

## **Online Supplement**

### **Physical Activity and Systemic Biomarkers in Persons With COPD: Insights from a Web-Based Pedometer-Mediated Intervention**

Megan N. Berube, BS<sup>1\*</sup> Stephanie A. Robinson, PhD<sup>2,3\*</sup> Emily S. Wan, MD, MPH<sup>1,4,5,6</sup> Maria A. Mongiardo, MPH<sup>1</sup> Elizabeth B. Finer, MA<sup>1</sup> Marilyn L. Moy, MD, MSc<sup>1,4,6</sup>

<sup>1</sup>Research and Development Service, VA Boston Healthcare System, Boston, Massachusetts, United States

<sup>2</sup>Center for Healthcare Organization and Implementation Research, VA Bedford Healthcare System, Boston, Massachusetts, United States

<sup>3</sup>The Pulmonary Center, Boston University School of Medicine, Boston, Massachusetts, United States

<sup>4</sup>Pulmonary and Critical Care Medicine Section, VA Boston Healthcare System, Boston, Massachusetts, United States

<sup>5</sup>Channing Division of Network Medicine, Brigham and Women's Hospital, Boston, Massachusetts, United States

<sup>6</sup>Harvard Medical School, Boston, Massachusetts, United States

\* *contributed equally to this work/co-first authors.*

Table E1. Associations between systemic biomarkers and categorical variables

	NT-proBNP (pg/ml)			sRAGE (pg/ml)			CKMM (ng/ml)		
	Mean	SD	<i>p</i>	Mean	SD	<i>p</i>	Mean	SD	<i>p</i>
Study			<.001			.245			.062
SAMO	191.47	3.76		978.52	1.66		543.31	1.45	
ESC	104.04	3.18		1079.95	1.67		531.48	1.49	
WEB	159.61	3.35		1055.50	1.63		481.86	1.60	
Sex			.009			.130			<.001
Male	157.46	3.57		1033.90	1.65		528.56	1.50	
Female	51.55	1.52		799.16	1.70		330.59	1.39	
Race			.108						.216
White	157.69	3.52		1062.15	1.64	<.001	526.26	1.50	
Other	103.24	4.04		652.40	1.52		473.68	1.55	
GOLD Stage			.688			<.001			.407
1	131.42	3.97		1133.09	1.69		480.17	1.46	
2	162.39	3.21		1088.82	1.65		535.90	1.50	
3	155.23	4.10		961.73	1.63		523.03	1.52	
4	134.78	3.49		765.02	1.53		514.61	1.59	
BMI Categories			.877			.235			<.001
Extremely Obese	171.22	3.18		1078.89	1.51		605.30	1.54	
Obese	149.45	3.61		1004.98	1.64		542.65	1.51	
Overweight	143.37	3.64		1077.89	1.70		535.01	1.47	
Normal	170.96	3.64		994.63	1.63		474.47	1.50	
Underweight	165.07	2.19		697.03	1.53		287.81	1.44	
Coronary Artery Disease			<.001			.040			.224
Yes	263.56	3.37		1126.87	1.61		546.40	1.45	
No	127.34	3.45		995.52	1.67		514.55	1.53	
Congestive Heart Failure			<.001			.018			.012
Yes	478.19	3.55		1232.50	1.59		612.23	1.58	
No	134.29	3.34		1005.96	1.66		512.96	1.49	
Oxygen			.008			.120			.007
Yes	213.22	4.12		951.36	1.65		581.71	1.53	
No	139.45	3.36		1050.06	1.66		506.72	1.49	
Acute Exacerbation			.772			.304			.910
None	151.69	3.45		1013.22	1.66		523.13	1.49	
≥1	159.07	4.02		1083.22	1.62		520.01	1.59	
Exposure			.115			.115			.308
Control	163.94	3.64		1000.13	1.63		529.97	1.48	
Intervention	130.28	3.35		1095.48	1.72		505.09	1.56	

Note: NT-proBNP = N-terminal pro- $\beta$ -type natriuretic peptide; sRAGE = soluble receptor for advanced glycation end products; CKMM = muscle-type creatine kinase; SD=Standard deviation; BMI=body mass index; Extremely Obese: BMI > 40 kg/m<sup>2</sup>; Obese: BMI = 30 to < 40 kg/m<sup>2</sup>; Overweight: BMI= 25 to < 30 kg/m<sup>2</sup>; Normal: BMI=18.5 to < 25 kg/m<sup>2</sup>; Underweight: BMI < 18.5 kg/m<sup>2</sup>. *p*-value from independent samples t-tests (2 levels) and analyses of variances (ANOVAs; 3 or more levels).

