SUPPLEMENTARY FIGURE LEGENDS

Supplementary Figure 1. UACR is not strongly associated with 6MWD, SGRQ, or radiographic measures of COPD. (A-E) UACR (log2 mg/g) and association with 6MWD **(A)**, SGRQ **(B)**, %LAA < -950 HU **(C)**, PRM^{EMPH} **(D)**, and PRM^{FSAD} **(E)**, tested with unadjusted linear regression models (never smokers n=56-63, smokers without airflow obstruction n=94-107, mild/moderate COPD n=123-135, severe COPD n=148-165). Linear associations (**A-E**) were implemented with unadjusted linear regression models.

Supplementary Figure 2. U-mtDNA levels do not associate with FEV_1 % predicted in the SPIROMICS cohort. U-mtDNA (log2 copies mtDNA/g creatinine) and association with post-bronchodilator FEV_1 % predicted in each subgroup**:** never smokers (n=62; red), smokers without airflow obstruction ("smokers", n=107; green), participants with mild/moderate COPD (n=139; blue), and severe COPD (n=166; purple). Linear associations were implemented with unadjusted linear regression models.

Supplementary Figure 3. U-mtDNA levels are associated with UACR. U-mtDNA (log2 copies mtDNA/g creatinine) and association with UACR (log 2 mg/g), tested with unadjusted linear regression models (never smokers n=63, smokers without airflow obstruction n=107, mild/moderate COPD n=136, severe COPD n=166). Linear association was implemented with unadjusted linear regression models.

Supplementary Figure 4. Unadjusted u-mtDNA is not associated with radiographic measures of emphysema. (A-C) U-mtDNA (log 2 copies mtDNA/g creatinine) and association with %LAA < -950 HU **(A)**, PRM^{EMPH} **(B)**, and PRM^{FSAD} **(C)**, tested with unadjusted linear regression models (never-smokers n=56-63, smokers without airflow obstruction n=94-107, mild/moderate COPD n=126-138, severe COPD n=148-165).

Supplementary Figure 5. UACR does not differ between males and females. UACR (log 2 mg/g) levels in males (n=252) compared to females (n=220) in all participants. Data is presented as median with box indicating upper and lower quartiles, whiskers indicating extrema, and with p-values calculated by non-parametric Kruskal-Wallis test.

Supplementary Table 1. Baseline characteristics of the urine mtDNA study compared to the overall SPIROMICS cohort

Parameter	Urine mtDNA Study (n=475)	SPIROMICS Cohort (n=2491)	*P-value**
Age, median [IQR]	65.0 [55.0-70.0]	64.0 [57.0-70.0]	0.656
Male N (%)	253 (53.3)	1319 (53.0)	0.940
Body Mass Index, median [IQR]	27.7 [24.5-32.0]	27.5 [24.1-31.5]	0.319
Current Non-Smoker N (%)	332 (71.7)	1502 (61.0)	<0.001
Subgroup N (%) Non-Smokers Smoker without COPD Mild/Moderate COPD Severe COPD	 63 (13.3) 107 (22.5) 139 (29.3) 166 (34.9)	 138 (5.5) 832 (33.4) 1065 (42.8) 456 (18.3)	<0.001
Genitourinary Condition N (%)	163 (35.2)	886 (36.6)	0.605

*Kruskal-Wallis or Chi-square test comparing participants in this study with the entire SPIROMICS cohort
Abbreviations: IQR=interquartile range

Supplementary Table 2. Urine albumin/creatinine ratio and clinical characteristics

	Unadjusted		Adjusted for Age, Sex, BMI, & Smoking Status	
	$\hat{\beta}$ (CI)	*P-value**	$\hat{\beta}$ (CI)	*P-value**
FEV_1 % Predicted	-0.11 (-0.20,-0.03)	0.011	-0.08 (-0.17,0.01)	0.086
6MWD (meters)	-0.01 (-0.02,0.001)	0.081	-0.01 (-0.02,0.004)	0.250
SGRQ	0.005 (-0.001,0.01)	0.120	0.004 (-0.003,0.01)	0.264
CAT (≥10)	0.38 (0.10,0.66)	0.009	0.31 (0.02,0.59)	0.034
Emphysema % (<950 HU)	0.001 (-0.01,0.01)	0.826	-0.004 (-0.02,0.01)	0.550
PRM^{EMPH}	-0.0001 (-0.01,0.01)	0.992	-0.005 (-0.02,0.01)	0.433
PRM^{FSAD}	0.01 (0.0005,0.02)	0.039	0.002 (-0.01,0.01)	0.719

