Title: The contribution of anemia to adverse outcomes in a COPD population with high burden of comorbidites, an analysis from SPIROMICS.

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Online Supplementary Information:

e-Table 1: Associations of hemoglobin with outcomes (continuous), among those with normocytic anemia and normal hemoglobin.

	Coefficient	95 % CI	p-value
Clinical measures			
6MWD	**11.36**	**(6.05, 16.68)**	**<0.001**
FEV1 % pred	**1.67**	**(0.35, 0.66)**	**0.001**
SGRQ	**-0.69**	**(-1.34, -0.043)**	**0.037**
Total CAT	**-0.29**	**(-0.58, -0.0062)**	**0.045**
# exac in past yr	-0.017	(-0.057, 0.023)	0.406
# severe exac in past yr	**-0.038**	**(-0.067, -0.0096)**	**0.009**
MMRC	**-0.069**	**(-0.11, -0.031)**	**<0.001**
Pre-walk oxygen saturation	**-0.30**	**(-0.48, -0.12)**	**0.001**
Post-walk oxygen saturation	**-0.42**	**(-0.63, -0.20)**	**<0.001**
Exacerbations over follow-up (IRR)	0.98	(0.91, 1.04)	0.469
Severe exacerbations over follow-up (IRR)	0.99	(0.89, 1.11)	0.911
All regression models adjusted for age, gender, race, FEV1 % predicted, current smoking status, education level, comorbidity count.			

e-Table 2: Differences in biomarker levels between those with and without normocytic anemia						
	Unadjusted			**Adjusted***		
	β	95% CI	p-value	β	95% CI	p-value
VWF	12.69	(0.86, 24.53)	0.036	6.83	(-4.56, 18.21)	0.240
VEGFα	-11.45	(-43.76, 20.86)	0.487	-16.3	(-50.5, 17.91)	0.350
TNFα	-1.05	(-7.00, 4.90)	0.730	-1.03	(-7.34, 5.28)	0.749
IL-15	0.059	(-0.027, 0.14)	0.177	0.055	(-0.035, 0.15)	0.228
IFNγ	-0.12	(-0.55, 0.31)	0.571	-0.016	(-0.47, 0.44)	0.943
IgA	0.34	(-0.014, 0.69)	0.060	0.21	(-0.14, 0.56)	0.236
CRP	**7.50**	**(5.01, 9.98)**	**<0.001**	**6.97**	**(4.35, 9.58)**	**<0.001**
APOa4	0.72	(-0.48, 1.93)	0.240	0.70	(-0.57, 1.96)	0.280
sRAGE~~AGER~~	**0.96**	**(0.39, 1.53)**	**0.001**	**1.35**	**(0.78, 1.93)**	**<0.001**
VCAM1	20.35	(-26.77, 67.48)	0.397	20.09	(-22.74, 62.92)	0.358
SOD1	-4.92	(-9,82, -0.027)	0.049	-3.64	(-8.80, 1.53)	0.167
SHBG	0.41	(-8.19, 9.01)	0.926	1.14	(-6.87, 9.14)	0.780
CDH1	**1312.19**	**(940.55, 1683.82)**	**<0.001**	**1213.20**	**(832.85, 1593.55)**	**<0.001**
Multivariable linear regression analysis included adjustment for age, gender, race, FEV1 % predicted, current smoking status, educational attainment, comorbidity count, and batch number. A P value of 0.00384 was considered statistically significant after correction for multiple comparisons.						

e-Table 3: Interactions between normocytic anemia and cardiometabolic phenotype. Coefficients indicate difference between those with normocytic anemia and those without, in subgroups with and without cardiometabolic phenotype.							
	Not cardiometabolic phenotype			**Cardiometabolic phenotype**			
	β	95% CI	p-value	β	95% CI	p-value	p-int
IL-15	-0.032	(-0.17, 0.10)	0.642	**0.12**	**(0.021, 0.21)**	**0.017**	0.050
sRAGE~~AGER~~	0.55	(-0.21, 1.31)	0.156	**2.36**	**(1.55, 3.18)**	**<0.001**	0.001
ApoA4	-0.21	(-1.92, 1.51)	0.812	**2.00**	**(0.18, 3.83)**	**0.032**	0.079
CDH-1	**763. 28**	**(335.17, 1191.39)**	**<0.001**	**1767.53**	**(1087.34, 2447.72)**	**<0.001**	0.018
Adjusted for age, gender, race, FEV1 % predicted, current smoking status, educational attainment and batch number.							