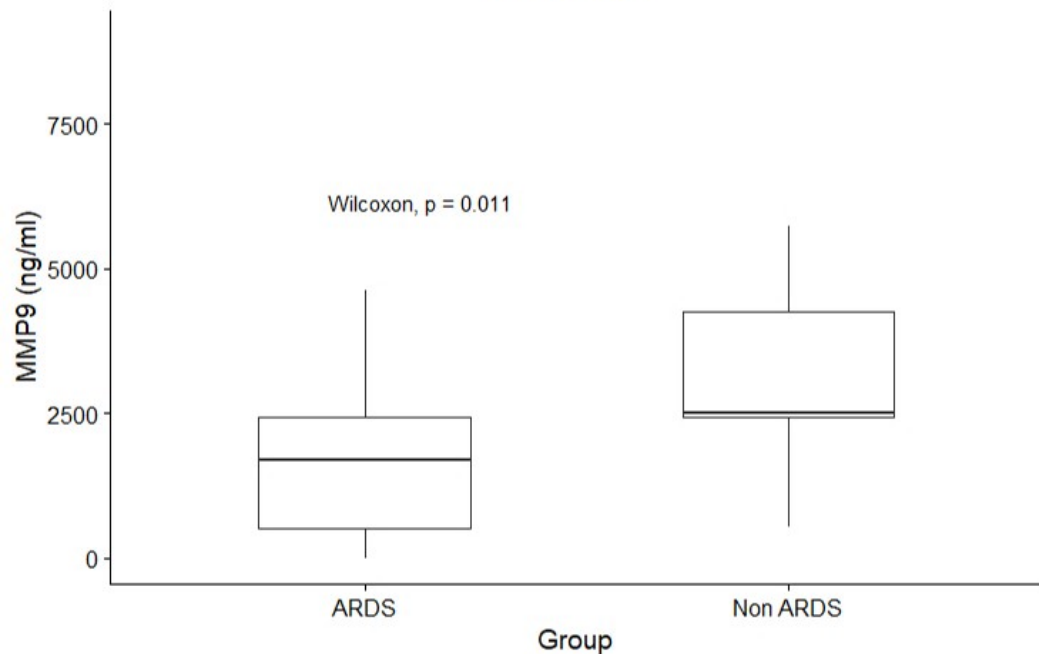


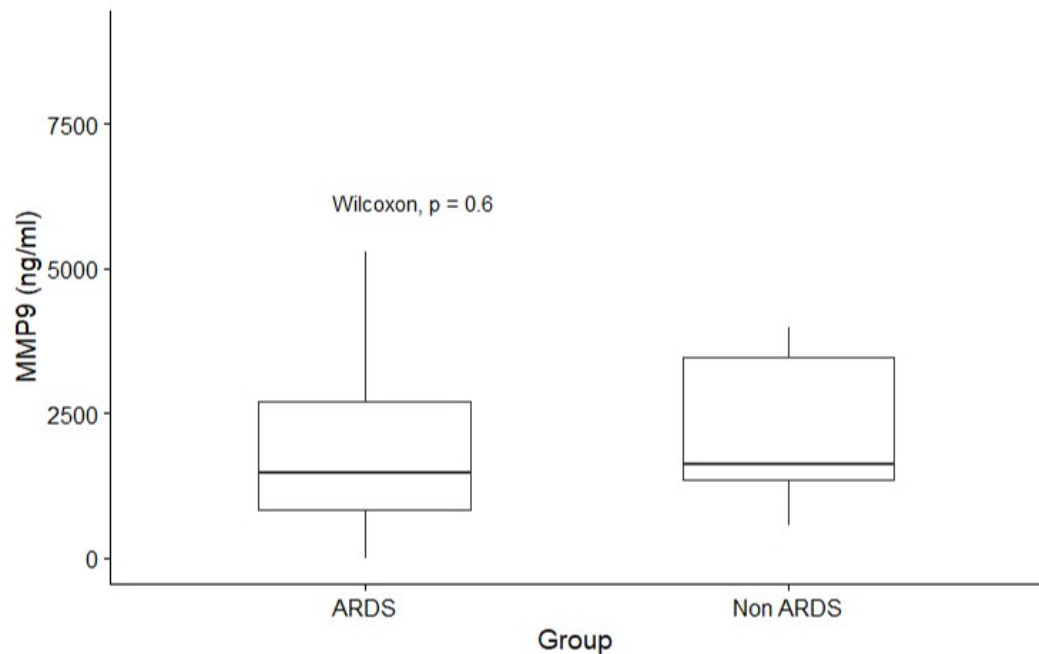
Specimen	TNFa	IL6	IL8	IL10	Ang2	IFNg	IL17	RAGE	GrB	sICAM-1	SPD	TNFRSF1A	IL18	MMP-9	PAI1	MPO
ARDS_001_ND1	22.4	41.4	35.1	10.6	22620.6	102.1	26.8	2100.6	127.3	309985.3	103123.2	4756.5	350.5	13559.9	591.6	22903.7
ARDS_002_ND1	32.7	14.4	1318.1	53.9	16103.1	111.3	15.3	684.4	150.8	940979.6	100567.6	14935.0	1760.2	392.4	1504.8	857.6
ARDS_003_ND1	9.3	10.6	17.0	0.0	3419.1	67.1	0.0	4725.3	113.2	434614.2	27851.5	1372.0	435.1	1976.7	2420.7	3667.2
ARDS_004_ND1	32.9	10649.2	9840.6	88.8	73238.4	126.6	61.5	11189.9	452.5	916168.0	8128.9	13644.7	2303.3	47.3	7593.8	2839.1
ARDS_005_ND1	14.3	58.4	199.0	32.4	3551.2	55.4	5.6	12557.2	265.1	799914.1	49921.5	3036.0	1505.7	2716.4	3273.1	5482.8
ARDS_006_ND1	9.5	9.6	18.8	9.0	5362.4	16.2	8.6	3862.8	63.6	427532.1	20714.1	1103.2	257.9	486.9	988.2	2473.4
ARDS_007_ND1	9.1	13.3	730.4	13.1	1878.0	30.2	5.6	3545.1	73.4	553128.9	34334.2	2378.1	563.5	2316.6	995.9	5357.7
ARDS_008_ND1	20.0	21.3	41.1	12.7	9087.0	30.3	18.2	11355.2	175.2	1050918.0	10454.4	4710.9	2720.5	12893.2	1115.9	33652.2
ARDS_009_ND1	25.1	3053.8	6675.3	7.2	14914.9	130.3	19.4	1042.6	137.7	473942.4	39912.5	3341.2	5079.5	0.0	110.7	0.0
ARDS_010_ND1	9.4	69.1	4.6	1.6	8935.6	11.2	3.3	2673.9	31.3	299467.4	12790.1	1563.3	279.9	2210.3	937.5	6489.5
ARDS_011_ND1	19.6	9.6	25.9	13.9	14148.7	35.0	2.8	3737.3	357.6	813805.8	28654.4	3745.1	1790.5	575.8	1747.0	2771.2
ARDS_012_ND1	4.3	4.4	14.2	0.0	2420.7	4.4	0.9	4625927.5	3.0	508387.9	28035.0	1147.5	207.4	3843.8	1081.2	5508.8
ARDS_013_ND1	8.6	18.4	27.0	0.0	5918.6	14.4	1.2	3642.6	10.7	518626.1	47473.6	1497.2	49.7	9485.0	2351.4	3601.9
ARDS_014_ND1	10.5	33.8	65.4	4.3	2453.2	19.0	3.2	4910.8	23.5	608850.2	35204.4	2939.2	74.3	1231.7	1461.5	5343.6
ARDS_015_ND1	4.8	15.4	16.7	0.0	1546.4	10.1	0.1	6014.1	6.2	450993.7	13042.7	1033.0	109.3	1787.6	966.7	1353.0
ARDS_016_ND1	16.4	657.9	320.0	4.8	4621.0	18.8	2.6	14183.5	14.9	1236587.4	31503.6	4163.6	418.3	331.7	599.1	1659.5
ARDS_017_ND1	11.9	25.5	51.1	13.6	5528.4	25.2	2.9	10450.9	46.1	525761.2	13494.6	3056.0	384.5	1738.4	3179.1	2926.6
ARDS_018_ND1	11.0	13.8	89.2	11.4	1696.1	24.5	0.1	8666.2	77.8	748646.5	49240.7	3428.5	543.9	1648.5	2043.3	4884.8
ARDS_019_ND1	8.4	1.6	30.9	0.9	6003.9	14.4	0.0	3468.9	52.1	725006.4	39340.3	1634.2	473.9	1219.0	1935.3	2932.2
ARDS_020_ND1	5.0	4.6	27.9	0.0	1333.9	10.1	0.1	2969.9	5.9	435297.5	14564.9	1392.9	103.5	10526.7	2120.5	7363.4
ARDS_021_ND1	52.1	443.2	42.3	30.3	125237.7	51.4	1.0	4334.8	105.8	1462469.0	8946.3	16841.3	13206.3	1454.0	1615.7	27315.6
ARDS_023_ND1	15.5	1981.1	120.5	9.7	12869.8	22.6	6.4	18364.1	35.3	884811.1	80236.8	4462.5	590.3	992.7	995.0	11267.3
ARDS_025_ND1	12.9	296.4	9.4	2.0	5913.8	40.2	7.1	4167.0	73.7	522129.9	5112.8	2792.5	564.9	11668.6	2288.9	21172.3
ARDS_026_ND1	25.5	202.0	1897.6	6.2	4062.6	72.9	20.5	5860.0	207.4	912801.4	52893.3	1829.6	5827.0	0.0	1008.9	31.7
ARDS_027_ND1	34.2	201.7	565.3	21.4	6922.4	78.5	46.2	4041.2	104.2	889351.9	37695.6	12509.6	776.4	989.0	937.7	1081.0
ARDS_029_ND1	193.7	18517.8	5325.8	215.4	58087.1	99.4	20.8	24592.2	524.2	1560122.2	11256.4	22825.4	771.3	296.0	5050.5	24741.8
ARDS_030_ND1	8.8	8.2	8.8	0.6	2502.8	19.3	5.6	992.2	31.5	230912.5	4311.1	734.5	94.8	2549.1	961.4	1217.7
ARDS_031_ND1	12.0	113.9	11.6	4.5	11132.6	33.2	7.1	3158.4	55.7	592662.7	16921.9	1941.8	231.7	2175.6	644.0	6303.8
ARDS_034_ND1	16.1	29.8	114.8	2.7	3641.9	15.8	0.0	9278.0	40.3	418110.3	36533.7	4158.4	496.9	3316.9	1357.0	7465.6
ARDS_035_ND1	15.7	6.7	4.7	0.4	7570.3	6.4	0.0	2553.9	28.3	609521.3	22489.3	2876.0	376.0	1067.0	927.4	4318.0
ARDS_036_ND1	11.9	447.3	48.8	5.5	2262.1	8.2	0.0	7175.7	60.8	779172.1	30409.8	2366.7	483.4	927.6	1015.9	2739.6
ARDS_037_ND1	19.0	25.3	21.4	14.8	8184.9	13.3	0.0	3151.2	108.4	475976.6	6008.3	2788.6	236.2	1938.8	2158.6	7413.3
ARDS_038_ND1	9.5	2.7	18.8	1.4	7256.0	13.3	0.0	1927.9	22.9	621222.4	59352.9	2765.3	359.7	1260.5	387.0	3486.7
ARDS_039_ND1	4.2	34.0	13.4	1.0	13405.8	17.9	3.1	16717.3	8.9	1040443.8	33550.6	4336.6	216.1	192.3	185.6	1815.7
ARDS_040_ND1	16.1	124.3	25.2	5.2	13662.0	15.8	9.1	6130.7	9.8	819607.2	11067.2	3331.1	268.3	2232.5	1028.3	5666.4
ARDS_041_ND1	12.9	220.4	15.9	6.2	5112.2	12.9	1.7	1866.7	6.6	764218.2	18768.2	2681.2	386.1	2084.3	1432.2	5783.7
ARDS_042_ND1	7.2	32.9	35.2	11.7	2110.3	21.7	1.0	14573.6	33.6	563502.7	17210.8	1590.0	312.3	1782.4	577.0	4586.8
ARDS_043_ND1	9.4	10.6	14.1	19.3	1147.0	22.1	1.7	7177.6	60.2	676731.0	48785.3	1447.1	332.6	637.6	1825.6	3612.8
ARDS_044_ND1	5.8	3.9	13.9	0.8	1989.1	16.2	1.4	3292.0	18.7	485282.5	5827.7	1377.8	167.7	5357.1	2985.2	5522.1
ARDS_045_ND1	5.1	10.6	7.4	3.5	7598.3	14.6	12.0	3539.8	11.2	566154.1	12603.0	1721.4	165.0	4624.2	2098.2	3765.4
ARDS_046_ND1	7.0	6.1	7.2	48.3	2868.8	13.8	0.0	1505.2	7.5	741457.2	16140.6	1913.7	149.5	2430.0	1353.7	3944.8
CHOP_ARDS_001	33.8	19.5	66.7	4.0	6707.4	9.9	0.0	16276.5	51.0	363210.7	14747.7	3786.5	1303.0	359.7	336.8	921.5
CHOP_ARDS_002	28.2	13.2	6.9	0.0	2817.5	11.6	0.0	6202.9	71.7	612631.3	17242.5	2014.3	391.7	2420.5	87.1	915.3
CHOP_ARDS_003	10.6	12.1	1.8	0.2	9009.2	10.7	0.0	3435.3	32.4	964291.9	25335.5	1735.9	294.0	221.7	59.7	741.4
CHOP_ARDS_005	18.1	316.4	1313.8	8.3	27054.4	26.6	0.0	2156.3	41.0	1027977.6	29767.8	3662.2	538.9	65.6	73.7	359.0
CHOP_ARDS_006	14.0	5.9	11.3	2.1	7133.6	16.6	0.0	2938.0	70.2	421215.6	46625.9	1252.7	294.7	310.4	132.5	2176.1



