Supplement

Supplemental Methods

The time to recovery endpoint was not pre-registered but was included post hoc as an endpoint after the authors decided it would be complementary to the mortality endpoint in a clinically meaningful way. Additionally, the greater number of recovery events would allow for a more precise analysis of the risk scores. The decision to include the recovery endpoint was made before the analysis for the endpoint was conducted. The deterioration endpoint was defined in the registration as time to progression to ordinal score 6 or 7. Before conducting the deterioration analysis, but after the concept sheet was registered, the authors agreed that modifying the endpoint to include death would better reflect the definition of deterioration.

NEWS2 and the Carr et al. extension of NEWS2 were not analyzed because hypercapnic respiratory failure status, a component of NEWS2, was not measured in the trial.

Supplemental Table 1. Ordinal scale used in ACTT-1 (33)

Ordinal Category	Definition
1	not hospitalized and no limitations on activities
2	not hospitalized, but with home oxygen requirement and/or limitations on activities
3	hospitalized but not requiring either supplemental oxygen or ongoing medical care
4	hospitalized and not requiring oxygen but requiring medical care
5	hospitalized and requiring supplemental oxygen
6	hospitalized and requiring noninvasive ventilation or high-flow oxygen
7	hospitalized and receiving invasive mechanical ventilation or ECMO[a]
8	death

a. ECMO: extracorporeal membrane oxygenation

Supplemental Table 2. Demographics table for ACTT-1 cohort Ordinal scale used in ACTT-1 (33)

Characteristic	Placebo (n=512)	Remdesivir (n=531)	All (n=1043)
Age - mean (sd)	59.1 (15.5)	58.6 (14.6)	58.9 (15.0)
Male sex - no. (%)	325 (63.4)	347 (65.3)	672 (64.4)
Race - no. (%)			
American Indian or Alaska Native	3 (0.6)	4 (0.8)	7 (0.7)
Asian	56 (10.9)	79 (14.9)	135 (12.9)
Black or African American	113 (22.1)	105 (19.8)	218 (20.9)
Multi-Racial	1 (0.2)	2 (0.4)	3 (0.3)
Native Hawaiin or Other Pacific Islander	2 (0.4)	2 (0.4)	4 (0.4)
White	283 (55.3)	272 (51.2)	555 (53.2)
Unknown	54 (10.5)	67 (12.6)	121 (11.6)
Hispanic or Latino - no. (%)			
Hispanic or Latino	113 (22.1)	132 (24.9)	245 (23.5)
Not Hispanic or Latino	367 (71.7)	374 (70.4)	741 (71.0)
Not Reported	14 (2.7)	15 (2.8)	29 (2.8)
Unknown	18 (3.5)	10 (1.9)	28 (2.7)
Days from symptom onset to randomization - median (IQR)	9 (7-13)	9 (6-12)	9 (6-12)
Number of comorbidities - no./total no. (%)			
None	96/510 (18.8)	96/530 (18.1)	192/1040 (18.5)
One	132/510 (25.9)	139/530 (26.2)	271/1040 (26.1)
Two or more	282/510 (55.3)	295/530 (55.7)	577/1040 (55.5)
Specific comorbidities - no./total no. (%)			
Type 2 diabetes	158/512 (30.9)	163/531 (30.7)	321/1043 (30.8)
Hypertension	260/512 (50.8)	269/531 (50.7)	529/1043 (50.7)

Obesity	231/511 (45.2)	241/530 (45.5)	472/1041 (45.3)
Baseline ordinal score - no. (%)			
4. Hospitalized and not requiring oxygen but requiring medical care	63 (12.3)	75 (14.1)	138 (13.2)
5. Hospitalized and requiring supplemental oxygen	202 (39.5)	231 (43.5)	433 (41.5)
6. Hospitalized and requiring noninvasive ventilation or high-flow oxygen	98 (19.1)	94 (17.7)	192 (18.4)
7. Hospitalized and receiving invasive mechanical ventilation or ECMO	149 (29.1)	131 (24.7)	280 (26.8)

Supplemental Table 3. Descriptive statistics of NEWS components. Summaries reported as either counts (%) or medians (interquartile range).

	Placebo		**Remdesivir**	
	Day 1 (n=512)	**Day 2 (n=510)**	**Day 1 (n=531)**	**Day 2 (n=526)**
NEWS				
0-3	133 (26%)	138 (27%)	149 (28%)	167 (32%)
4-6	164 (32%)	148 (29%)	191 (36%)	162 (30%)
7+	215 (42%)	224 (44%)	191 (36%)	197 (37%)
Respiratory Rate (breaths/min)	20 (18-24)	20 (18-24)	20 (18-24)	20 (18-24)
Oxygen Saturations (%)	95 (93-97)	95 (94-97)	95 (94-97)	95 (94-97)
Any Supplemental Oxygen	443 (87%)	437 (86%)	448 (84%)	426 (81%)
Temperature (Celsius)	37.1 (36.7-37.8)	37 (36.6-37.5)	37.1 (36.7-37.7)	37 (36.6-37.5)
Systolic Blood Pressure (mmHg)	120 (109-134)	120 (109-134)	120 (109-133)	120 (108-133)
Heart Rate (beats/min)	85 (73-95)	82 (72-92)	84 (74-94)	80 (71-90)
AVPU				
Alert	367 (72%)	337 (66%)	402 (76%)	382 (73%)
Voice	36 (7%)	42 (8%)	32 (6%)	33 (6%)
Pain	19 (4%)	26 (5%)	20 (4%)	27 (5%)
Unresponsive	89 (17%)	105 (21%)	75 (14%)	82 (16%)
Age (years)	60 (49-70)	60 (49-70)	59 (48.75-69)	59 (48.75-69)

Supplemental table 4. PPV/NPV of 14-day mortality for different NEWS cutoffs. Values used for Table 2 of the main manuscript are in bold.

