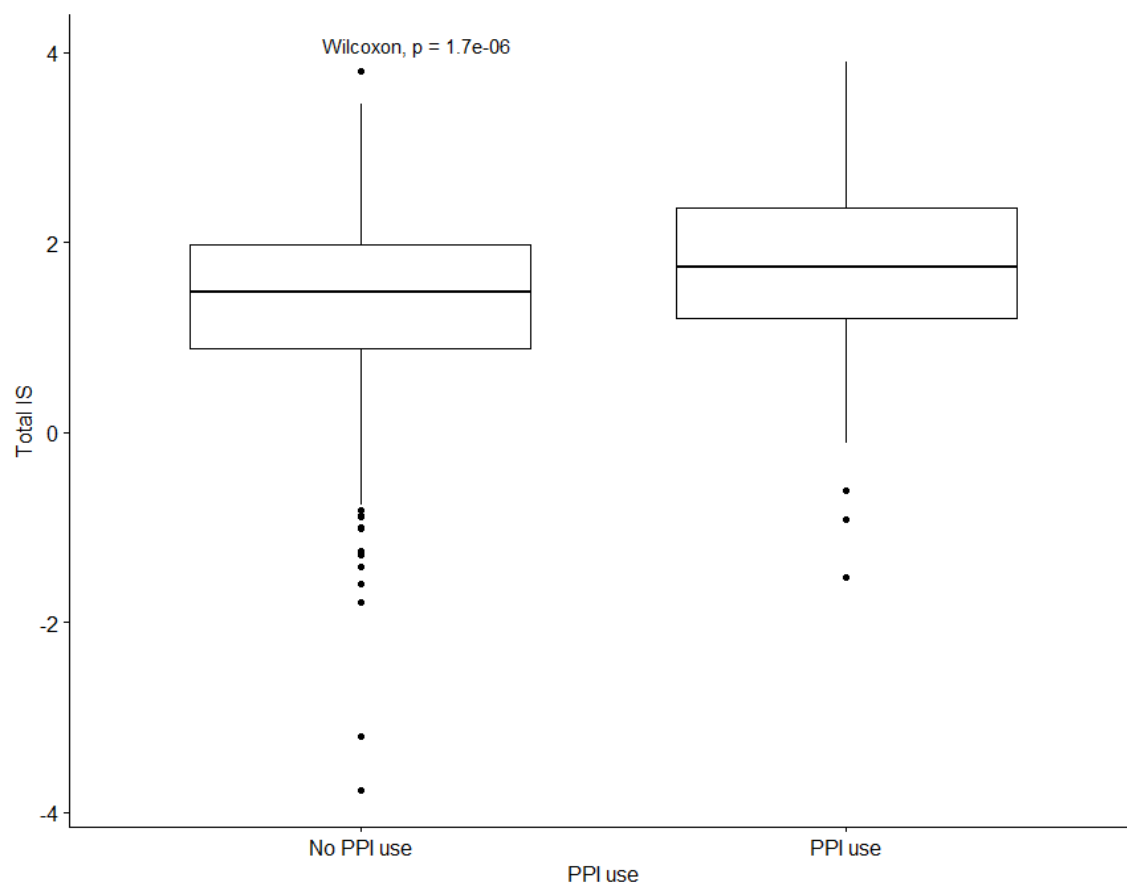
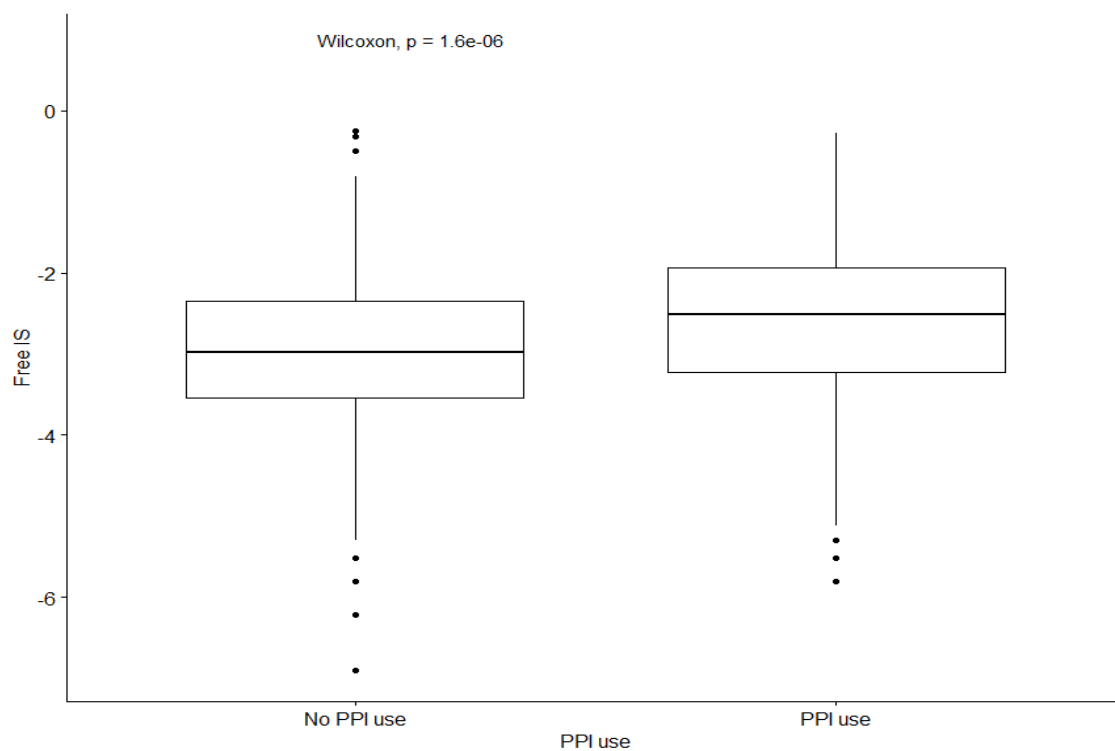


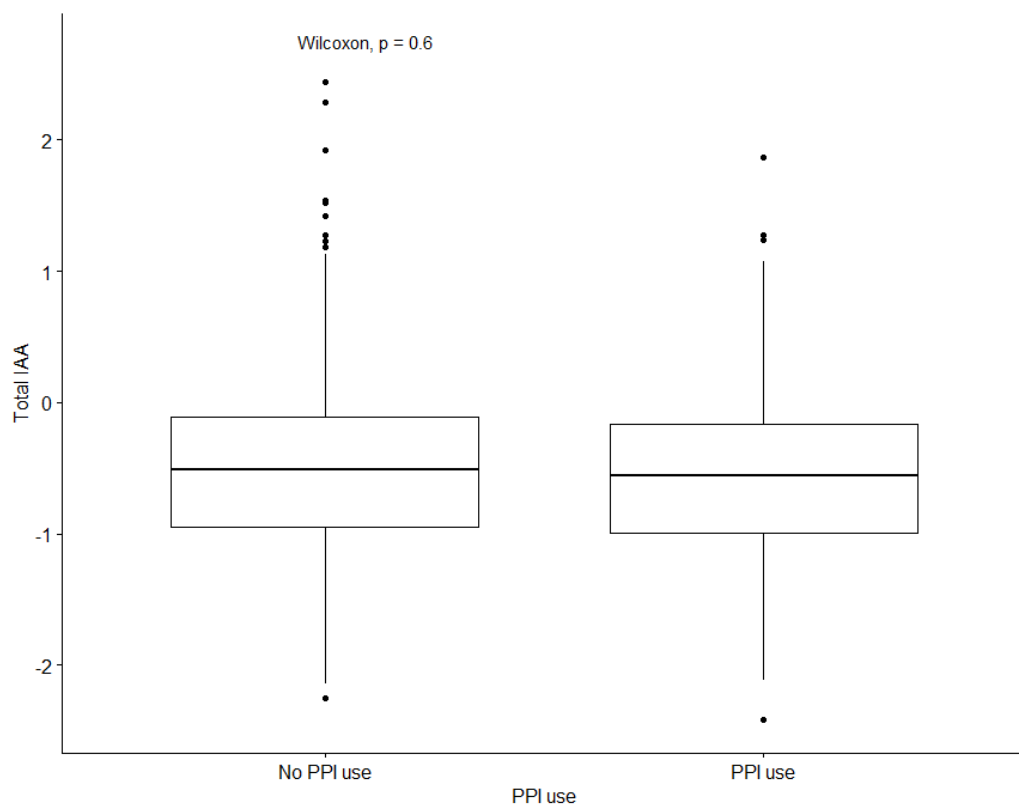
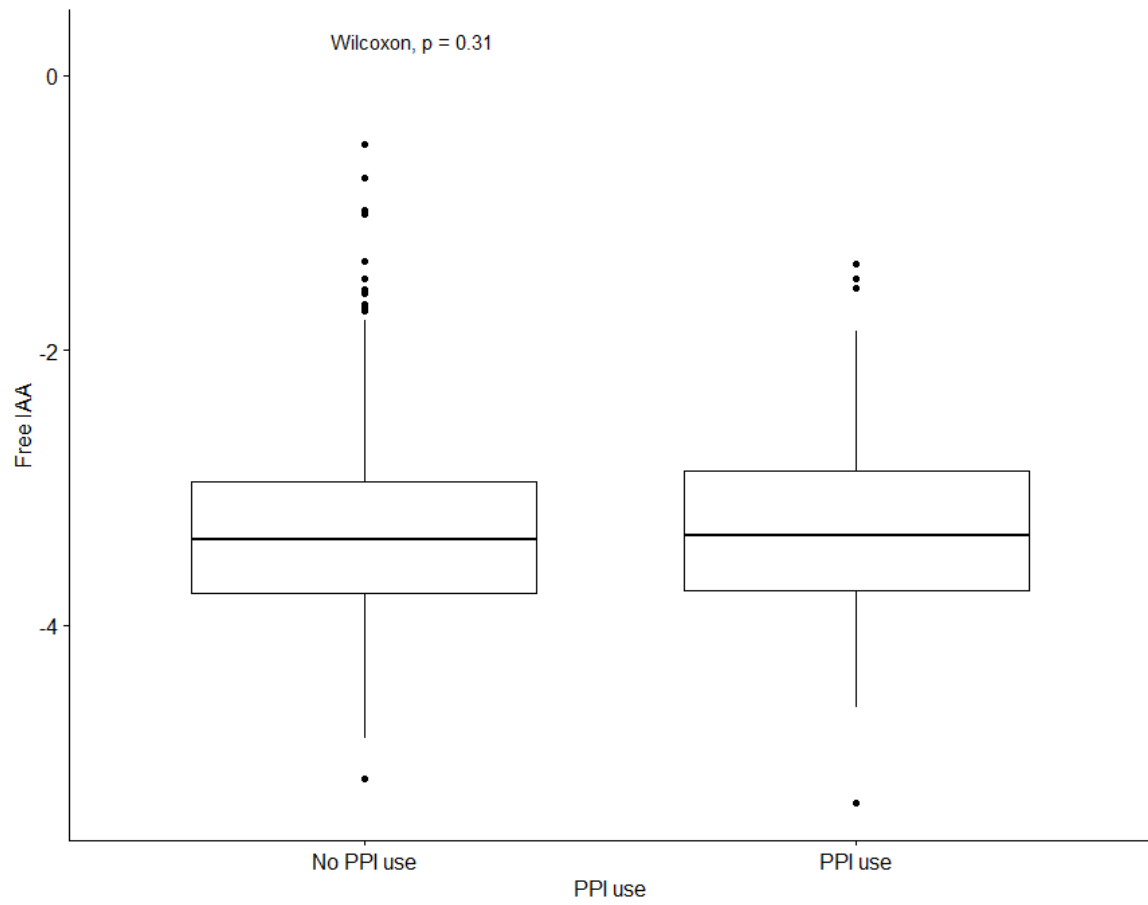
The dotted line indicates the reference value for healthy subjects.