*Univariable or multivariable linear regression
Abbreviations: BMI=body mass index, β=beta, CI=confidence interval, FEV_1=forced expiratory volume in 1 second, 6MWD=six-minute walk distance, SGRQ=St. George's Respiratory Questionnaire, CAT=COPD Assessment Test, HU=Hounsfield units, PRM^{EMPH}=emphysema by parametric response mapping, PRM^{FSAD}=functional small airway disease by parametric response mapping

Supplementary Table 3. Urine mtDNA and imaging parameters

	Unadjusted		Adjusted for Age, Sex, BMI, & Smoking Status	
	$\hat{\beta}$ (CI)	*P-value**	$\hat{\beta}$ (CI)	*P-value**
Emphysema % (<950 HU)	0.002 (-0.01,0.01)	0.693	0.01 (0.0002,0.02)	0.048
PRM^{EMPH}	0.004 (-0.01,0.01)	0.472	0.01 (0.0000,0.02)	0.050
PRM^{FSAD}	-0.0004 (-0.01,0.01)	0.925	0.01 (-0.01,0.02)	0.228

*Univariable or multivariable linear regression
Abbreviations: BMI=body mass index, β=beta, CI=confidence interval, HU=Hounsfield units, PRM^{EMPH}=emphysema by parametric response mapping, PRM^{FSAD}=functional small airway disease by parametric response mapping

Supplementary Table 4. Urine albumin/creatinine ratio in females compared to males

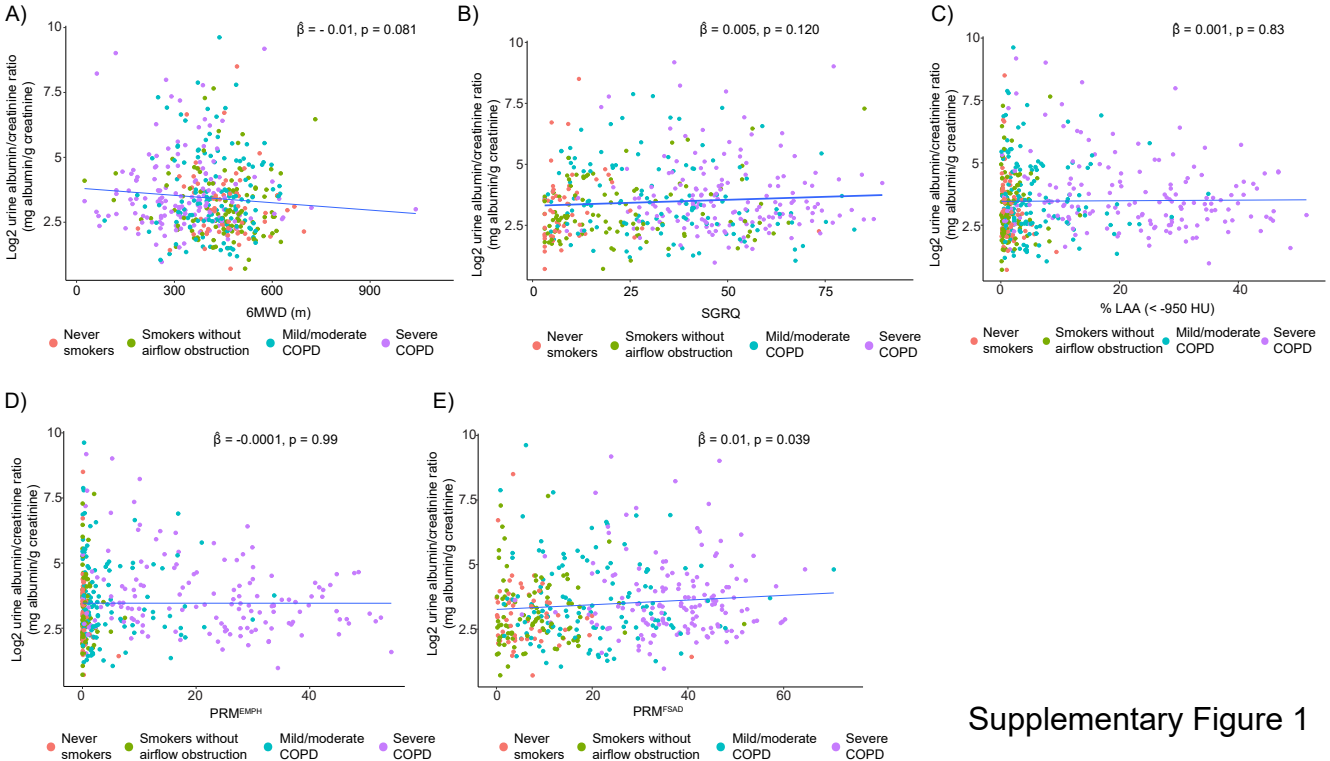
Unadjusted		Adjusted for Age, BMI, & Smoking Status	
$\hat{\beta}$ (CI)	*P-value**	$\hat{\beta}$ (CI)	*P-value**
-0.02 (-0.28,0.24)	0.894	0.09 (-0.17,0.36)	0.486