		>2	>3	>4	>5	>6	>7	>8
Placebo	**PPV**	0.13	0.14	0.14	0.14	**0.14**	0.15	0.15
(14-day mortality rate: 0.12)	**NPV**	0.96	**0.95**	0.92	0.91	0.90	0.90	0.89
Remdesivir	**PPV**	0.07	0.08	0.09	0.10	**0.12**	0.13	0.15
(14-day mortality rate: 0.07)	**NPV**	0.97	**0.97**	0.98	0.96	0.96	0.96	0.95

Supplemental table 5. PPV/NPV of 14-day recovery for different NEWS cutoffs. Values used for Table 2 of the main manuscript are in bold.

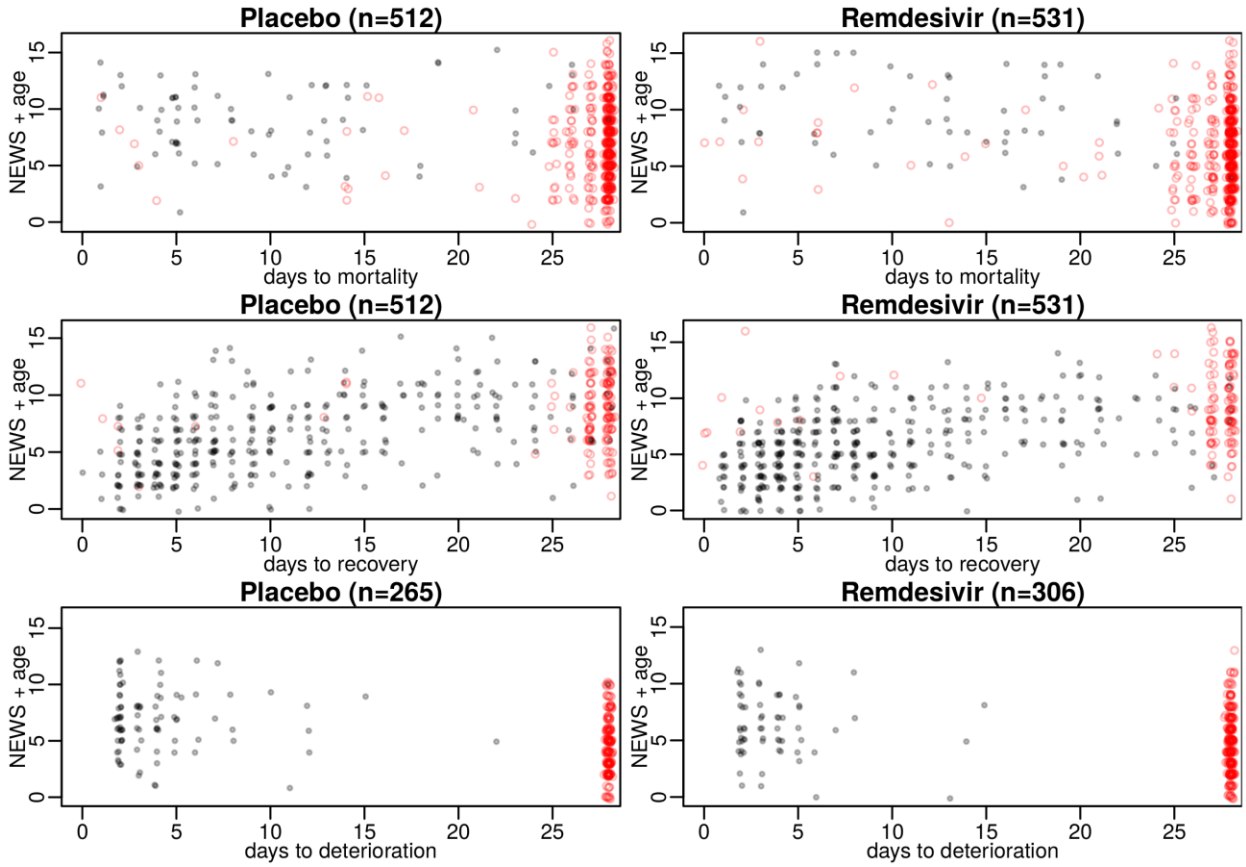
		<=2	<=3	<=4	<=5	<=6	<=7	<=8
Placebo	**PPV**	0.80	**0.77**	0.74	0.72	0.67	0.64	0.59
(14-day recovery rate: 0.49)	**NPV**	0.56	0.61	0.65	0.71	**0.75**	0.80	0.82
Remdesivir	**PPV**	0.88	**0.84**	0.83	0.81	0.77	0.75	0.71
(14-day recovery rate: 0.61)	**NPV**	0.45	0.49	0.54	0.62	**0.68**	0.75	0.80

Supplemental table 6. PPV/NPV of 14-day deterioration for different NEWS cutoffs. Values used for Table 2 of the main manuscript are in bold.