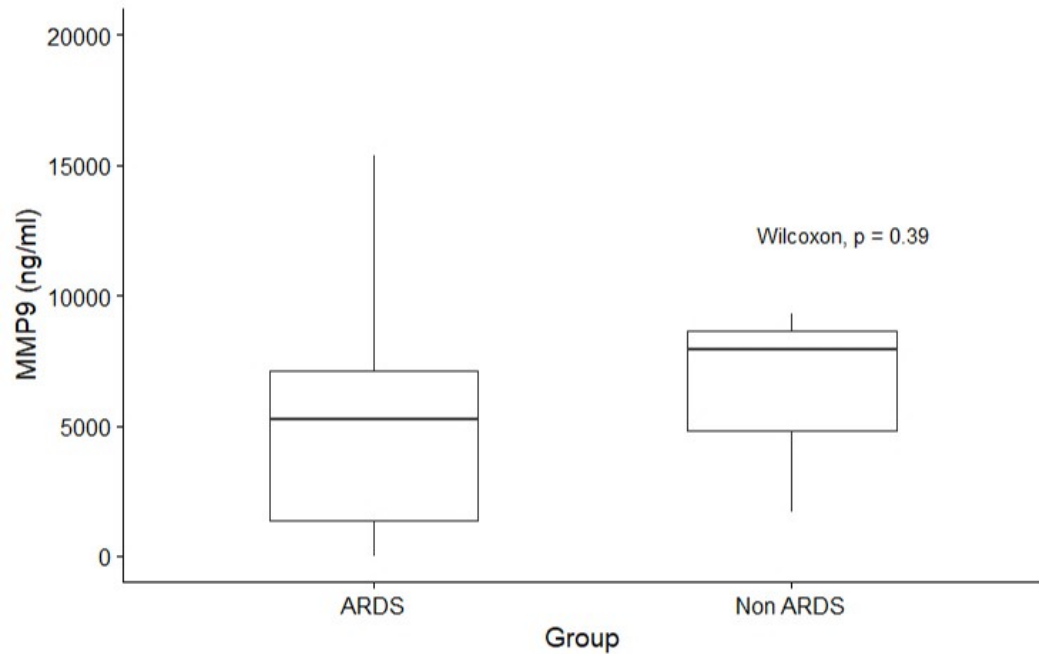
MMP9 Day 1



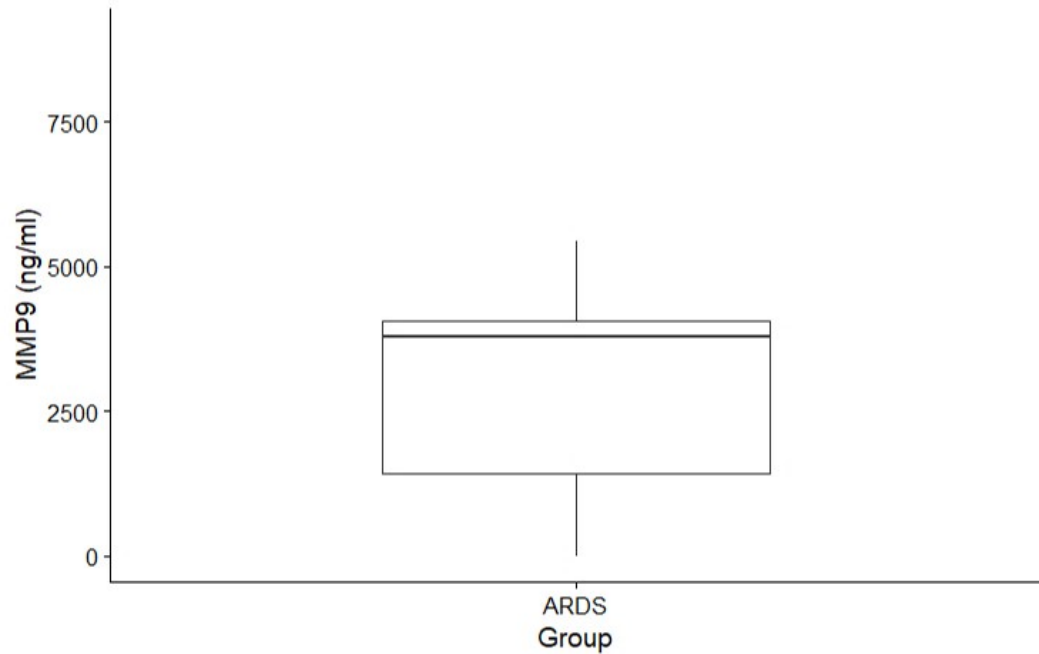
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