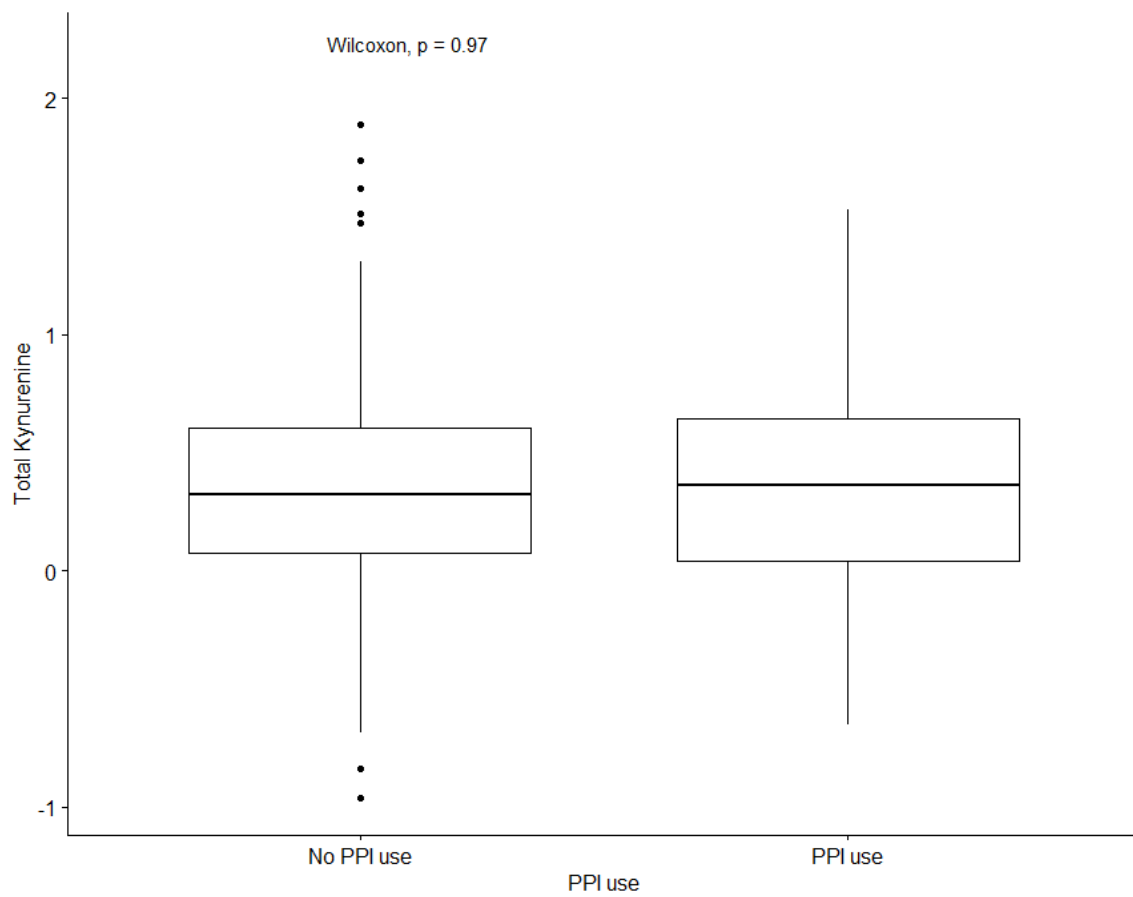
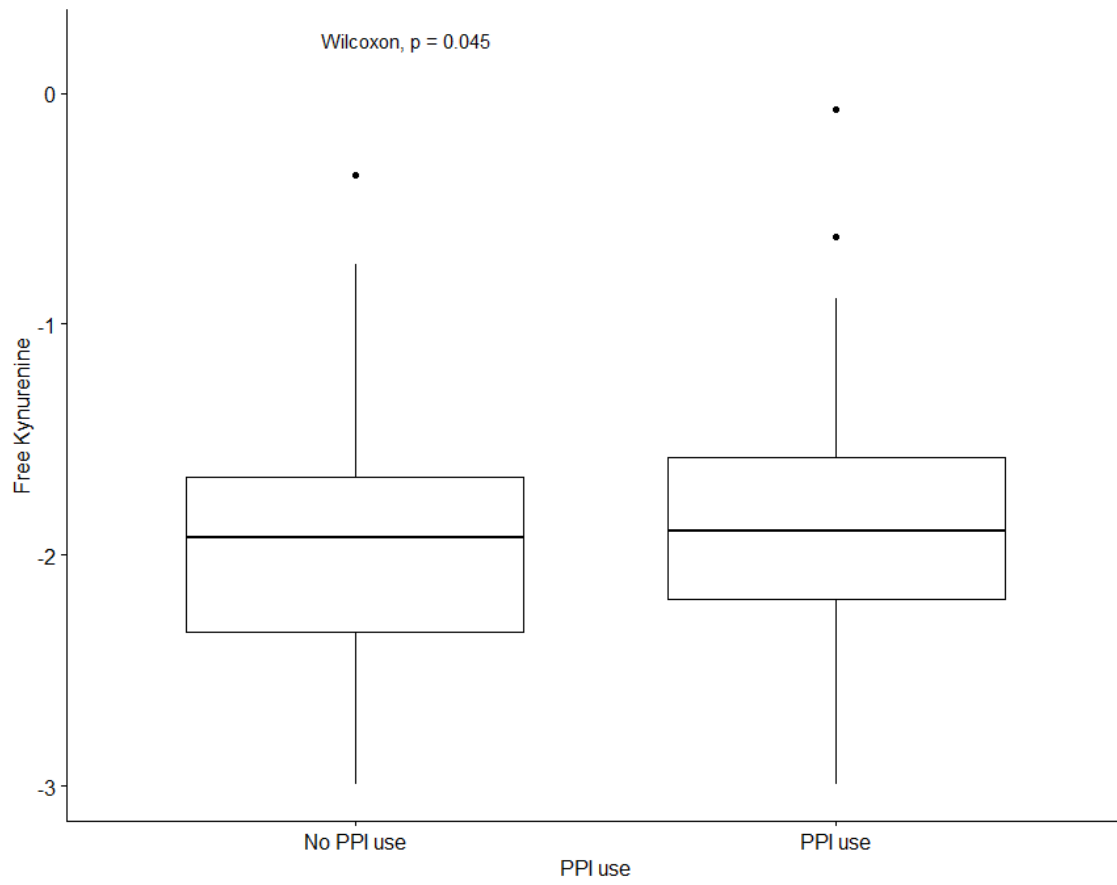
P -values : ns : non significant ; * : <0.05 ; ** : <0.01 ; *** : <0.001 ; **** : <0.0001 .

