

## **SUPPLEMENTARY FIGURE LEGENDS**

**Supplementary Figure 1. UACR is not strongly associated with 6MWD, SGRQ, or radiographic measures of COPD.** (A-E) UACR (log<sub>2</sub> mg/g) and association with 6MWD (A), SGRQ (B), %LAA < -950 HU (C), PRM<sup>EMPH</sup> (D), and PRM<sup>FSAD</sup> (E), tested with unadjusted linear regression models (never smokers n=56-64, smokers without airflow obstruction n=96-109, mild/moderate COPD n=124-135, severe COPD n=149-162). Linear associations (A-E) were implemented with unadjusted linear regression models.

**Supplementary Figure 2. U-mtDNA levels do not associate with FEV<sub>1</sub> % predicted in the SPIROMICS cohort.** U-mtDNA (log<sub>2</sub> copies mtDNA/g creatinine) and association with post-bronchodilator FEV<sub>1</sub> % predicted in each subgroup: never smokers (n=63; red), smokers without airflow obstruction ("smokers", n=109; green), participants with mild/moderate COPD (n=142; blue), and severe COPD (n=168; purple). Linear associations were implemented with unadjusted linear regression models.

**Supplementary Figure 3. U-mtDNA levels are associated with UACR.** U-mtDNA (log<sub>2</sub> copies mtDNA/g creatinine) and association with UACR (log<sub>2</sub> mg/g), tested with unadjusted linear regression models (never smokers n=64, smokers without airflow obstruction n=109, mild/moderate COPD n=139, severe COPD n=168). 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<sup>EMPH</sup> **(B)**, and PRM<sup>FSAD</sup> **(C)**, tested with unadjusted linear regression models (never-smokers n=56-64, smokers without airflow obstruction n=96-101, mild/moderate COPD n=127-129, severe COPD n=150-155).

**Supplementary Figure 5. UACR does not differ between males and females.** UACR (log 2 mg/g) levels in males (n=257) compared to females (n=223) 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=483)	SPIROMICS cohort (n=2974)	<i>P-value*</i>
Age, median [IQR]	65.0 [55.0-70.0]	64.0 [56.0-70.0]	0.601
Male N (%)	258 (53.4)	1577 (53.0)	0.912
Body mass index, median [IQR]	27.7 [24.6-32.0]	27.5 [24.2-31.6]	0.378
Current non-smoker N (%)	337 (71.5)	1839 (62.7)	<0.001
Subgroup N (%)			
Never smokers	64 (13.3)	202 (6.8)	<0.001
Smoker without airflow obstruction	109 (22.6)	941 (31.6)	
Mild/moderate COPD	142 (29.4)	1207 (40.6)	
Severe COPD	168 (34.8)	624 (21.0)	
Genitourinary condition N (%)	167 (35.5)	1053 (36.4)	0.728
*Kruskal-Wallis or Chi-square test comparing participants in this study with the entire SPIROMICS cohort Abbreviations: IQR=interquartile range; 25% and 75% percentiles			

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

	Unadjusted		Adjusted for age, sex, BMI, & smoking status	
	$\hat{\beta}$ (CI)	<i>P</i> -value*	$\hat{\beta}$ (CI)	<i>P</i> -value*
FEV <sub>1</sub> % predicted	-0.12 (-0.20,-0.03)	0.009	-0.08 (-0.17,0.01)	0.069
6MWD (meters)	-0.01 (-0.02,0.002)	0.055	-0.01 (-0.02,0.003)	0.179
SGRQ	0.005 (-0.001,0.01)	0.114	0.004 (-0.002,0.01)	0.221
CAT (≥10)	0.37 (0.09,0.65)	0.009	0.31 (0.03,0.59)	0.033
%LAA (<-950 HU)	0.002 (-0.01,0.01)	0.720	-0.002 (-0.01,0.01)	0.689
PRM <sup>EMPH</sup>	0.0006 (-0.01,0.01)	0.911	-0.004 (-0.02,0.01)	0.563
PRM <sup>FSAD</sup>	0.01 (0.0008,0.02)	0.033	0.002 (-0.01,0.01)	0.636
<p>*Univariable or multivariable linear regression  Abbreviations: BMI=body mass index, <math>\hat{\beta}</math>=estimated change log<sub>2</sub> UACR with a one unit increase in clinical characteristic, CI=confidence interval, FEV<sub>1</sub>=forced expiratory volume in 1 second, 6MWD=six-minute walk distance, SGRQ=St. George's Respiratory Questionnaire, CAT=COPD Assessment Test, LAA=low attenuation area, HU=Hounsfield units, PRM<sup>EMPH</sup>=emphysema by parametric response mapping, PRM<sup>FSAD</sup>=functional small airway disease by parametric response mapping</p>				