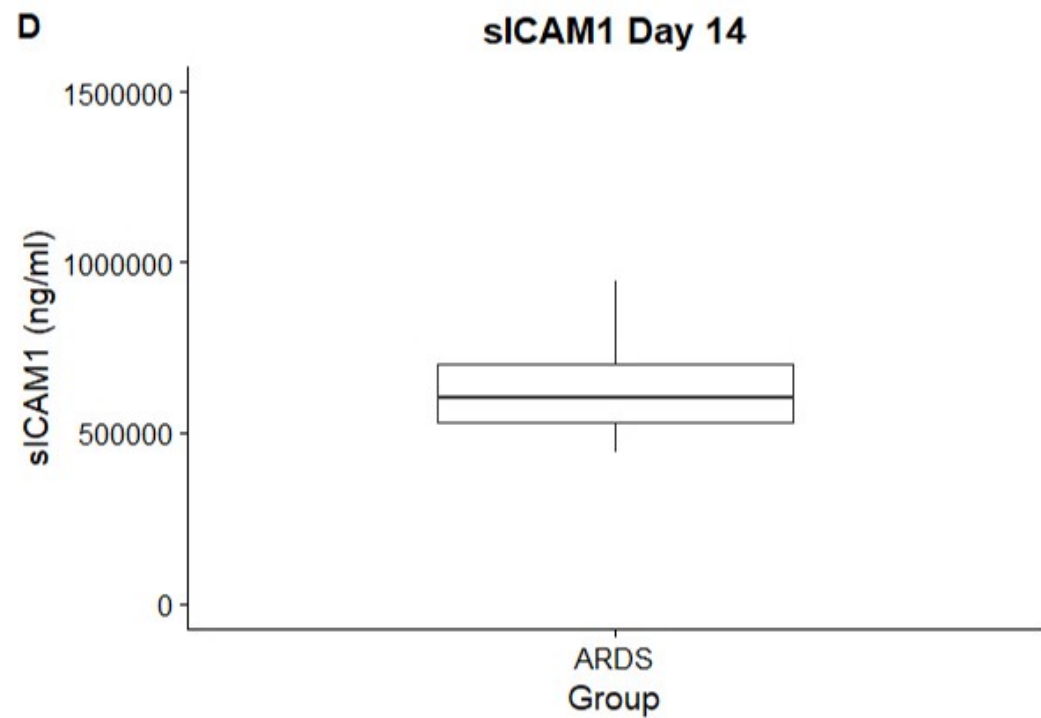
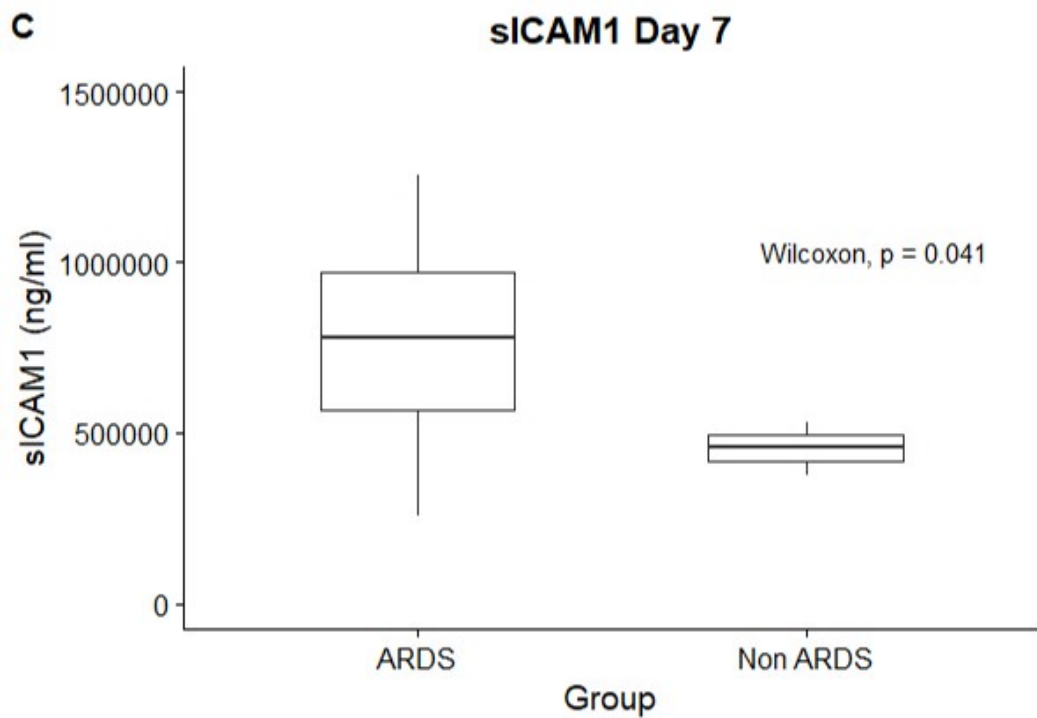
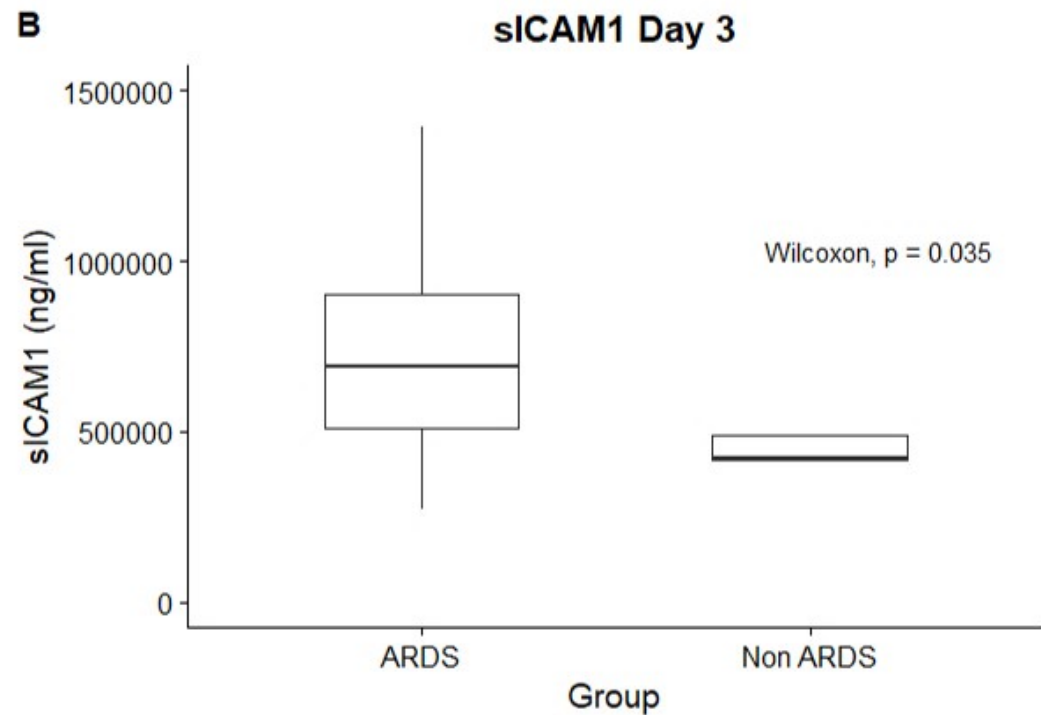
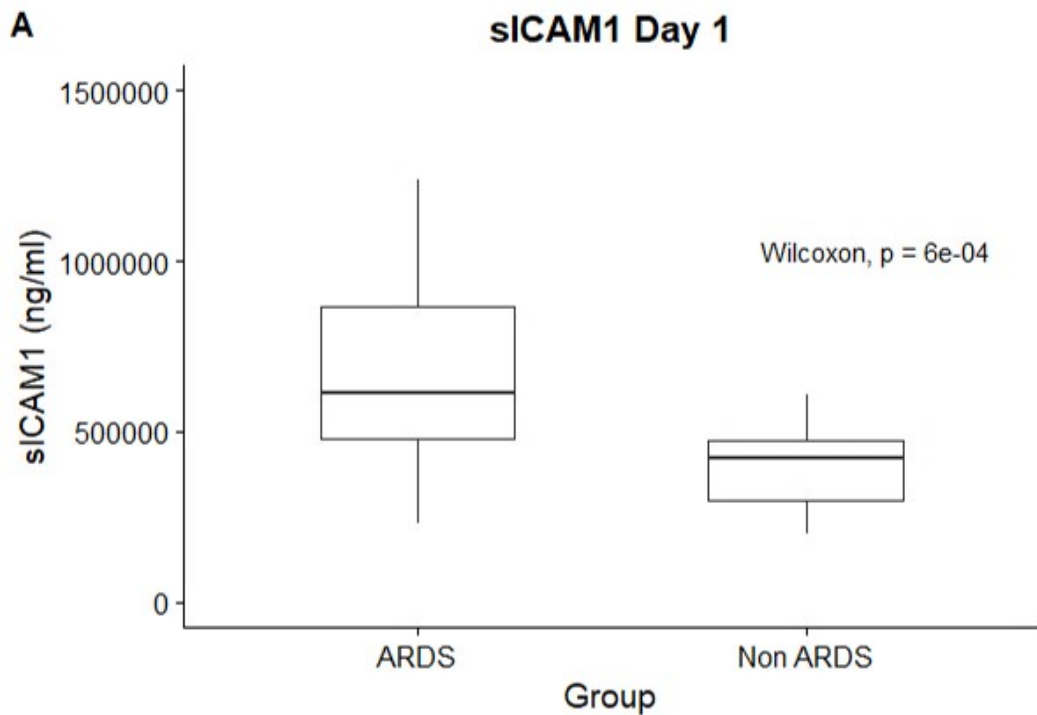