*Univariable or multivariable linear regression
Abbreviations: BMI=body mass index, β=beta, CI=confidence interval

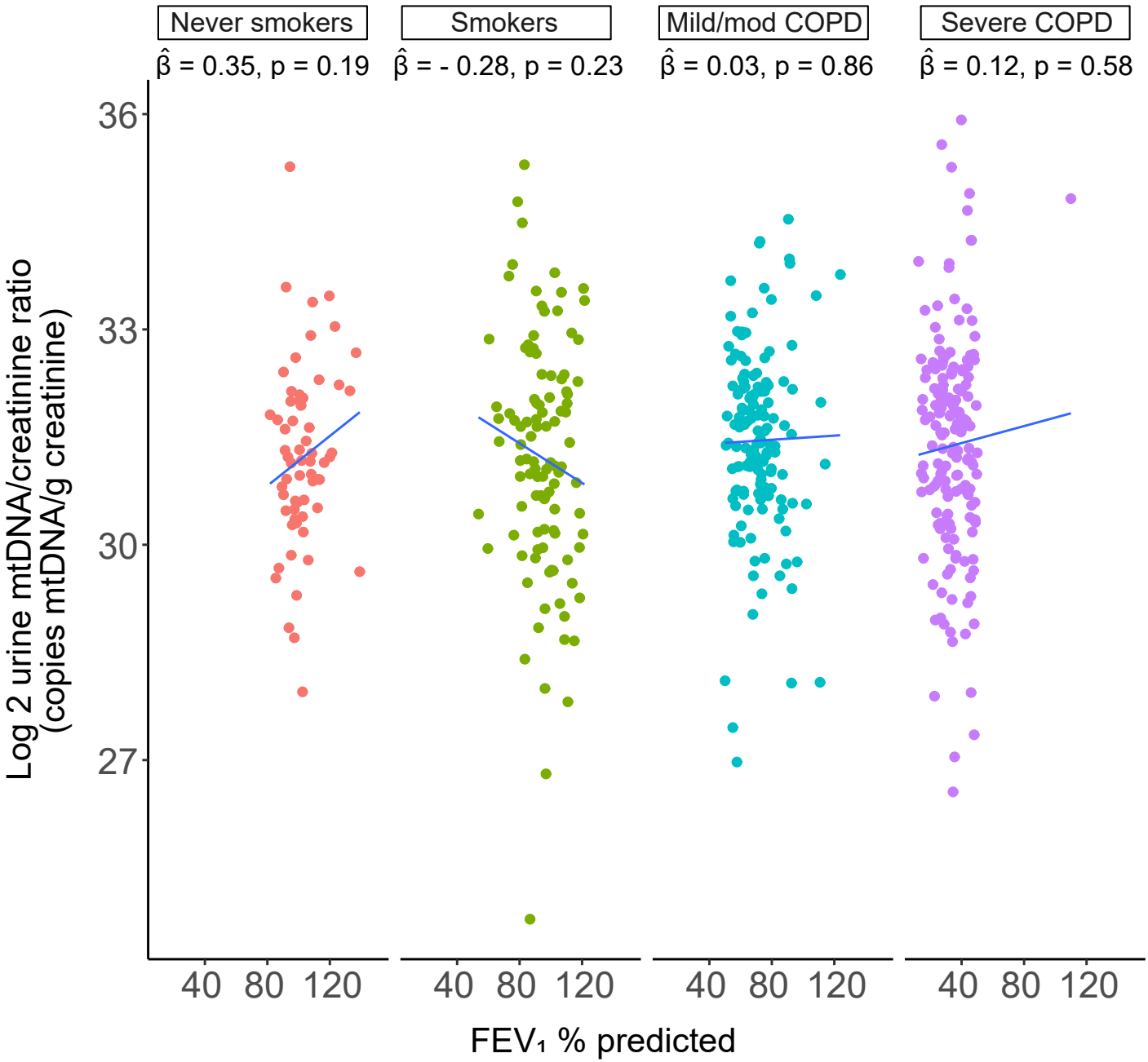
Supplementary Table 5. Urine albumin/creatinine ratio and clinical characteristics within males and females