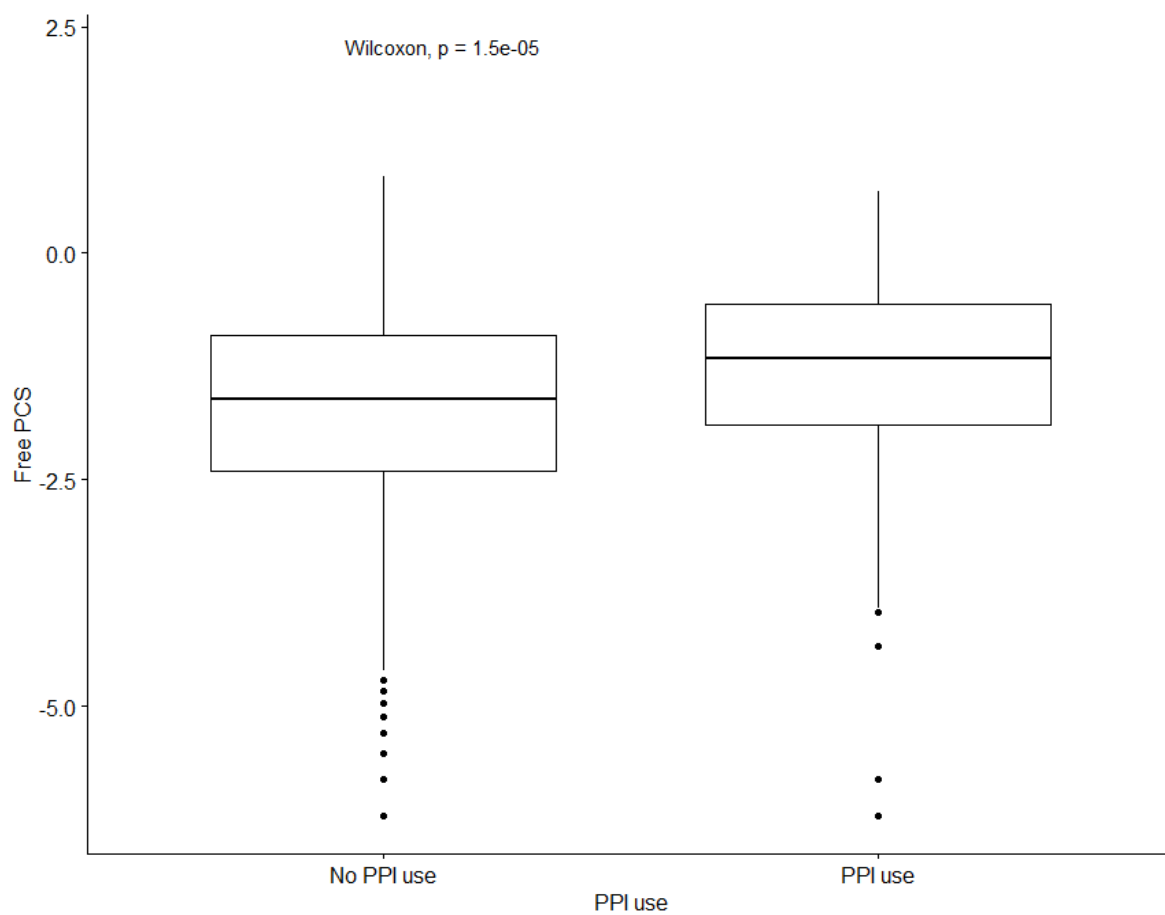
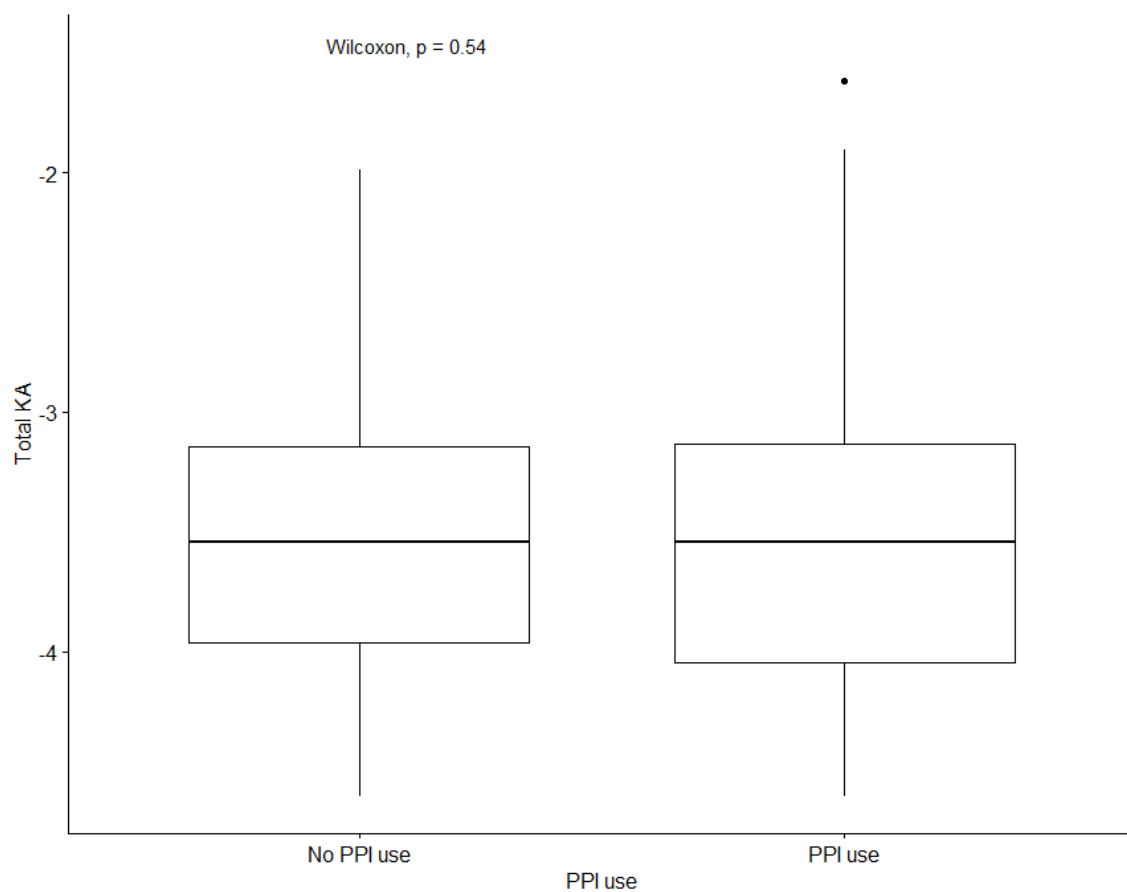
Abbreviations : IS, indoxyl sulfate ; IAA, indole-3-acetic acid ; KA, kynurenic acid ; PCS, p-cresyl sulfate ; PCG, p-cresyl glucuronide ; PAG, phenylacetylglutamine ; HA, hippuric acid ; CMPF, 3-carboxy-4-ethyl-5-propyl-2-furanpropanoic acid ; TMAO, trimethylamine N-oxide.

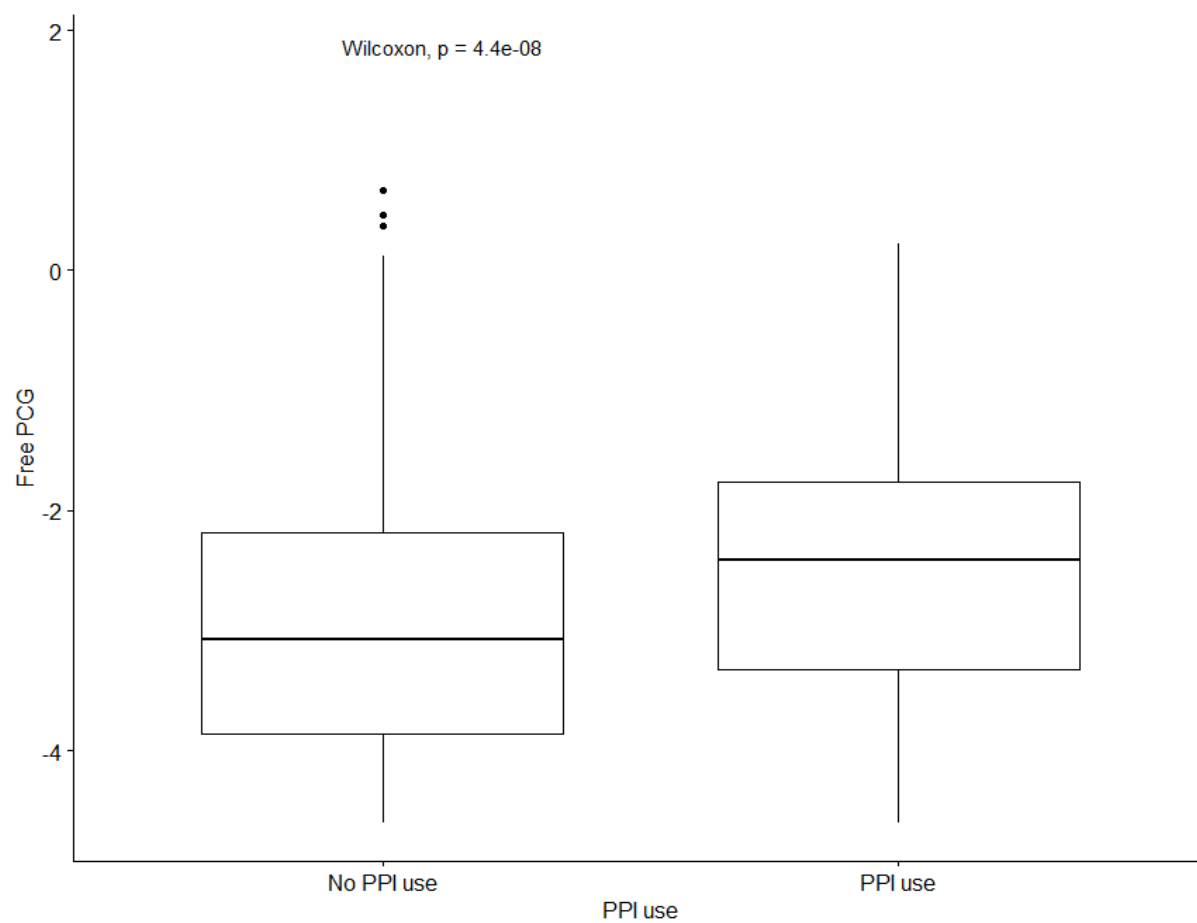
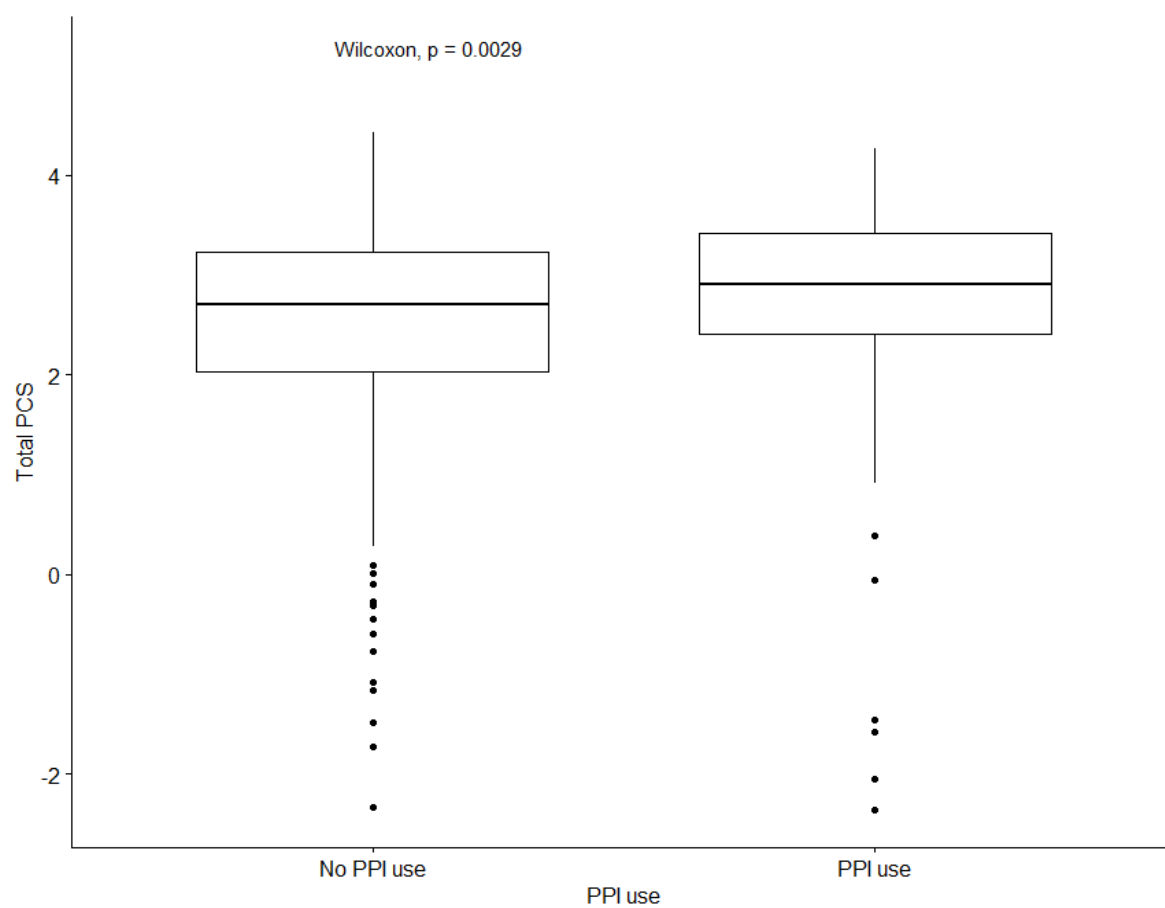