Table E2. Pearson correlation coefficients for systemic biomarkers and continuous variables

	Age	FEV <sub>1</sub> % predicted	Pack-Years	6MWT distance	Daily Step Count	NT-proBNP	sRAGE
FEV <sub>1</sub> % predicted	0.12	--					
<i>p</i> -value	.025	--					
Pack-Years	.035	-0.04	--				
<i>p</i> -value	.500	.485	--				
6MWT distance	-0.43	0.20	-0.06	--			
<i>p</i> -value	<.001	<.001	.217	--			
Daily Step Counts	-0.31	0.21	-0.07	0.52	--		
<i>p</i> -value	<.001	<.001	.204	<.001	--		
NT-proBNP	0.56	8.60E-4	9.20E-4	-0.43	-0.29	--	
<i>p</i> -value	<.001	.987	.986	<.001	<.001	--	
sRAGE	0.28	0.21	0.01	-0.10	-0.07	0.36	--
<i>p</i> -value	<.001	<.001	.921	.050	.199	<.001	--
CKMM	0.38	-0.01	-0.02	-0.24	-0.15	0.31	0.25
<i>p</i> -value	<.001	.890	.734	<.001	.004	<.001	<.001

Note: FEV<sub>1</sub> = forced expiratory volume in the first second, 6MWT = 6-minute walk test; NT-proBNP = N-terminal pro-β-type natriuretic peptide; sRAGE = soluble receptor for advanced glycation end products; CKMM = muscle-type creatine kinase. *p*-value from Pearson correlations.

Table E3. General linear models between baseline daily step counts and baseline sRAGE levels (pg/mL)

	ln(sRAGE)		sRAGE		<i>p</i> -value
	Est.	SE	Est.	SE	
Daily Step Counts (1,000)	-0.01	0.01	-0.99	1.01	.545
Study (ref=SAM-O)					
ESC	0.14	0.06	1.15	1.07	.032
WEB	0.04	0.08	1.05	1.08	.559
Age	0.02	0.00	1.02	1.00	<.001
Race (ref=White)					
Other	-0.42	0.10	-0.66	1.11	<.001
Sex (ref=Male)					
Female	0.12	0.17	1.13	1.18	.473
FEV <sub>1</sub> % predicted	0.00	0.00	1.00	1.00	.009
BMI (ref=Normal)					
Extremely Obese	0.04	0.11	1.04	1.12	.721
Obese	0.00	0.07	-1.00	1.07	.970
Overweight	0.00	0.07	1.00	1.07	.984
Underweight	-0.25	0.20	-0.78	1.22	.208
CAD (ref=No)					
Yes	0.03	0.06	1.03	1.06	.611
CHF (ref=No)					
Yes	0.20	0.09	1.22	1.09	.024
Oxygen Use (ref=No)					
Yes	-0.10	0.06	-0.91	1.07	.139
Acute Exacerbation (ref=None)					
≥1 Event	0.06	0.07	1.06	1.08	.412

*Note.* sRAGE = soluble receptor for advanced glycation end products; Est. = Estimate; SE = Standard Error; BMI = Body Mass Index; CAD = Coronary artery disease; CHF = Congestive Heart Failure.

Table E4. General linear models between baseline daily step counts and baseline CKMM levels (ng/mL)