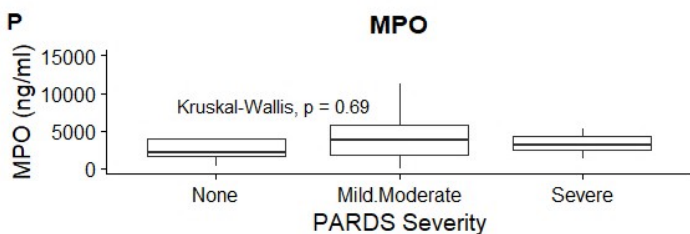
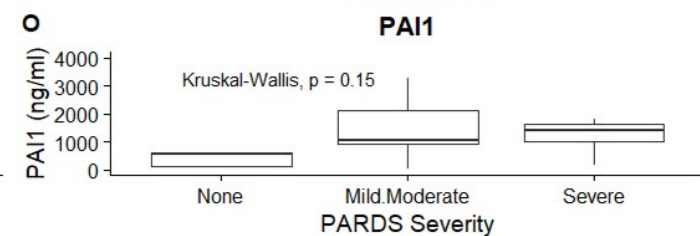
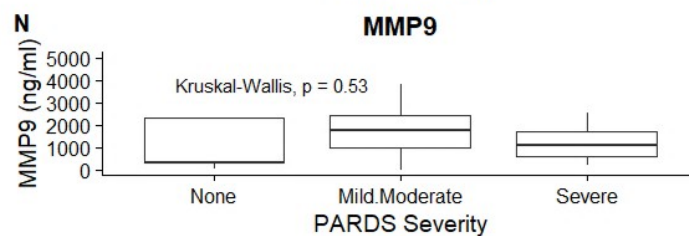
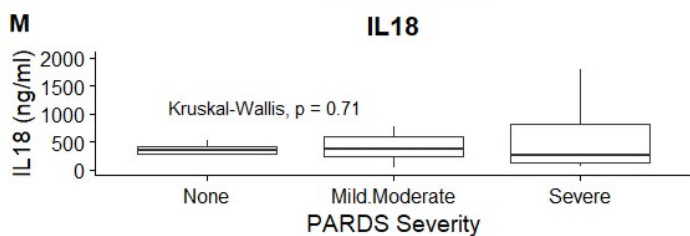
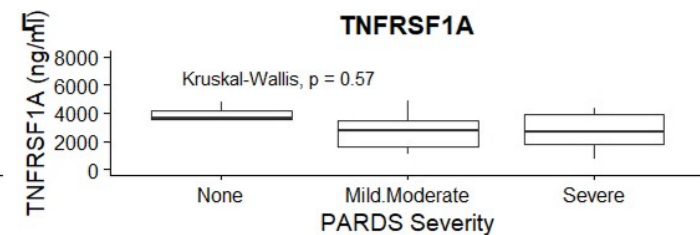
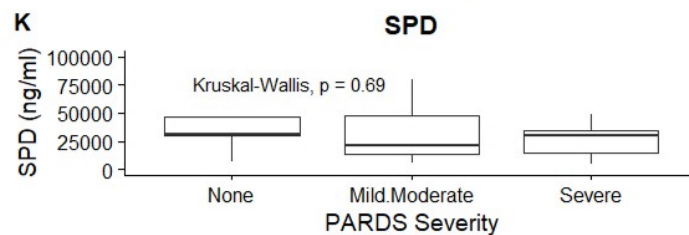
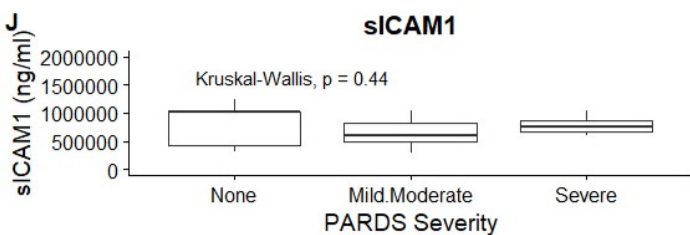
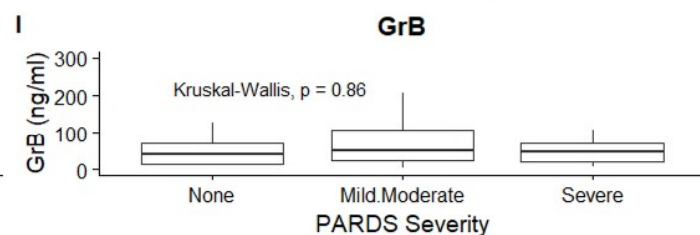
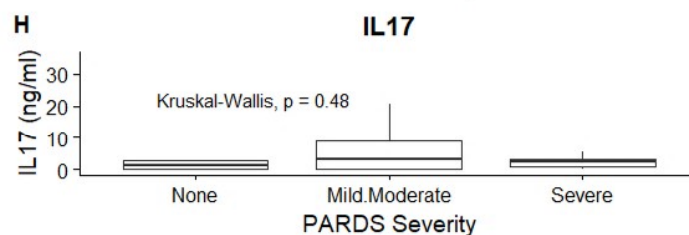
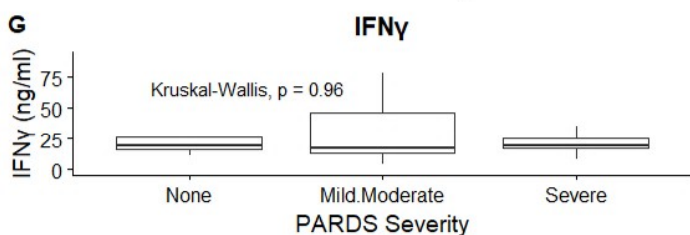
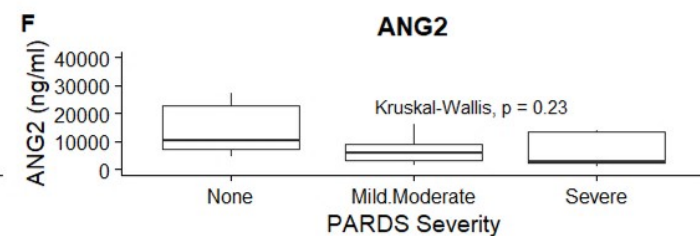
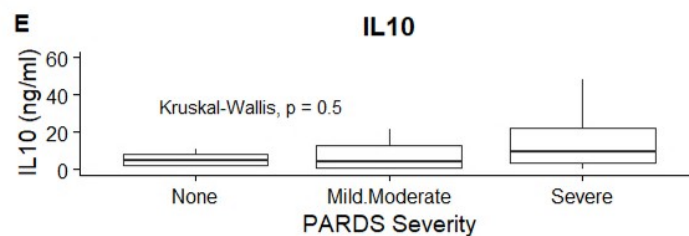
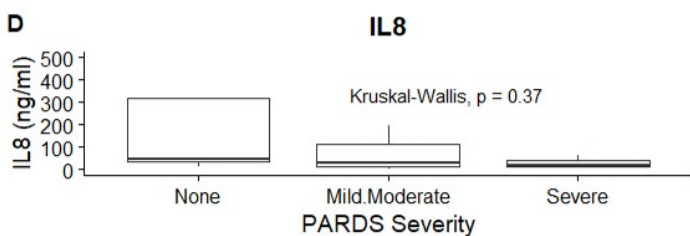
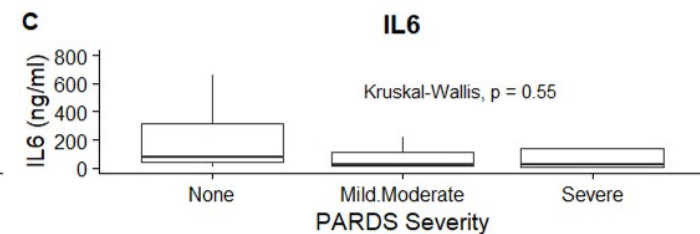
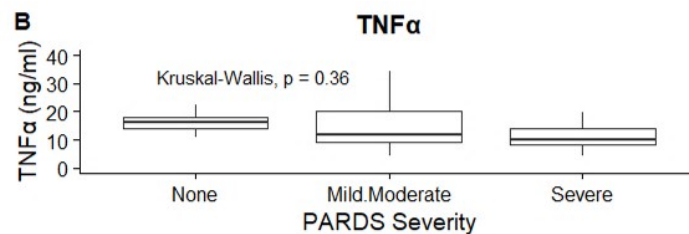
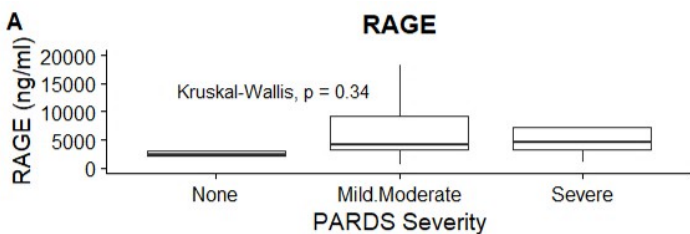
MMP9 Day 7