Figure S2. Distribution of log normalized uremic toxins according to proton-pump inhibitor use.

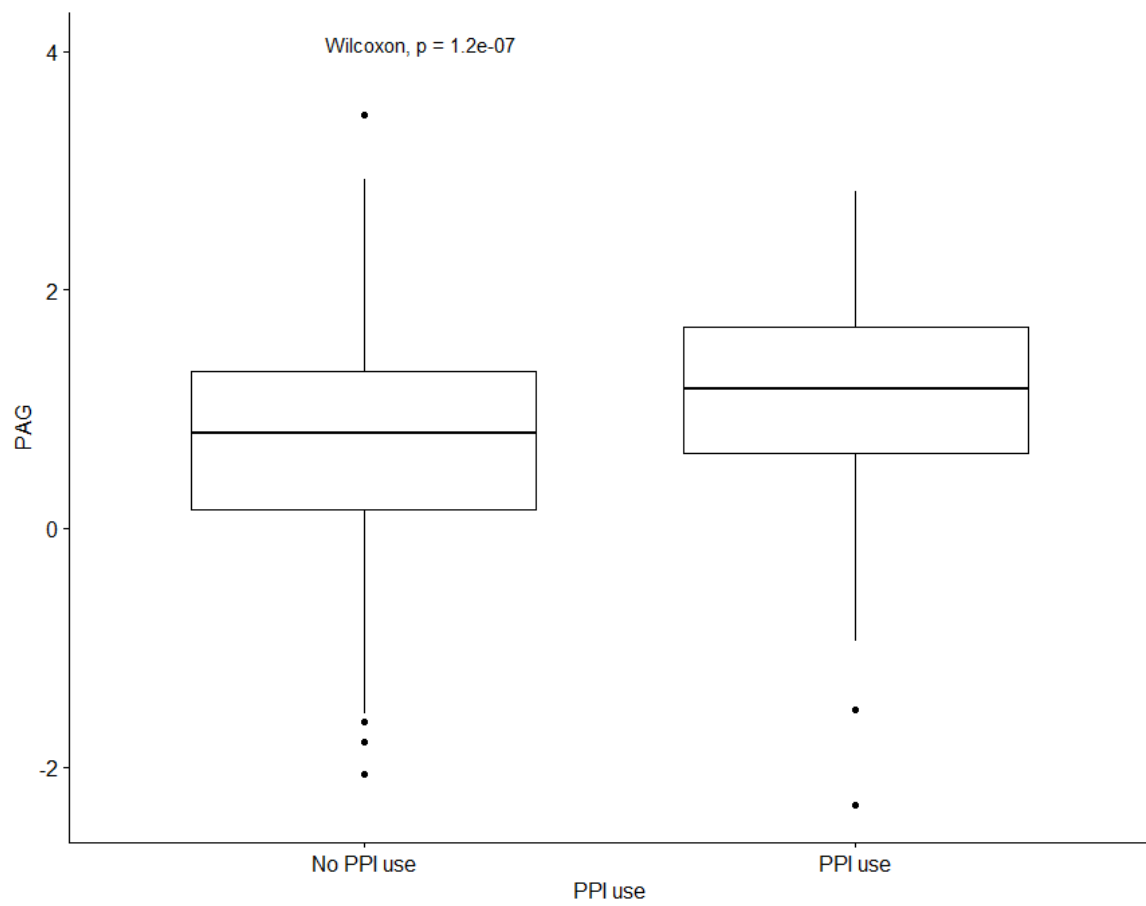
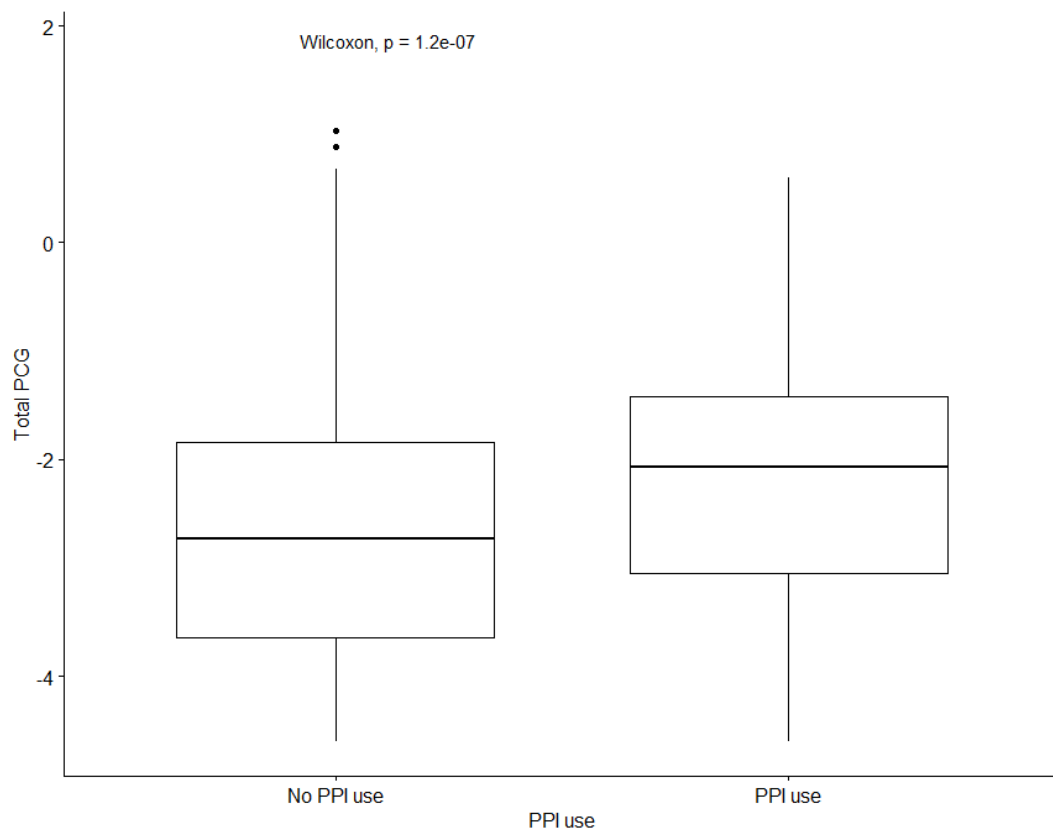


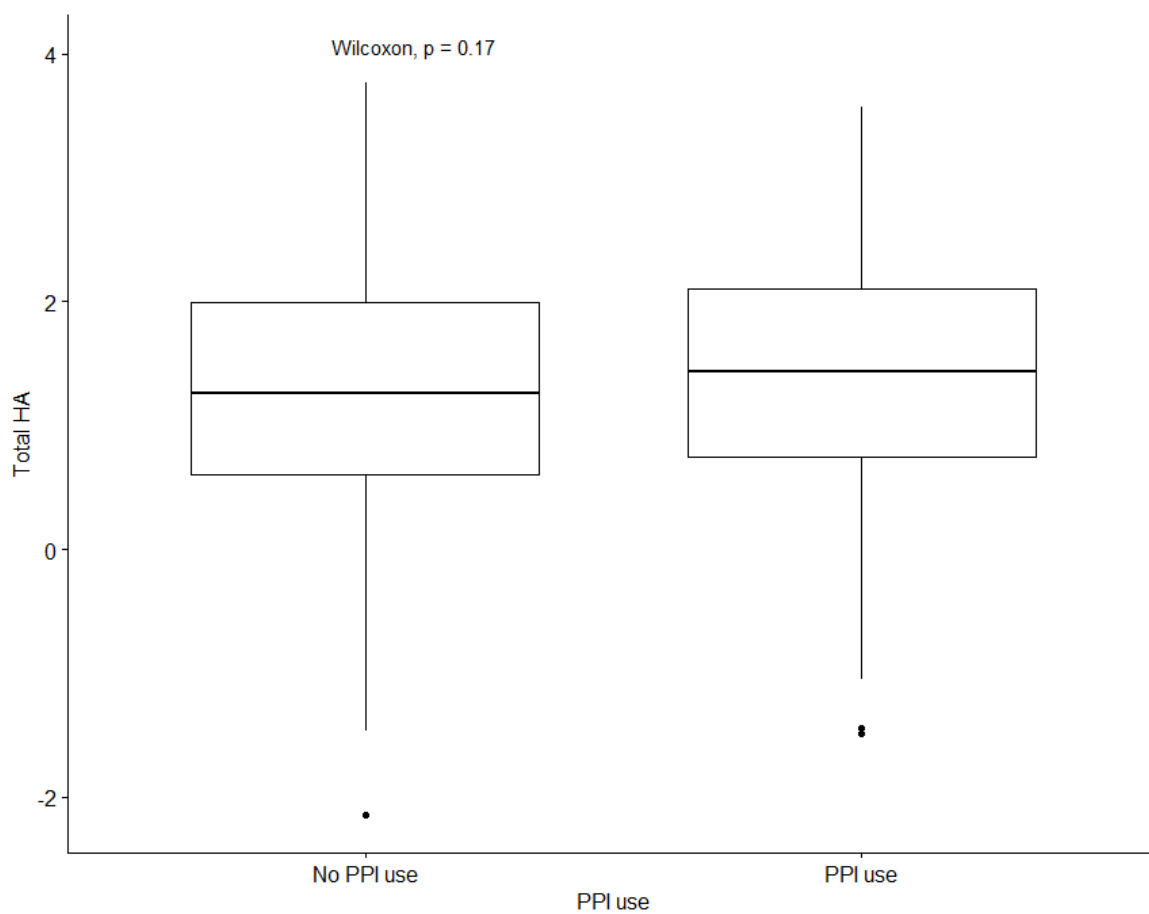