	Unadjusted		Adjusted for Age, BMI, & Smoking Status	
	$\hat{\beta}$ (CI)	*P-value**	$\hat{\beta}$ (CI)	*P-value**
FEV_1 % Predicted				
Males	-0.11 (-0.24,0.01)	0.082	-0.08 (-0.21,0.05)	0.237
Females	-0.12 (-0.24,-0.004)	0.059	-0.08 (-0.20,0.04)	0.198
6MWD (meters)				
Males	-0.01 (-0.02,0.006)	0.229	-0.004 (-0.02,0.01)	0.567
Females	-0.01 (-0.03,0.005)	0.185	-0.01 (-0.03,0.06)	0.223
SGRQ				
Males	0.01 (-0.004,0.01)	0.250	0.004 (-0.005,0.01)	0.353
Females	0.004 (-0.004,0.01)	0.295	0.004 (-0.005,0.01)	0.378
CAT (≥10)				
Males	0.47 (0.06,0.88)	0.027	0.40 (-0.005,0.81)	0.054
Females	0.28 (-0.10,0.66)	0.155	0.22 (0.16,0.61)	0.261
Emphysema % (<950 HU)				
Males	-0.01 (-0.02,0.006)	0.214	-0.01 (-0.03,0.006)	0.196
Females	0.01 (0.0000,0.03)	0.052	0.01 (-0.01,0.02)	0.370
PRM^{EMPH}				
Males	-0.01 (-0.02,0.01)	0.243	-0.01 (-0.03,0.01)	0.266
Females	0.01 (-0.003,0.03)	0.118	0.01 (-0.01,0.02)	0.539
PRM^{FSAD}				
Males	0.01 (-0.004,0.02)	0.203	0.003 (-0.01,0.02)	0.654
Females	0.01 (-0.002,0.02)	0.118	0.001 (-0.01,0.01)	0.857