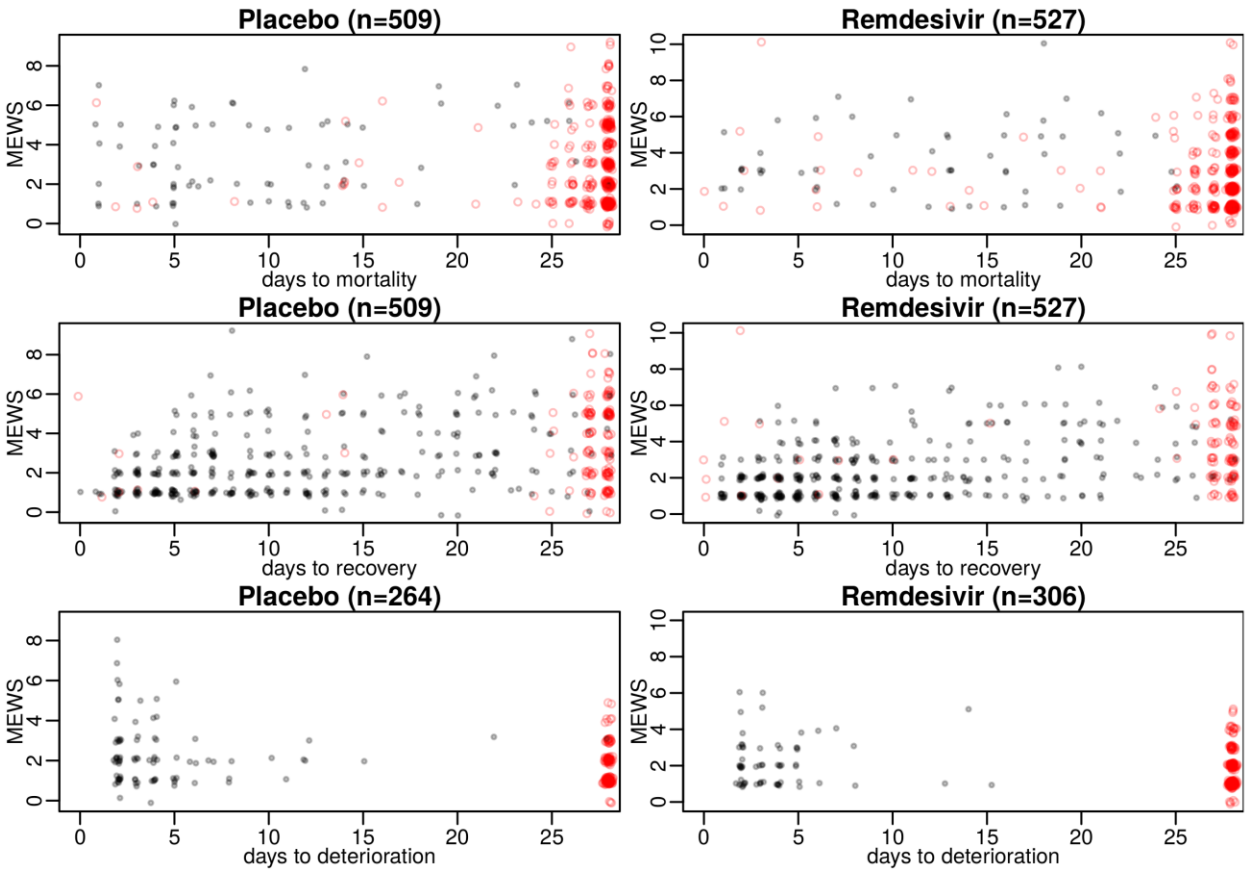
		>2	>3	>4	>5	>6	>7	>8
Placebo	**PPV**	0.40	0.46	0.48	0.57	**0.62**	0.70	0.80
(14-day deterioration rate: 0.33)	**NPV**	0.85	**0.83**	0.78	0.77	0.73	0.71	0.70
Remdesivir	**PPV**	0.24	0.28	0.31	0.33	**0.37**	0.42	0.50
(14-day deterioration rate: 0.21)	**NPV**	0.87	**0.89**	0.86	0.83	0.82	0.81	0.80