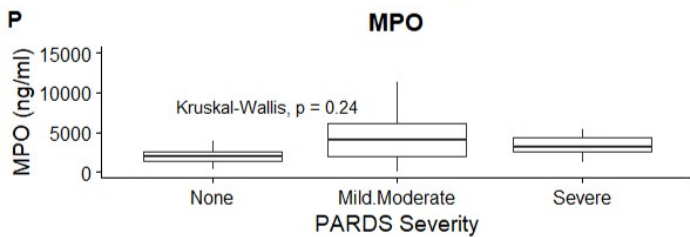
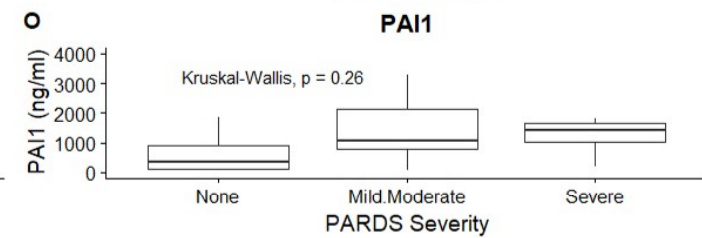
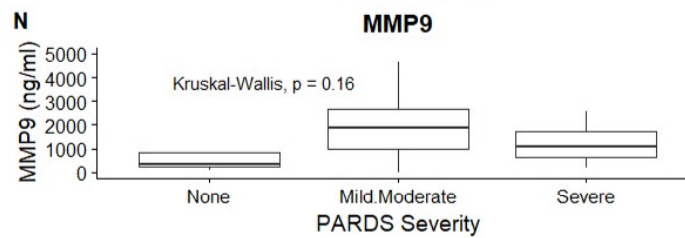
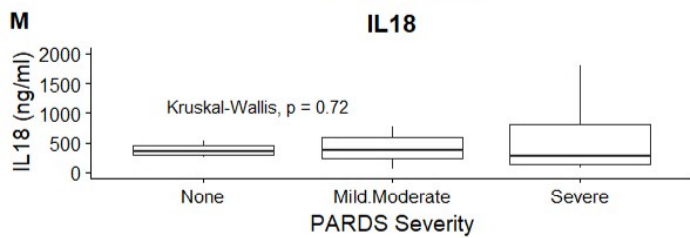
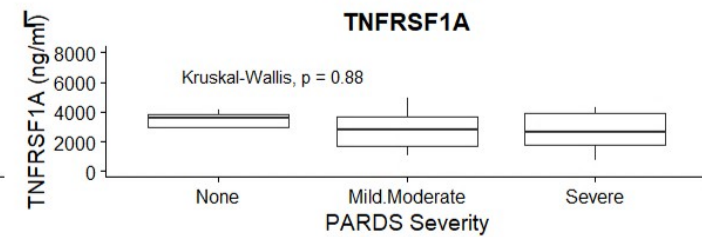
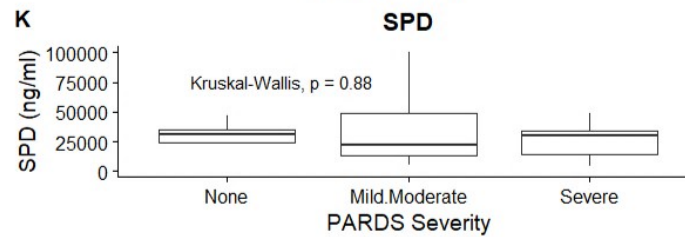
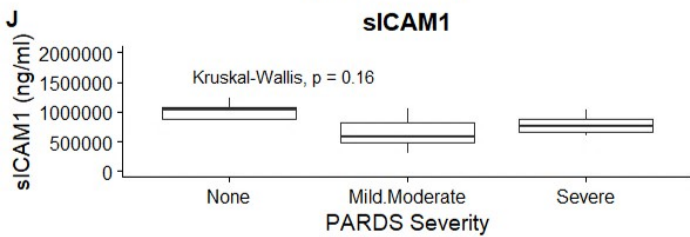
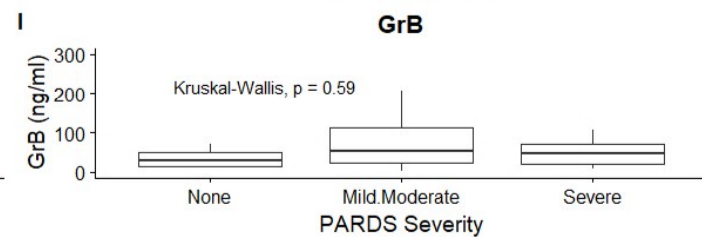
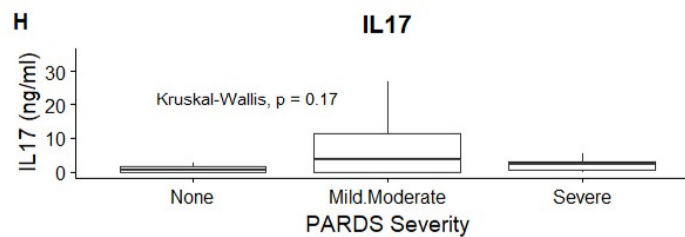
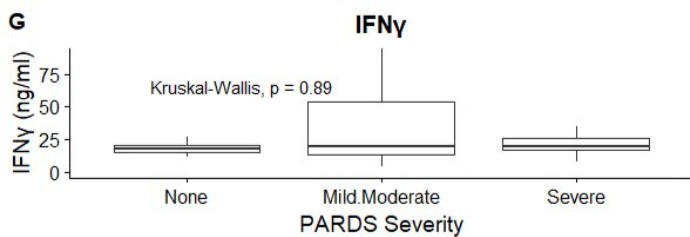
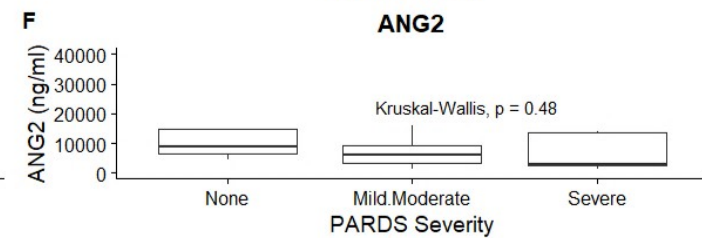
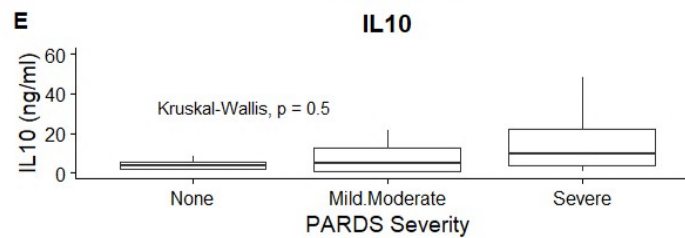
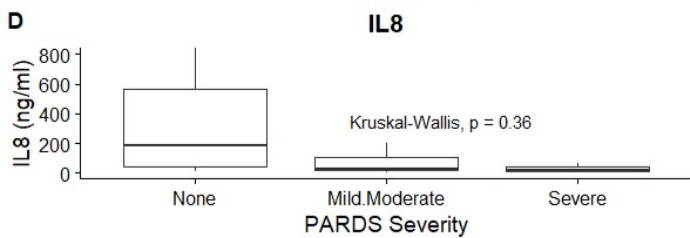
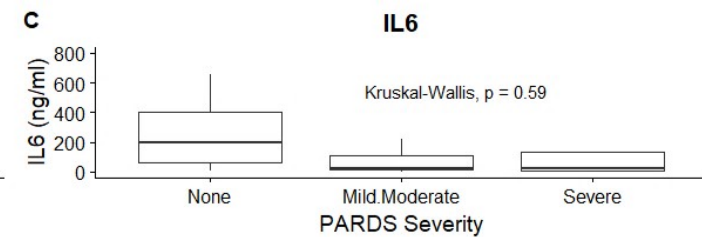
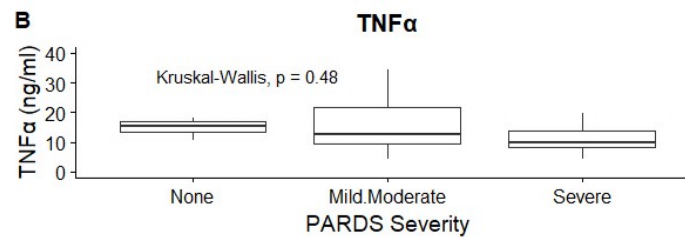
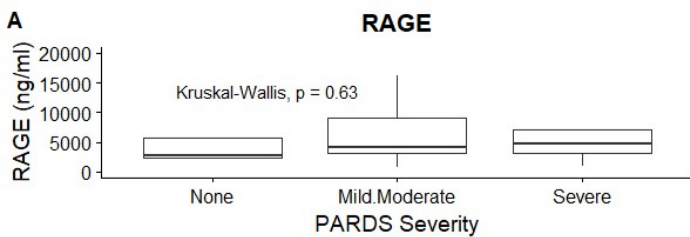