**Supplementary Table 3. Urine mtDNA and imaging parameters**

	Unadjusted		Adjusted for age, sex, BMI, & smoking status	
	$\hat{\beta}$ (CI)	<i>P</i> -value*	$\hat{\beta}$ (CI)	<i>P</i> -value*
%LAA (<-950 HU)	0.003 (-0.01,0.01)	0.573	0.01 (0.002,0.03)	0.028
PRM <sup>EMPH</sup>	0.005 (-0.01,0.02)	0.370	0.01 (0.002,0.03)	0.028
PRM <sup>FSAD</sup>	-0.0002 (-0.01,0.01)	0.958	0.01 (-0.003,0.02)	0.206
<p>*Univariable or multivariable linear regression  Abbreviations: BMI=body mass index, <math>\hat{\beta}</math>=estimated change log2 urine mtDNA with a one unit increase in clinical characteristic, CI=confidence interval, LAA=low attenuation area, HU=Hounsfield units, PRM<sup>EMPH</sup>=emphysema by parametric response mapping, PRM<sup>FSAD</sup>=functional small airway disease by parametric response mapping</p>				

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

Unadjusted		Adjusted for age, BMI, & smoking status	
$\hat{\beta}$ (CI)	<i>P-value</i> *	$\hat{\beta}$ (CI)	<i>P-value</i> *
-0.03 (-0.29,0.23)	0.805	0.08 (-0.18,0.34)	0.551
*Multivariable linear regression Abbreviations: BMI=body mass index, $\hat{\beta}$ =estimated change log2 UACR with a one unit increase in clinical characteristic, CI=confidence interval			

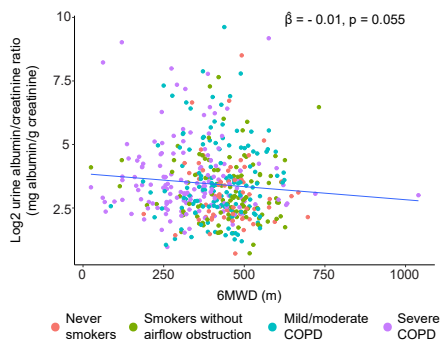
**Supplementary Table 5. Urine albumin/creatinine ratio and clinical characteristics within males and females**

	Unadjusted		Adjusted for age, BMI, & smoking status	
	$\hat{\beta}$ (CI)	<i>P</i> -value*	$\hat{\beta}$ (CI)	<i>P</i> -value*
<b>FEV<sub>1</sub> % predicted</b>				
Males	-0.12 (-0.24,0.01)	0.072	-0.09 (-0.21,0.04)	0.189
Females	-0.12 (-0.24,-0.0003)	0.051	-0.08 (-0.20,0.04)	0.185
<b>6MWD (meters)</b>				
Males	-0.01 (-0.02,0.004)	0.168	-0.01 (-0.02,0.01)	0.407
Females	-0.01 (-0.03,0.004)	0.163	-0.01 (-0.03,0.01)	0.210
<b>SGRQ</b>				
Males	0.01 (-0.003,0.02)	0.194	0.01 (-0.004,0.01)	0.250
Females	0.004 (-0.004,0.01)	0.356	0.003 (-0.005,0.01)	0.427
<b>CAT (<math>\geq 10</math>)</b>				
Males	0.47 (0.06,0.87)	0.025	0.41 (0.01,0.81)	0.047
Females	0.26 (0.12,0.64)	0.180	0.21 (0.17,0.59)	0.289
<b>%LAA (&lt;950 HU)</b>				
Males	-0.01 (-0.02,0.01)	0.262	-0.01 (-0.03,0.01)	0.303
Females	0.02 (0.0004,0.03)	0.045	0.01 (-0.01,0.02)	0.350
<b>PRM<sup>EMPH</sup></b>				
Males	-0.01 (-0.02,0.01)	0.296	-0.01 (-0.02,0.01)	0.394
Females	0.01 (-0.0004,0.03)	0.112	0.01 (-0.01,0.02)	0.529
<b>PRM<sup>FSAD</sup></b>				
Males	0.01 (-0.004,0.02)	0.194	0.004 (-0.01,0.02)	0.568
Females	0.01 (-0.002,0.02)	0.106	0.001 (-0.01,0.01)	0.824

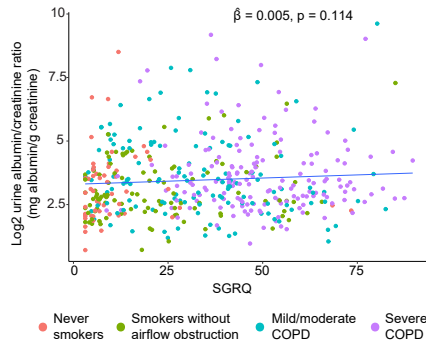
\*Univariable or multivariable linear regression

Abbreviations: BMI=body mass index,  $\hat{\beta}$ =estimated change log<sub>2</sub> urine mtDNA with a one unit increase in clinical characteristic, CI=confidence interval, FEV<sub>1</sub>=forced expiratory volume in 1 second, 6MWD=six-minute walk distance, SGRQ=St. George's Respiratory Questionnaire, CAT=COPD Assessment Test, LAA=low attenuation area, HU=Hounsfield units, PRM<sup>EMPH</sup>=emphysema by parametric response mapping, PRM<sup>FSAD</sup>=functional small airway disease by parametric response mapping