Supplemental Figures 1. Descriptive scatterplots

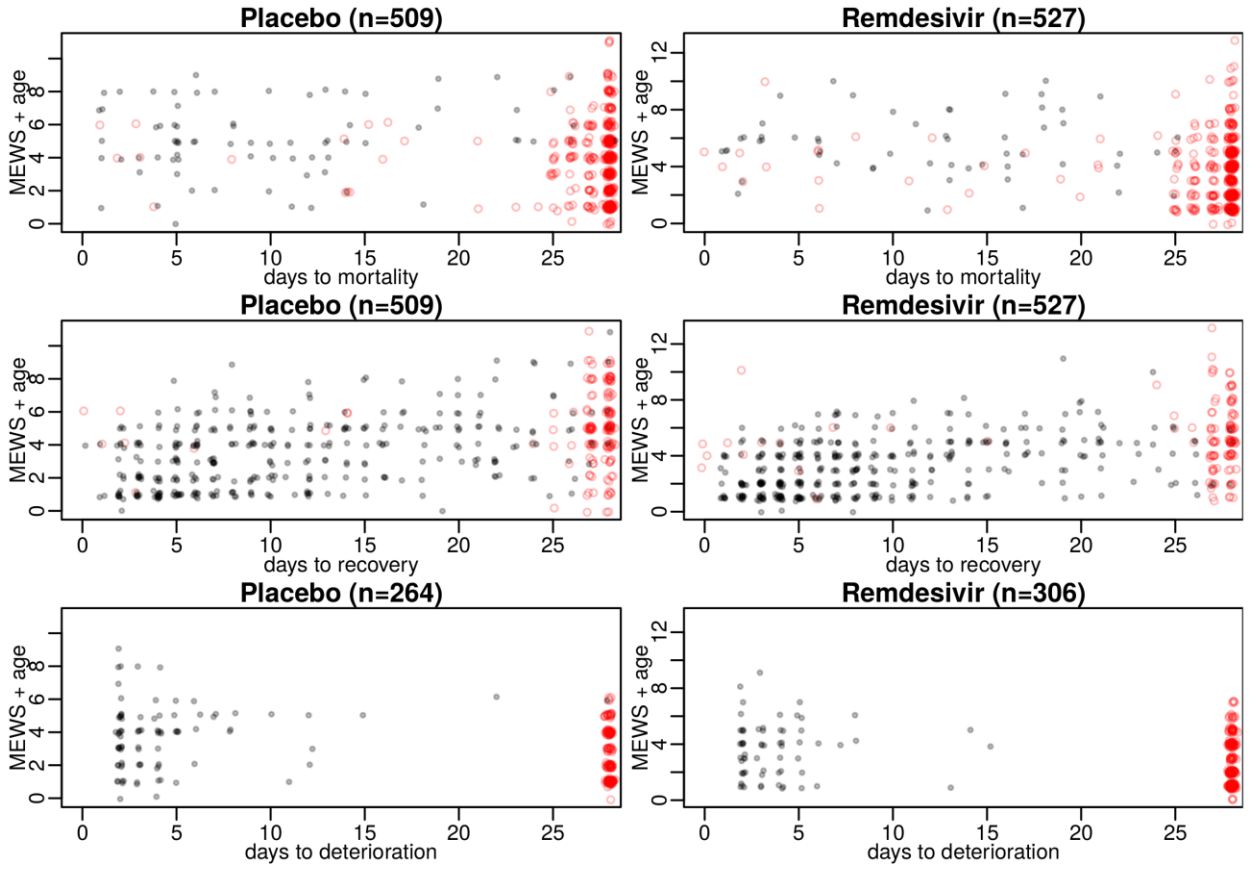
1A. Illustration of baseline NEWS+age plotted against different endpoints, by placebo arm and remdesivir arm. Gray dots represent events and red dots represent censoring. Points are jittered to address overplotting.



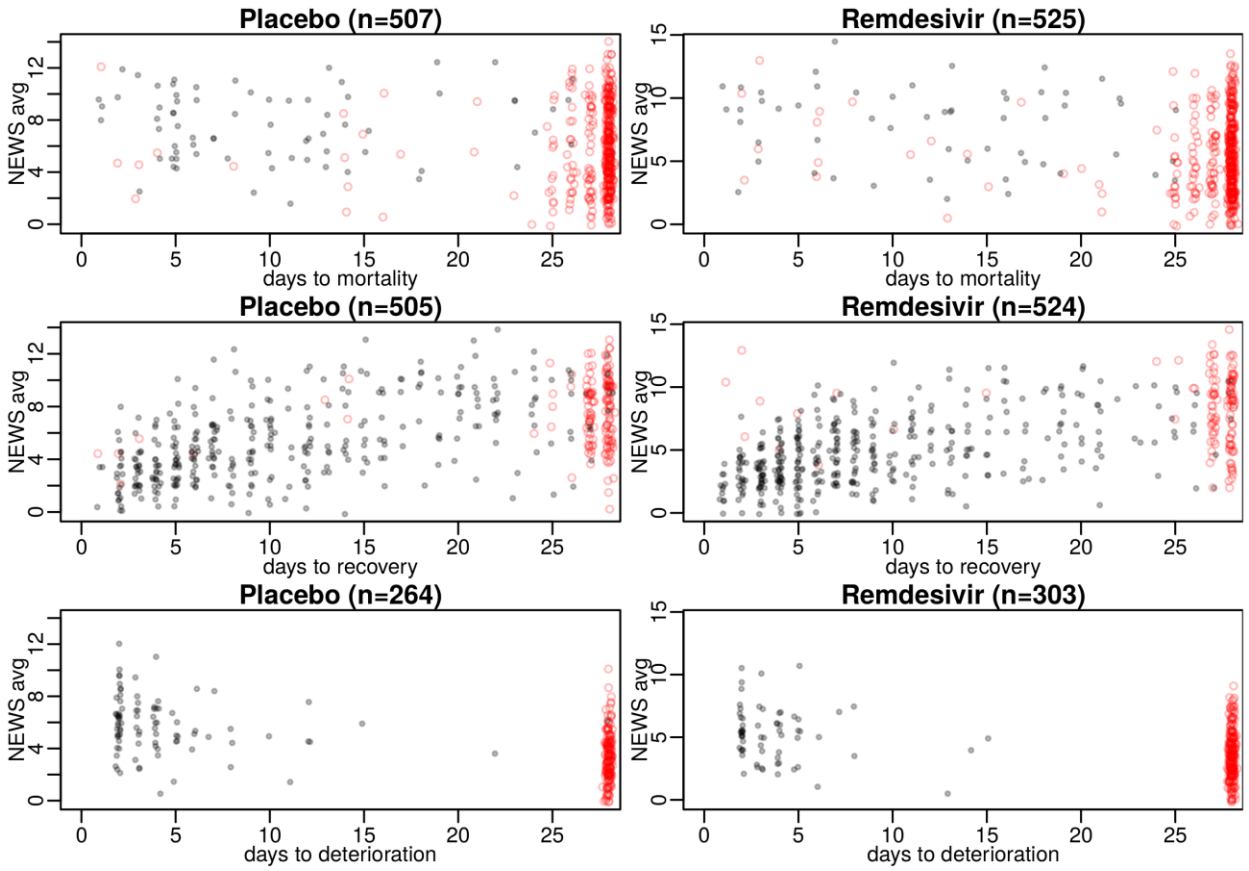
1B. Illustration of baseline MEWS plotted against different endpoints, by placebo arm and remdesivir arm. Gray dots represent events and red dots represent censoring. Points are jittered to address overplotting.