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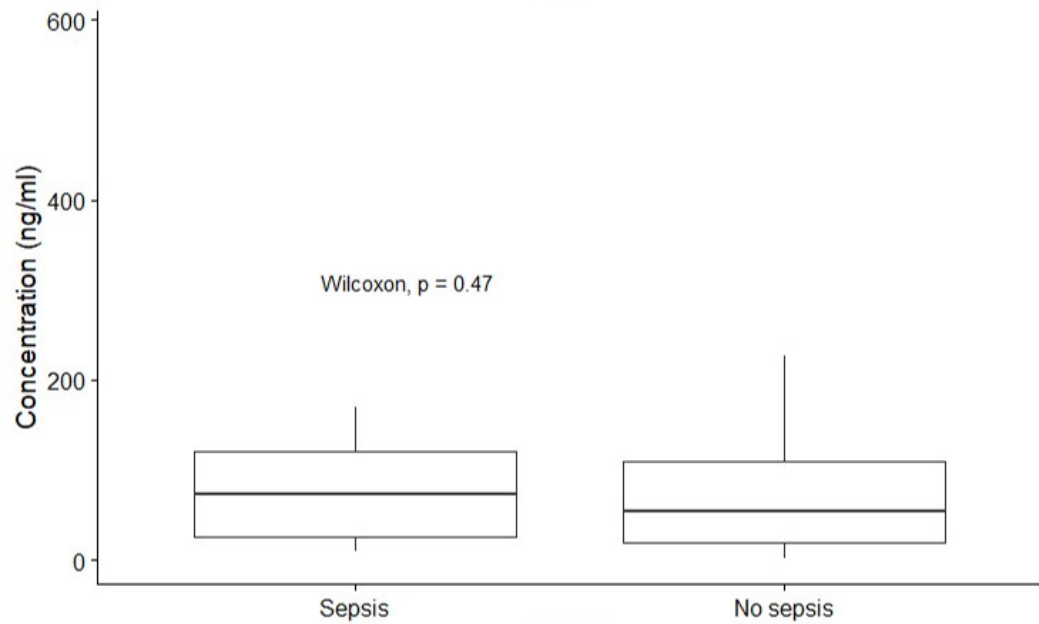