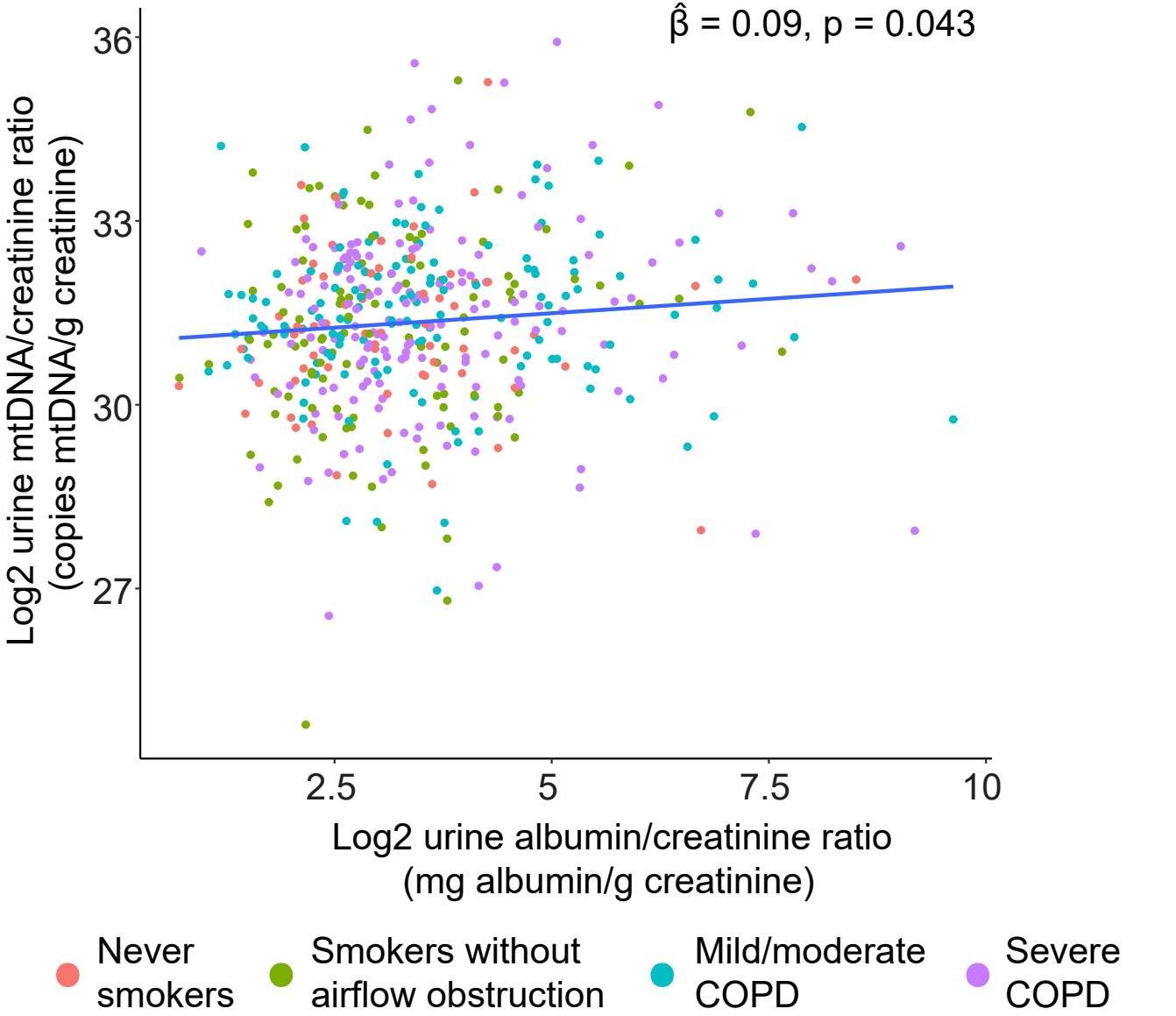
*Univariable or multivariable linear regression
Abbreviations: BMI=body mass index, β=beta, CI=confidence interval, FEV_1=forced expiratory volume in 1 second, 6MWD=six-minute walk distance, SGRQ=St. George's Respiratory Questionnaire, CAT=COPD Assessment Test, HU=Hounsfield units, PRM^{EMPH}=emphysema by parametric response mapping, PRM^{FSAD}=functional small airway disease by parametric response mapping