	ln(CKMM)		CKMM		<i>p</i> -value
	Est.	SE	Est.	SE	
Daily Step Counts (1,000)	0.00	0.01	1.00	1.01	.628
Study (ref=SAM-O)					
ESC	0.03	0.05	1.03	1.05	.595
WEB	-0.16	0.06	-0.85	1.06	.009
Age	0.02	0.00	1.02	1.00	<.001
Race (ref=White)					
Other	-0.01	0.08	-0.99	1.08	.920
Sex (ref=Male)					
Female	-0.11	0.13	-0.89	1.14	.399
FEV <sub>1</sub> % predicted	0.00	0.00	-1.00	1.00	.315
BMI (ref=Normal)					
Extremely Obese	0.28	0.09	1.33	1.09	.002
Obese	0.18	0.05	1.19	1.06	.001
Overweight	0.14	0.05	1.15	1.06	.010
Underweight	-0.37	0.16	-0.69	1.17	.016
CAD (ref=No)					
Yes	-0.07	0.05	-0.93	1.05	.132
CHF (ref=No)					
Yes	0.14	0.07	1.15	1.07	.038
Oxygen Use (ref=No)					
Yes	0.07	0.05	1.08	1.05	.145
Acute Exacerbation (ref=None)					
≥1 Event	0.10	0.06	1.11	1.06	.081

*Note.* CKMM = muscle type creatine kinase; Est. = Estimate; SE = Standard Error; BMI = Body Mass Index; CAD = Coronary artery disease; CHF = Congestive Heart Failure.

Table E5. General linear models between baseline 6MWT distance and baseline sRAGE levels (pg/mL)

Parameter	ln(sRAGE)		sRAGE		p-value
	Est.	SE	Est.	SE	
6MWT Distance (100 m)	-0.02	0.03	-0.98	1.03	.517
Study (ref=SAM-O)					
ESC	0.14	0.06	1.14	1.07	.034
WEB	0.04	0.08	1.04	1.08	.582
Age	0.01	0.00	1.02	1.00	<.001
Race (ref=White)					
Other	-0.42	0.10	-0.66	1.11	<.001
Sex (ref=Male)		.			
Female	0.11	0.17	1.11	1.19	.529
FEV <sub>1</sub> % predicted	0.00	0.00	1.00	1.00	.009
BMI (ref=Normal)					
Extremely Obese	0.04	0.11	1.04	1.12	.706
Obese	0.00	0.07	-1.00	1.07	.947
Overweight	0.00	0.07	-1.00	1.07	.995
Underweight	-0.25	0.20	-0.78	1.22	.204
CAD (ref=no)		.			
Yes	0.03	0.06	1.03	1.06	.636
CHF (ref=no)		.			
Yes	0.19	0.09	1.21	1.09	.029
Oxygen Use (ref=No)		.			
Yes	-0.10	0.07	-0.90	1.07	.127
Acute Exacerbation (ref=None)		.			
≥1 Event	0.06	0.07	1.06	1.08	.430

Note. sRAGE = soluble receptor for advanced glycation end products; Est. = Estimate; SE = Standard Error; BMI = Body Mass Index; CAD = Coronary artery disease; CHF = Congestive Heart Failure.

Table E6. General linear models between baseline 6MWT distance and baseline CKMM level (ng/mL)

Parameter	ln(CKMM)		CKMM		p-value
	Est.	SE	Est.	SE	
6MWT Distance (100 m)	-0.02	0.02	-0.98	1.02	.463
Study (ref=SAM-O)					
ESC	0.03	0.05	1.03	1.05	.594
WEB	-0.15	0.06	-0.86	1.06	.011
Age	0.02	0.00	1.02	1.00	<.001
Race (ref=White)					
Other	-0.01	0.08	-0.99	1.08	.892
Sex (ref=Male)					.
Female	-0.12	0.13	-0.89	1.14	.364
FEV <sub>1</sub> % predicted	0.00	0.00	-1.00	1.00	.444
BMI (ref=Normal)					
Extremely Obese	0.28	0.09	1.32	1.09	.002
Obese	0.17	0.05	1.19	1.06	.002
Overweight	0.14	0.05	1.15	1.06	.008
Underweight	-0.38	0.16	-0.68	1.17	.014
CAD (ref=no)					
Yes	-0.07	0.05	-0.93	1.05	.130
CHF (ref=no)					
Yes	0.13	0.07	1.14	1.07	.056
Oxygen Use (ref=No)					
Yes	0.06	0.05	1.06	1.05	.228
Acute Exacerbation (ref=None)					.
≥1 Event	0.10	0.06	1.10	1.06	.092

Note. CKMM = muscle type creatine kinase; Est. = Estimate; SE = Standard Error; BMI = Body Mass Index; CAD = Coronary artery disease; CHF = Congestive Heart Failure.