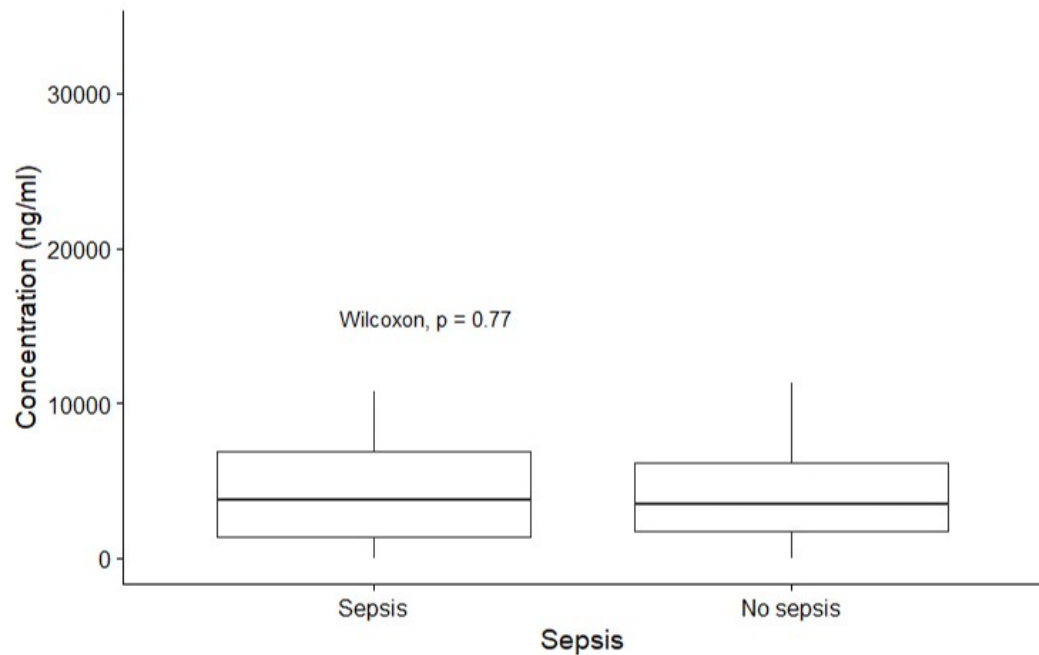




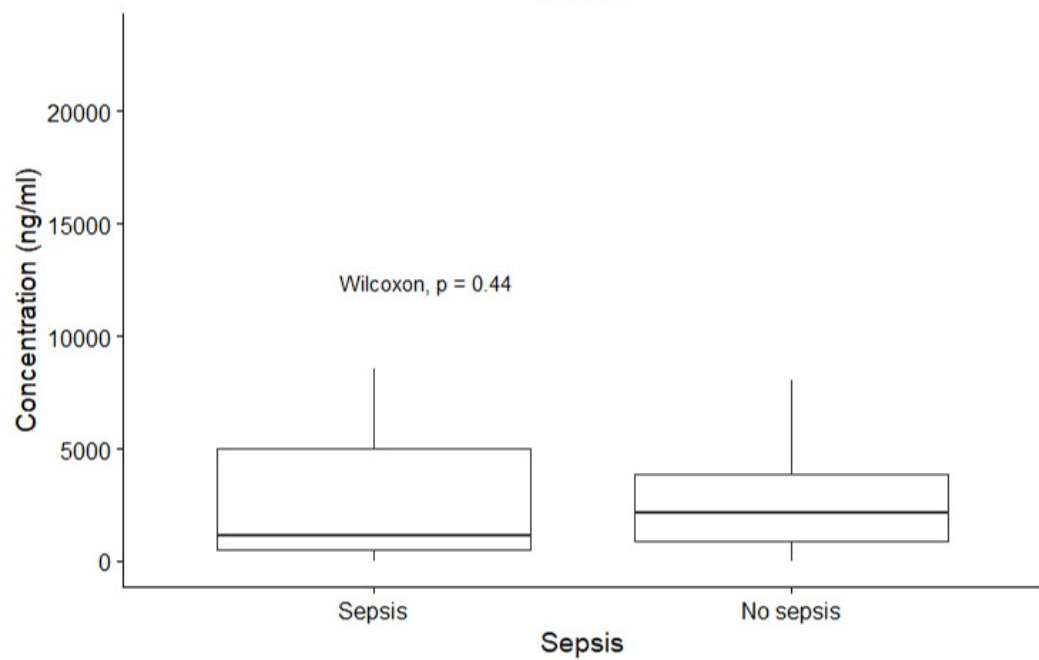
GrB



MPO



MMP9



Supplemental Figure 1: Batch Correction of Mean Fluorescent Intensities. Coefficients of variation before batch correction.

Supplemental Figure 2: Batch Correction of Mean Fluorescent Intensities. Coefficients of variation after batch correction.

Supplemental Figure 3: Changes in Biomarker Concentration with Changing OSI. A scatter plot of change in plasma biomarker concentration (ng/mL) and change in oxygenation saturation index (OSI) ($OSI = \text{mean airway pressure} \times \text{fraction of inspired oxygen (FiO}_2\text{)}/\text{oxygen saturation}$). Both R and p values are denoted with 95% confidence interval (CI) denoted by gray shaded area. All biomarkers were significantly and positively correlated with worsening lung injury except RAGE, IL6, IL8, IFN γ , and MMP-9. (A) Receptor For Advanced Glycation End Products (RAGE). (B) Tumor Necrosis Factor Alpha (TNF α). (C) Interleukin-6 (IL6). (D) Interleukin-8 (IL8). (E) Interleukin-10 (IL10). (F) Angiopoietin-2 (ANG2). (G) Interferon- γ (IFN γ). (H) Interleukin-17 (IL17). (I) Granzyme B (GrB). (J) Soluble Intercellular Adhesion Molecule-1 (sICAM1). (K) Surfactant Protein D (SPD). (L) TNF Receptor Soluble Factor 1A (TNFRSF1A). (M) Interleukin-18 (IL18). (N) Matrix Metalloproteinase 9 (MMP-9). (O) Plasminogen Activator Inhibitor-1 (PAI1). (P) Myeloperoxidase (MPO).