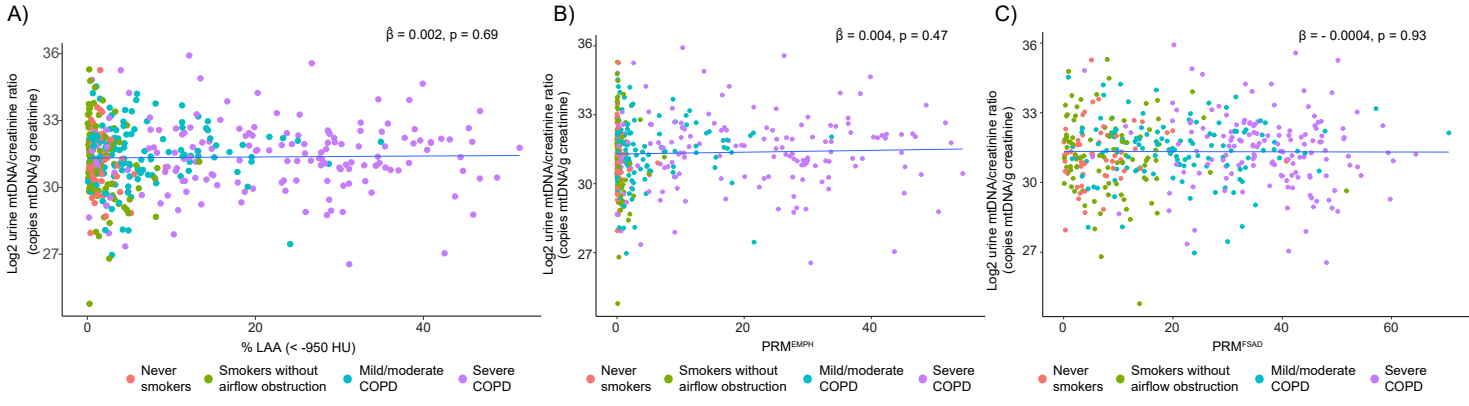
Supplementary Figure 1



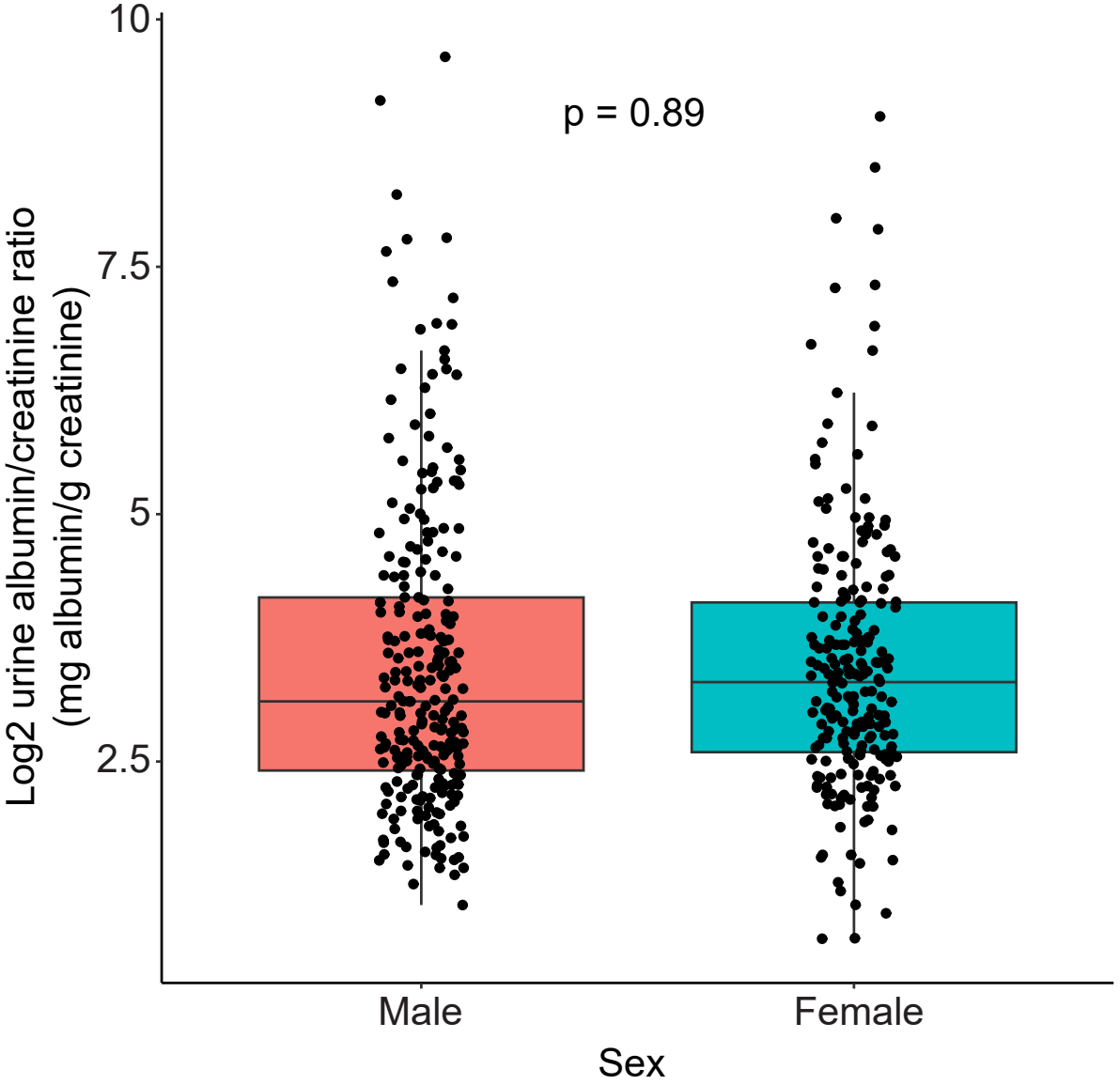
Supplementary Figure 2



Supplementary Figure 3



Supplementary Figure 4



Supplementary Figure 5