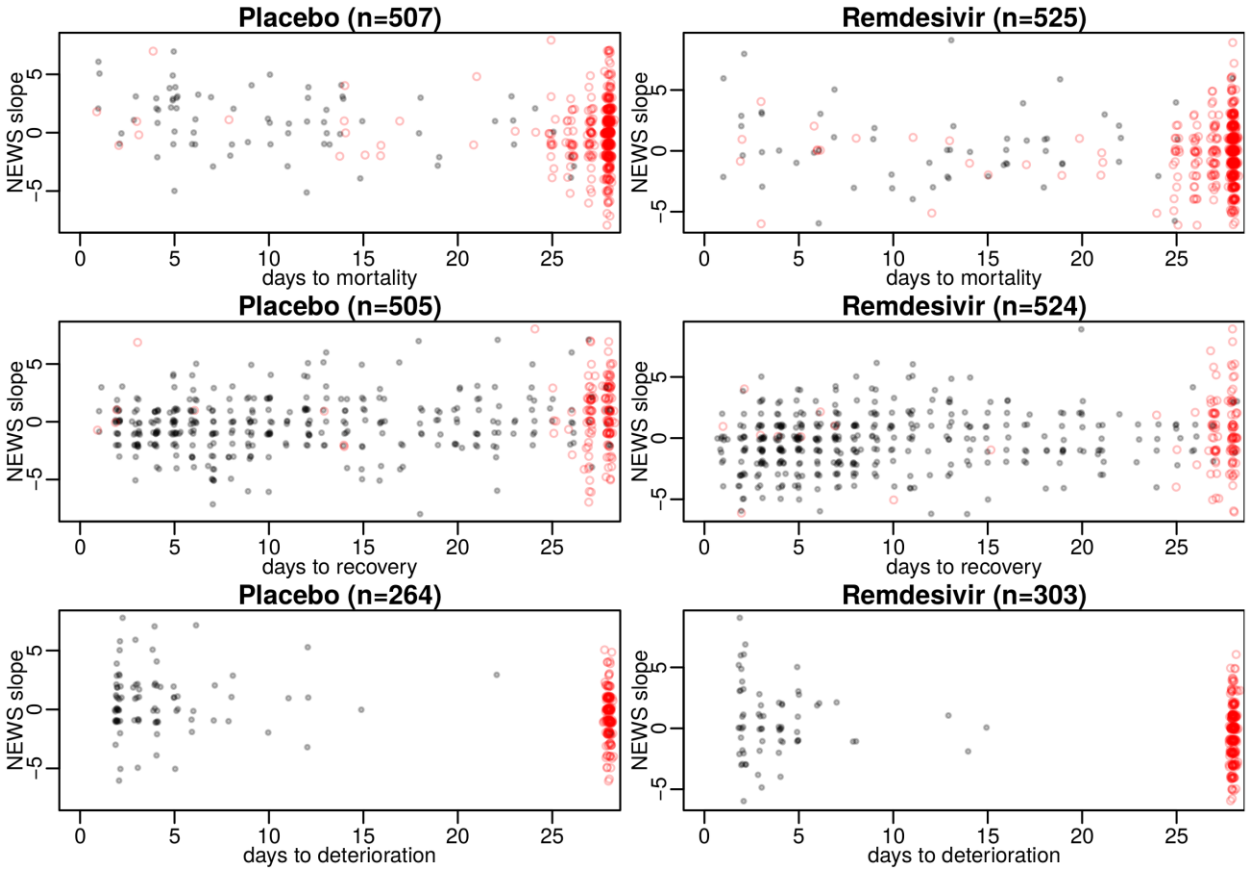
1C. Illustration of baseline MEWS+age plotted against different endpoints, by placebo arm and remdesivir arm. Gray dots represent events and red dots represent censoring. Points are jittered to address overplotting.