Supplemental Figure 4: Sensitivity Analysis of Change in Biomarker Concentration with Changing OSI. A scatter plot of change in plasma biomarker concentration (ng/mL) and change in oxygenation saturation index (OSI) ($OSI = \text{mean airway pressure} \times \text{fraction of inspired oxygen (FiO}_2\text{)}/\text{oxygen saturation}$). Both R and p values are denoted with 95% confidence interval (CI) denoted by gray shaded area. All biomarkers were significantly and positively correlated with worsening lung injury except RAGE, IL6, IL8, IFN γ , and MMP-9. (A) Receptor For Advanced

Glycation End Products (RAGE). (B) Tumor Necrosis Factor Alpha (TNF α). (C) Interleukin-6 (IL6). (D) Interleukin-8 (IL8). (E) Interleukin-10 (IL10). (F) Angiotensin-2 (ANG2). (G) Interferon- γ (IFN γ). (H) Interleukin-17 (IL17). (I) Granzyme B (GrB). (J) Soluble Intercellular Adhesion Molecule-1 (sICAM1). (K) Surfactant Protein D (SPD). (L) TNF Receptor Soluble Factor 1A (TNFRSF1A). (M) Interleukin-18 (IL18). (N) Matrix Metalloproteinase 9 (MMP-9). (O) Plasminogen Activator Inhibitor-1 (PAI1). (P) Myeloperoxidase (MPO).

Supplemental Figure 5: Day 1 plasma biomarker levels in PARDS (n = 50) and non PARDS (n = 13) subjects. Eight of the sixteen biomarkers tested were significantly higher in PARDS patients compared to non-PARDS patients while one biomarker (MMP9) was significantly higher in non-PARDS patients. Biomarker concentrations are in ng/ml and P-values are noted in plots. (A) Receptor For Advanced Glycation End Products (RAGE). (B) Tumor Necrosis Factor Alpha (TNF α). (C) Interleukin-6 (IL6). (D) Interleukin-8 (IL8). (E) Interleukin-10 (IL10). (F) Angiotensin-2 (ANG2). (G) Interferon- γ (IFN γ). (H) Interleukin-17 (IL17). (I) Granzyme B (GrB). (J) Soluble Intercellular Adhesion Molecule-1 (sICAM1). (K) Surfactant Protein D (SPD). (L) TNF Receptor Soluble Factor 1A (TNFRSF1A). (M) Interleukin-18 (IL18). (N) Matrix Metalloproteinase 9 (MMP-9). (O) Plasminogen Activator Inhibitor-1 (PAI1). (P) Myeloperoxidase (MPO).

Supplemental Figure 6: Sensitivity analysis of Day 1 plasma biomarker levels in PARDS (n = 50) and non PARDS (n = 13) subjects. Eight of the sixteen biomarkers tested were significantly higher in PARDS patients compared to non-PARDS patients while one biomarker (MMP9) was significantly higher in non-PARDS patients. Biomarker concentrations are in ng/ml and P-values are noted in plots. (A) Receptor For Advanced Glycation End Products (RAGE). (B) Tumor Necrosis Factor Alpha (TNF α). (C) Interleukin-6 (IL6). (D) Interleukin-8 (IL8). (E) Interleukin-10 (IL10). (F) Angiotensin-2 (ANG2). (G) Interferon- γ (IFN γ). (H) Interleukin-17 (IL17). (I)

Granzyme B (GrB). (J) Soluble Intercellular Adhesion Molecule-1 (sICAM1). (K) Surfactant Protein D (SPD). (L) TNF Receptor Soluble Factor 1A (TNFRSF1A). (M) Interleukin-18 (IL18). (N) Matrix Metalloproteinase 9 (MMP-9). (O) Plasminogen Activator Inhibitor-1 (PAI1). (P) Myeloperoxidase (MPO).

Supplemental Figure 7: Heatmap of each PARDS subject and biomarker concentration in ng/mL on day 1. PARDS subject 29 had very elevated levels of most biomarkers however most other subjects had no consistent pattern. Biomarkers included: Receptor For Advanced Glycation End Products (RAGE), Tumor Necrosis Factor Alpha (TNF α), Interleukin-6 (IL6), Interleukin-8 (IL8), Interleukin-10 (IL10), Angiopoietin-2 (ANG2), Interferon- γ (IFN γ), Interleukin-17 (IL17), Granzyme B (GrB), Soluble Intercellular Adhesion Molecule-1 (sICAM1), Surfactant Protein D (SPD), TNF Receptor Soluble Factor 1A (TNFRSF1A), Interleukin-18 (IL18), Matrix Metalloproteinase 9 (MMP-9), Plasminogen Activator Inhibitor-1 (PAI1), and Myeloperoxidase (MPO).

Supplemental Figure 8: The concentration of matrix metalloproteinase 9 (MMP-9) in PARDS (n = 50) and critically ill subjects without PARDS (n = 13) on day 1, day 3 (n = 33 PARDS and n = 5 non PARDS), day 7 (n = 25 PARDS and n = 3 non PARDS), and day 14 (n = 13 PARDS and n = 0 non PARDS). MMP-9 was more elevated in the plasma of the non-PARDS subjects on days 1, 3, and 7. This difference was only statistically significant on day 1. Only PARDS subjects were available for sample collection on day 14 as most non PARDS subjects had discharged home. Concentrations are in ng/mL and p values are noted in the graph.

Supplemental Figure 9: The concentration of soluble intercellular adhesion molecule 1 (sICAM1) in PARDS and critically ill subjects without PARDS on day 1 (n = 50 PARDS and n = 13 non

PARDS), day 3 (n = 33 PARDS and n = 5 non PARDS), day 7 (n = 25 PARDS and n = 3 non PARDS), and day 14 (n = 13 PARDS and n = 0 non PARDS). sICAM1 was more elevated in the plasma of PARDS subjects on days 1, 3, and 7, and was statistically significant. Only PARDS subjects were available for sample collection on day 14 as most non PARDS subjects had discharged home. Concentrations are in ng/mL and p values are noted in the graph.

Supplemental Figure 10: The correlation between day 1 plasma biomarker concentration and day 1 PARDS severity in PARDS (n = 50) subjects. There was no statistically significant correlation between biomarker concentration and severity for any of the biomarkers we tested. (A) Receptor For Advanced Glycation End Products (RAGE). (B) Tumor Necrosis Factor Alpha (TNF α). (C) Interleukin-6 (IL6). (D) Interleukin-8 (IL8). (E) Interleukin-10 (IL10). (F) Angiopoietin-2 (ANG2). (G) Interferon- γ (IFN γ). (H) Interleukin-17 (IL17). (I) Granzyme B (GrB). (J) Soluble Intercellular Adhesion Molecule-1 (sICAM1). (K) Surfactant Protein D (SPD). (L) TNF Receptor Soluble Factor 1A (TNFRSF1A). (M) Interleukin-18 (IL18). (N) Matrix Metalloproteinase 9 (MMP-9). (O) Plasminogen Activator Inhibitor-1 (PAI1). (P) Myeloperoxidase (MPO).

Supplemental Figure 11: Sensitivity analysis of the correlation between day 1 biomarker level and day 1 PARDS severity in PARDS (n = 50) subjects. There was no correlation between biomarkers concentration and PARDS severity. (A) Receptor For Advanced Glycation End Products (RAGE). (B) Tumor Necrosis Factor Alpha (TNF α). (C) Interleukin-6 (IL6). (D) Interleukin-8 (IL8). (E) Interleukin-10 (IL10). (F) Angiopoietin-2 (ANG2). (G) Interferon- γ (IFN γ). (H) Interleukin-17 (IL17). (I) Granzyme B (GrB). (J) Soluble Intercellular Adhesion Molecule-1 (sICAM1). (K) Surfactant Protein D (SPD). (L) TNF Receptor Soluble Factor 1A (TNFRSF1A). (M) Interleukin-18 (IL18). (N) Matrix Metalloproteinase 9 (MMP-9). (O) Plasminogen Activator Inhibitor-1 (PAI1). (P) Myeloperoxidase (MPO).

Supplemental Figure 12: Concentrations of granzyme B (GrB), myeloperoxidase (MPO), and matrix metalloproteinase 9 (MMP-9) in PARDS patients with sepsis and without sepsis across all study time points. There was no difference in any of the three biomarkers between groups. Biomarker concentrations are in ng/ml and p values are noted on the plots.