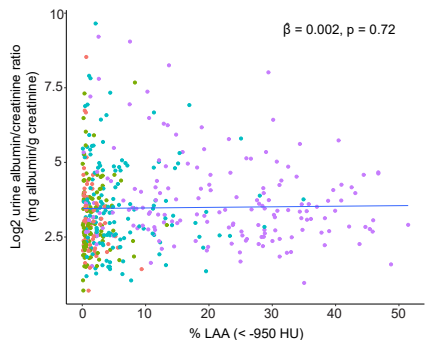
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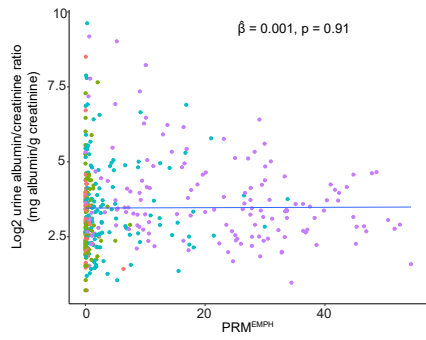
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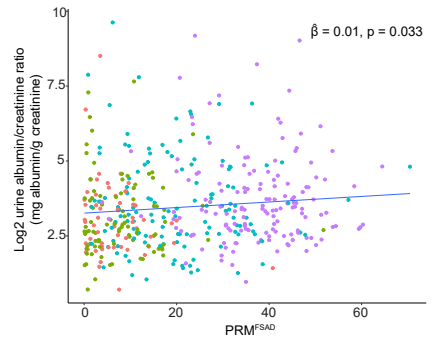
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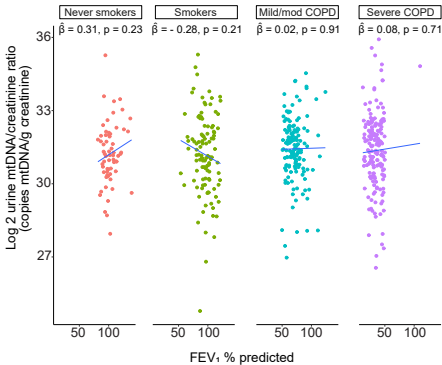
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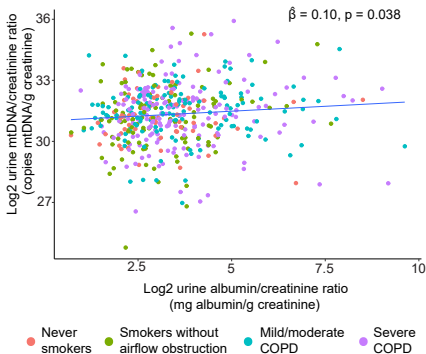
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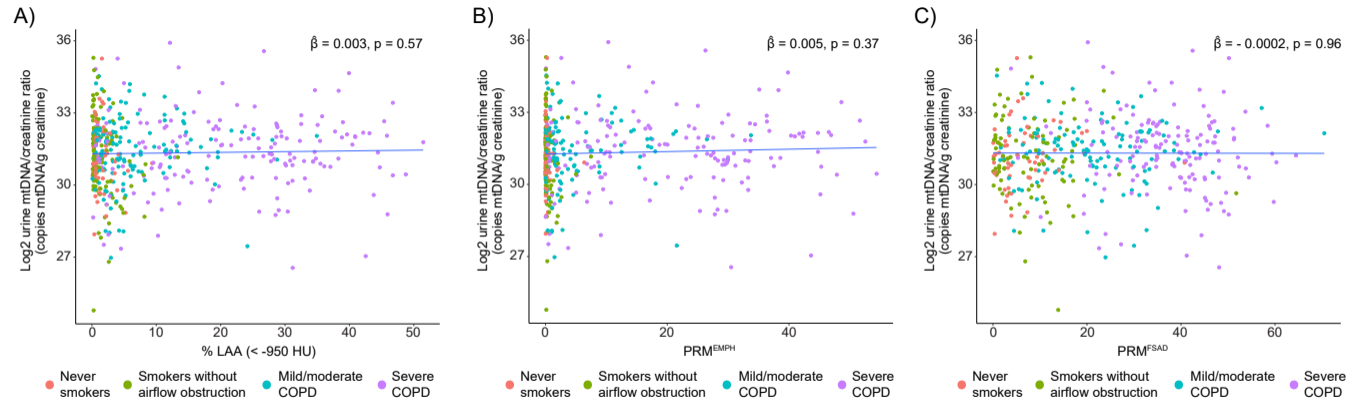
Supplementary Figure 1



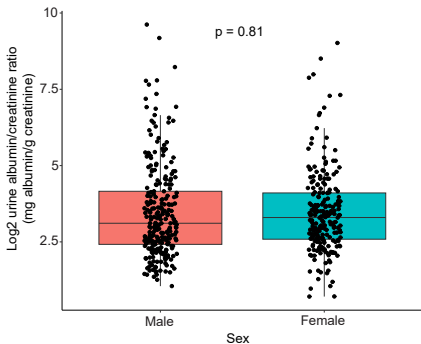
Supplementary Figure 2



Supplementary Figure 3



Supplementary Figure 4



Supplementary Figure 5