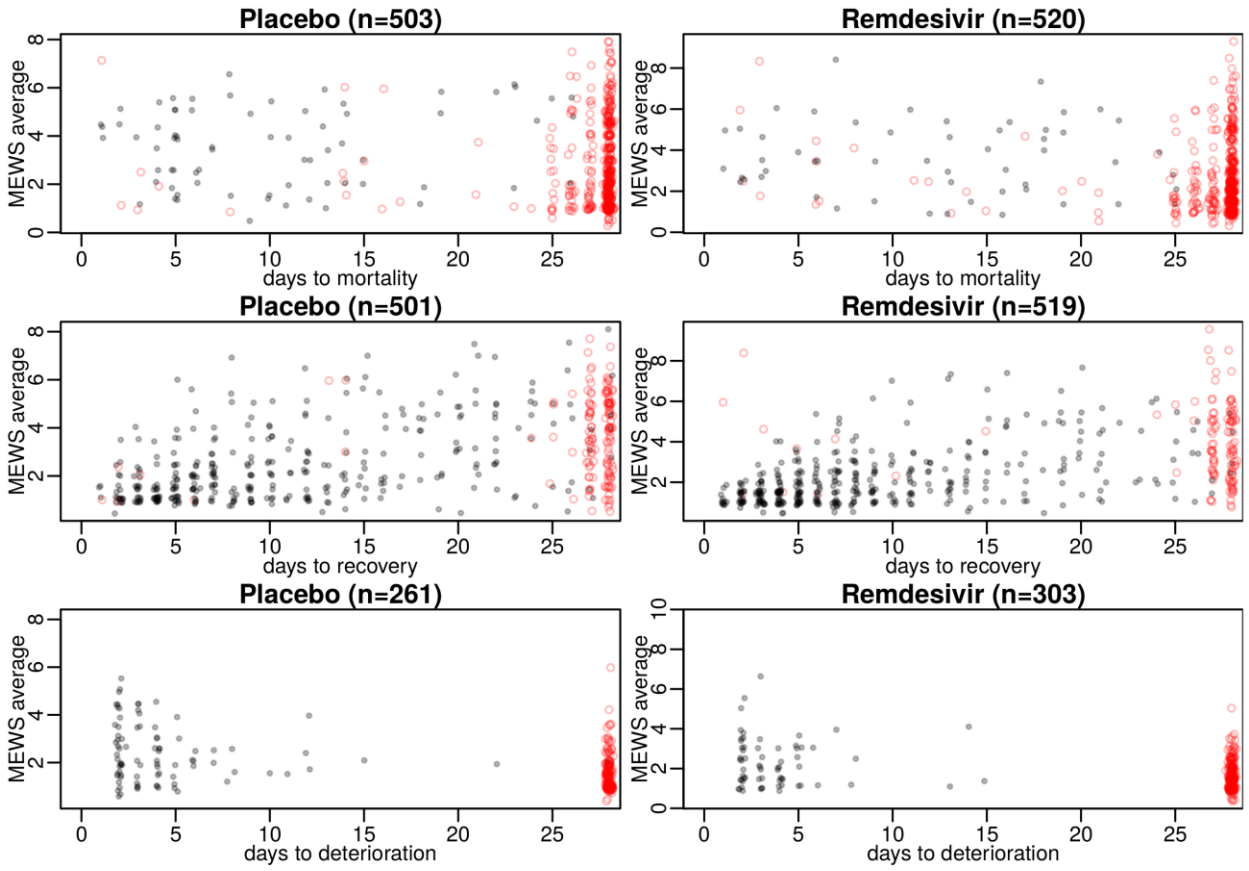
1D. Illustration of average of first two NEWS scores plotted against different endpoints, by placebo arm and remdesivir arm. Gray dots represent events and red dots represent censoring. Points are jittered to address overplotting.