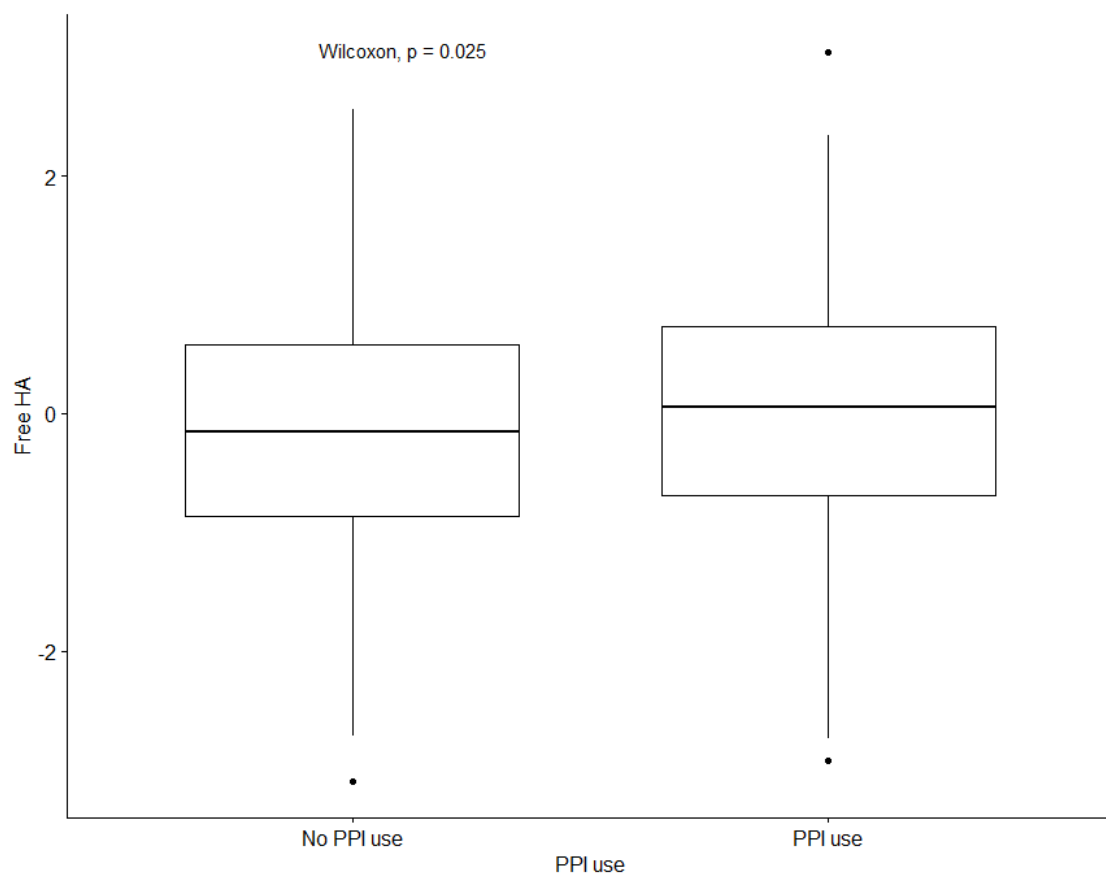


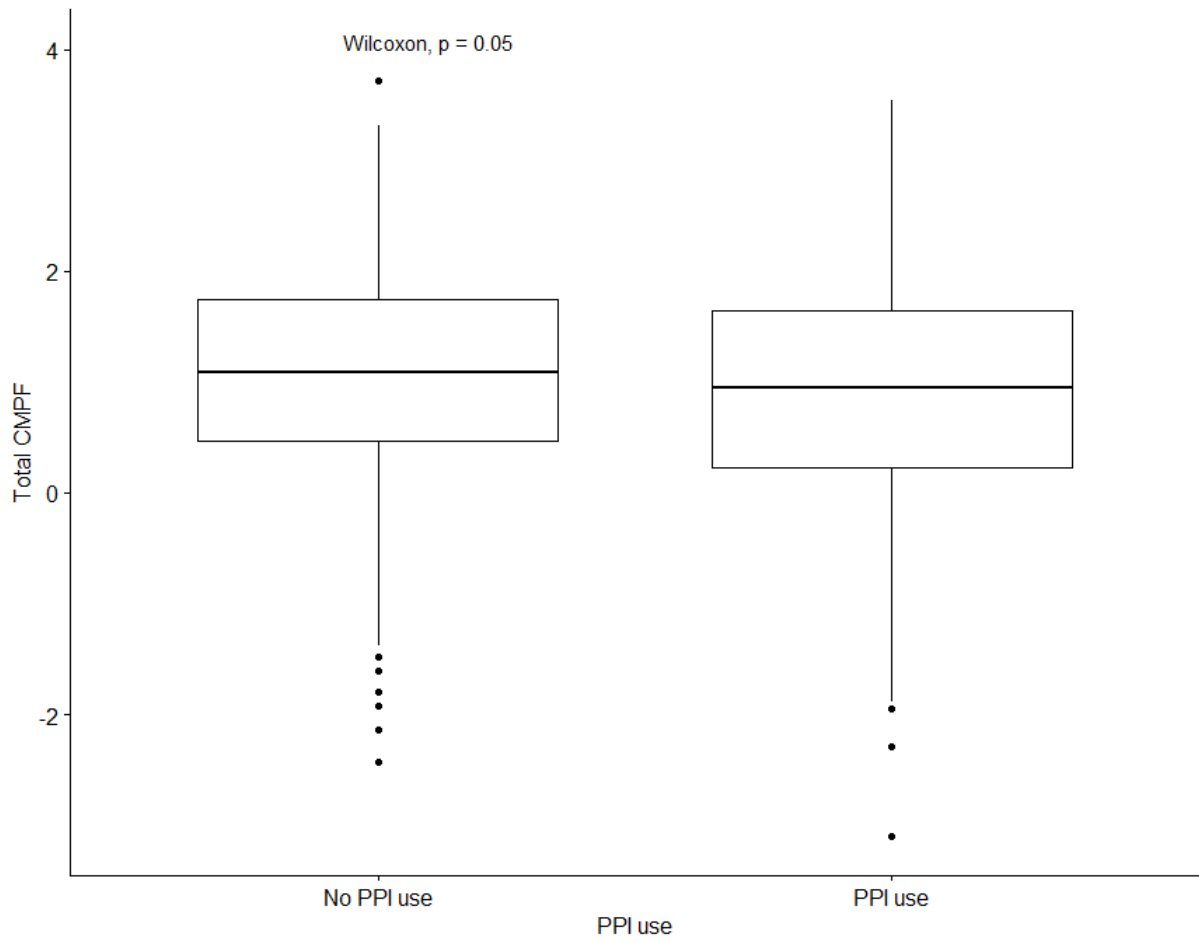
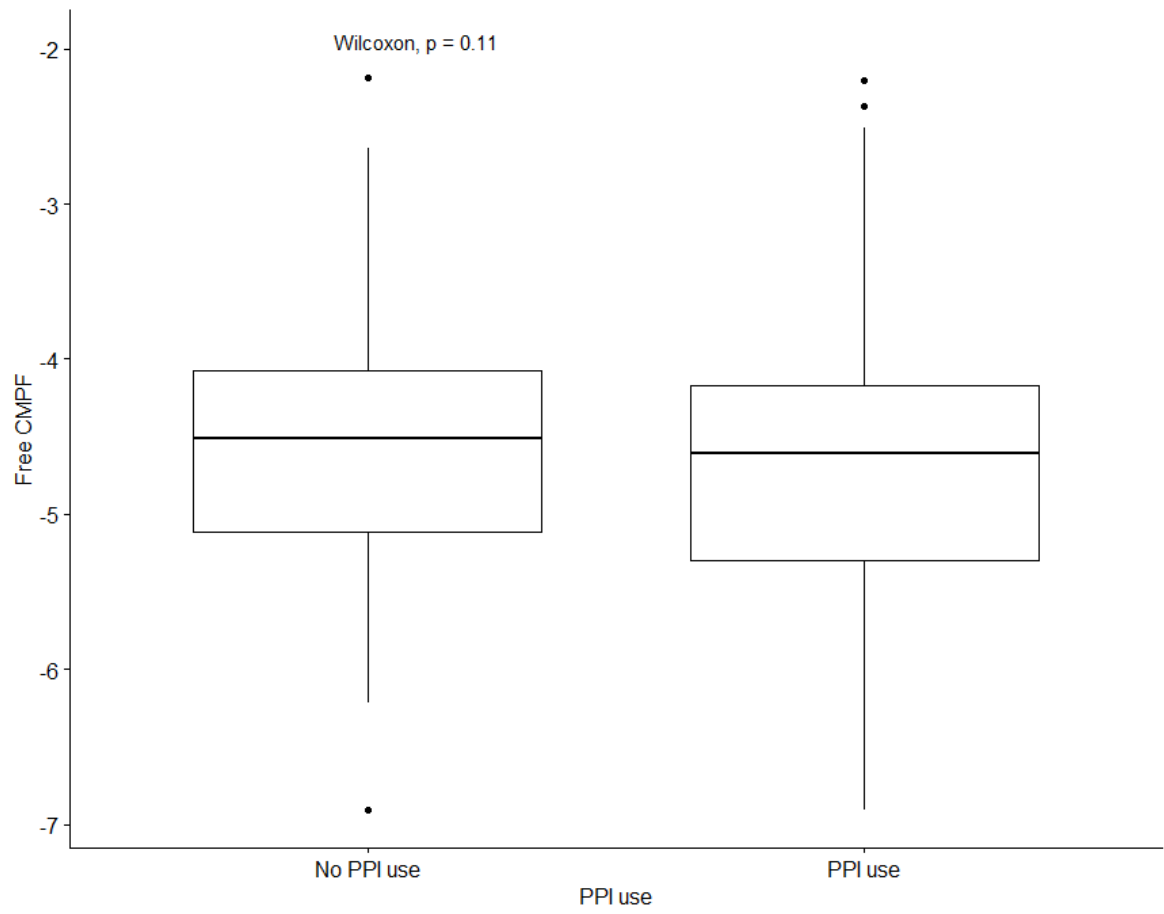


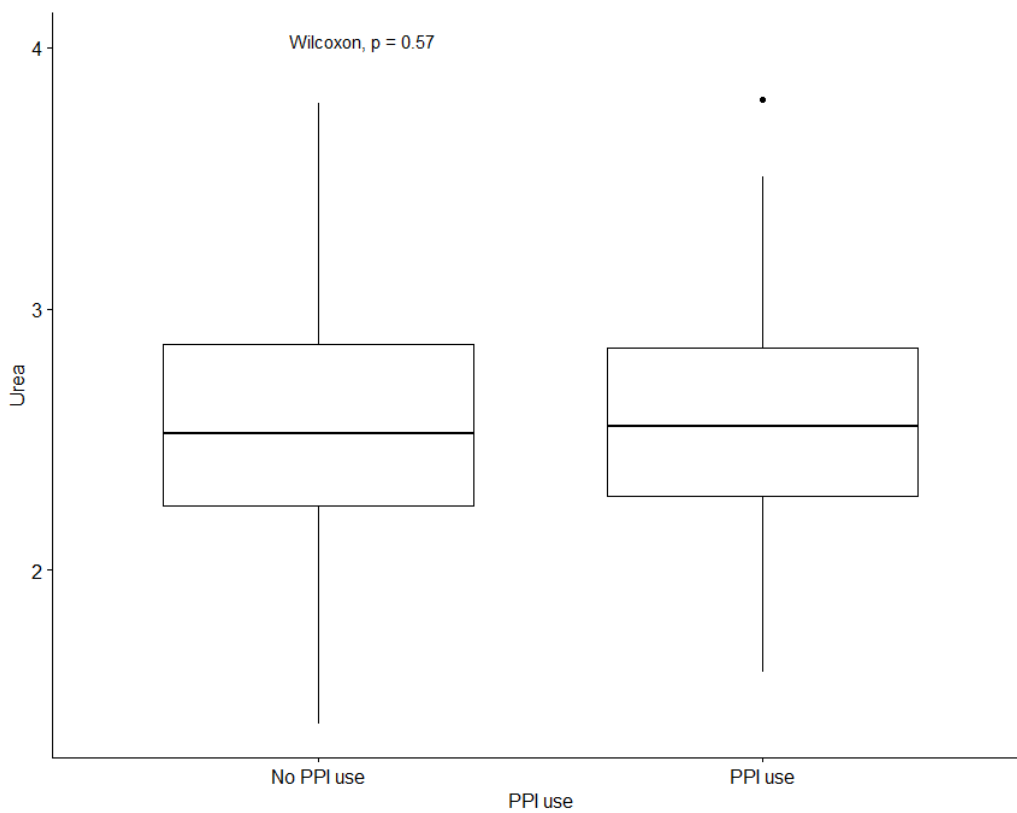
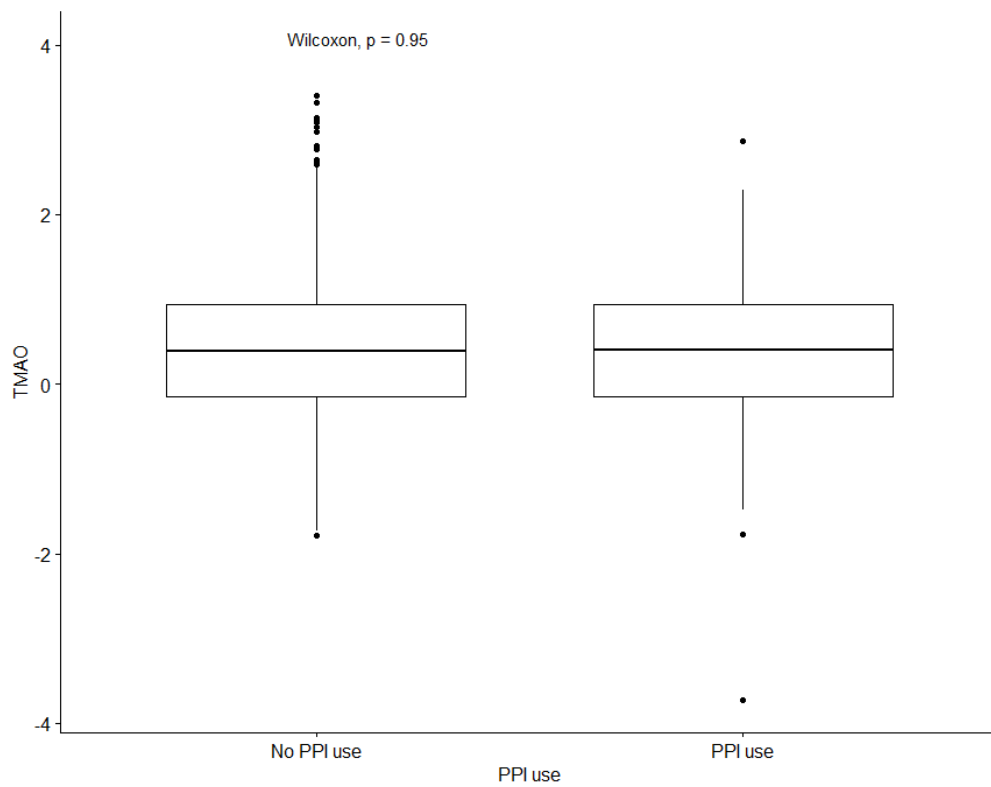












Abbreviations : PPI : proton pump inhibitor ; IS, indoxyl sulfate ; IAA, indole-3-acetic acid ; KA, kynurenic acid ; PCS, p-cresyl sulfate ; PCG, p-cresyl glucuronide ; PAG, phenylacetylglutamine ; HA, hippuric acid ; CMPF, 3-carboxy-4-ethyl-5-propyl-2-furanpropanoic acid ; TMAO, trimethylamine N-oxide.

List of biological resources centers

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