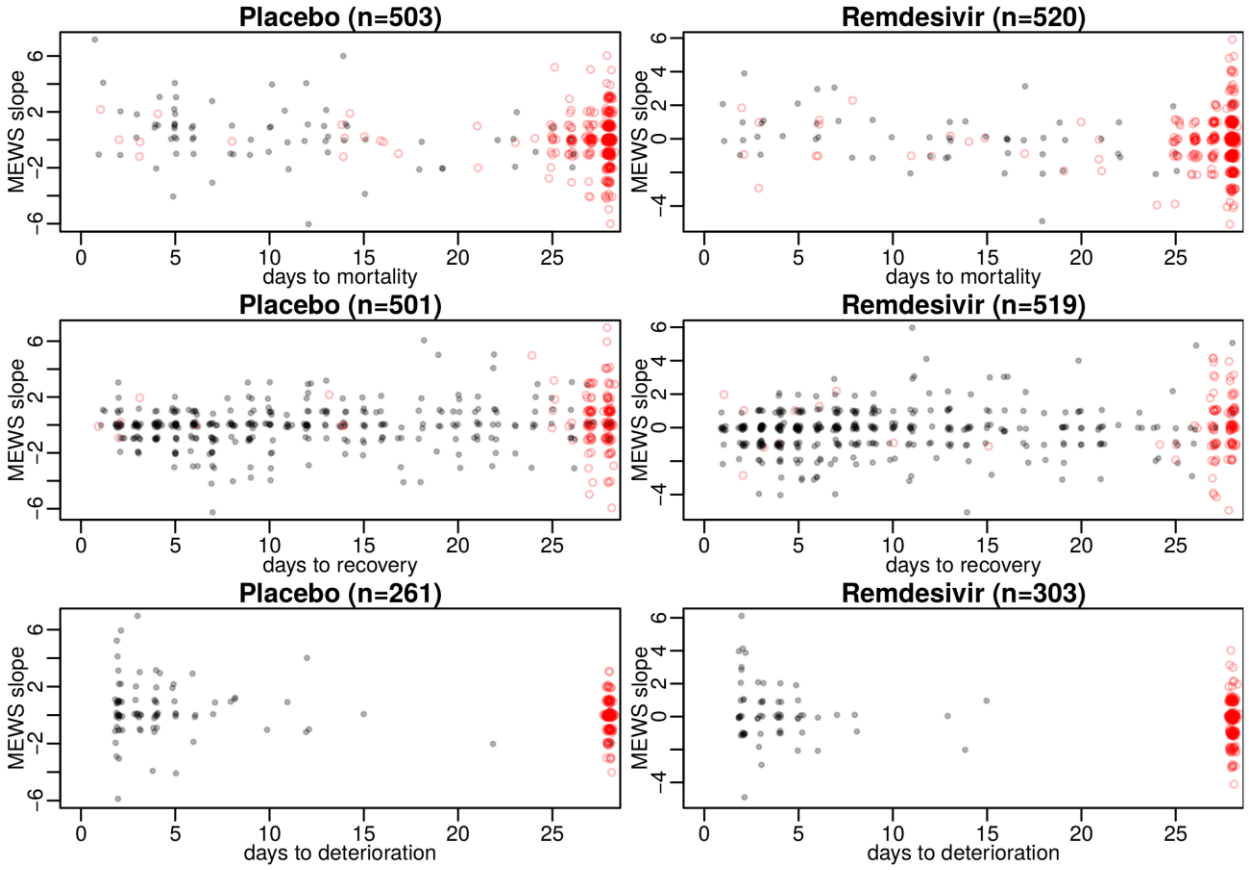
1E. Illustration of change in NEWS from day one to day two plotted against different endpoints, by placebo arm and remdesivir arm. Gray dots represent events and red dots represent censoring. Points are jittered to address overplotting.



1F. Illustration of average of first two MEWS scores plotted against different endpoints, by placebo arm and remdesivir arm. Gray dots represent events and red dots represent censoring. Points are jittered to address overplotting.

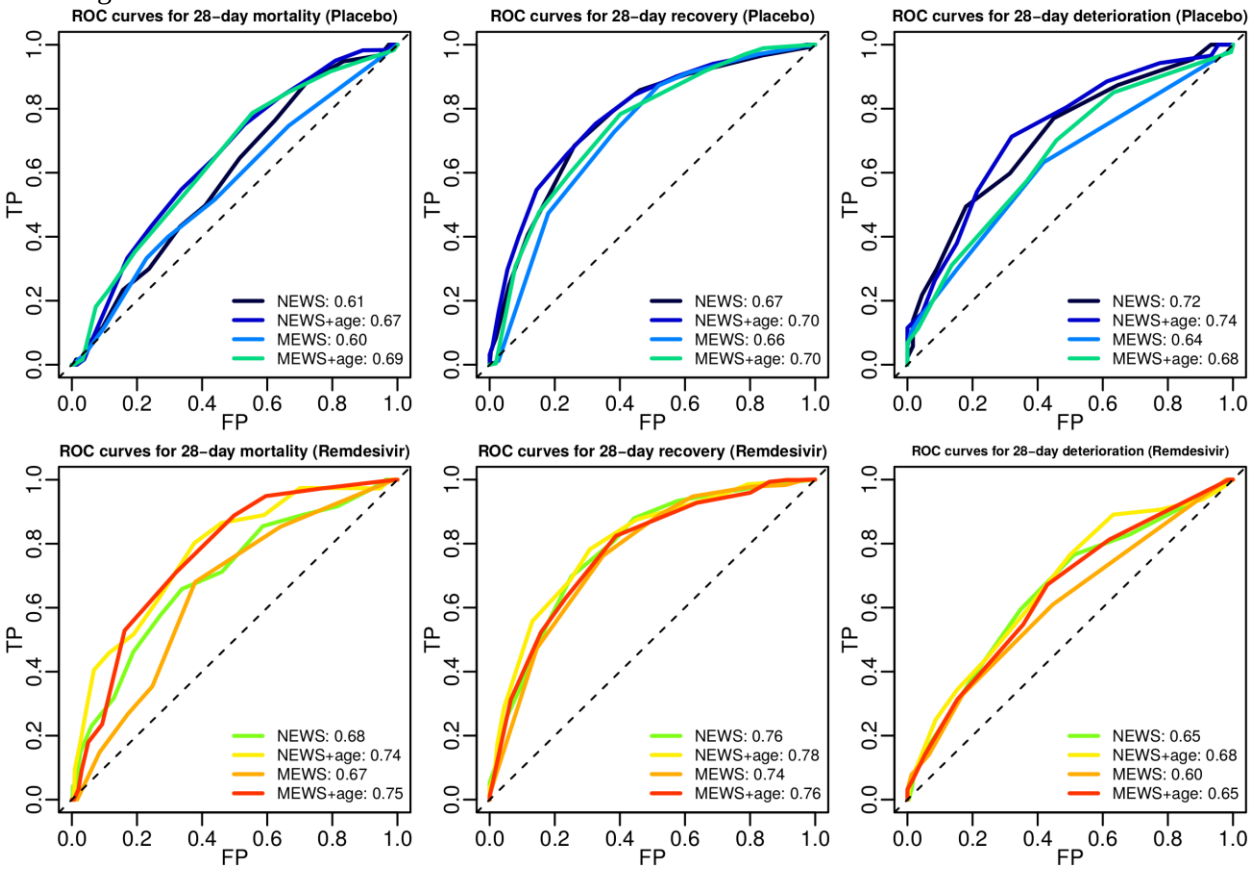


1G. Illustration of change in MEWS from day one to day two plotted against different endpoints, by placebo arm and remdesivir arm. Gray dots represent events and red dots represent censoring. Points are jittered to address overplotting.

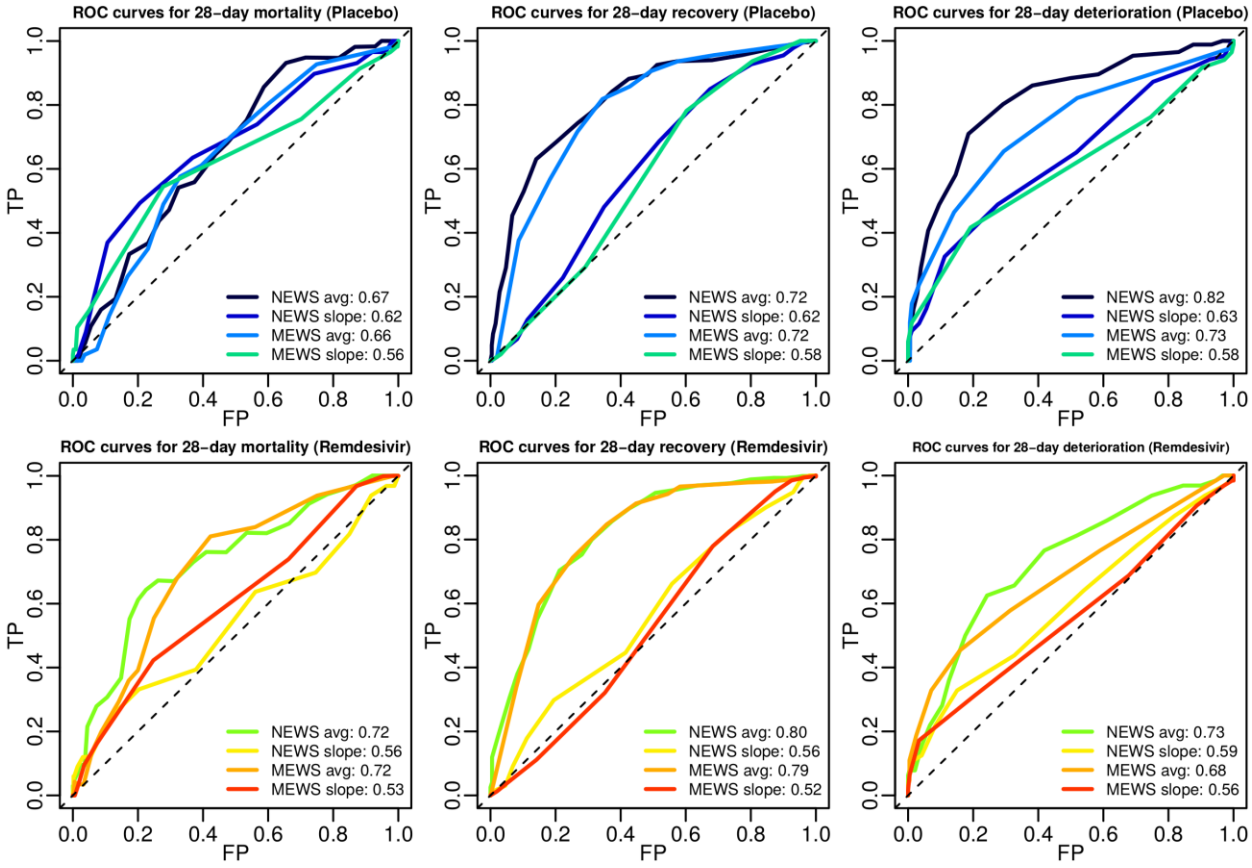


Supplemental Figures 2. ROC Curves

2A. ROC curves summarizing sensitivity and specificity of NEWS, MEWS, NEWS + age, and MEWS + age for the endpoints of 28-day mortality, recovery, and deterioration. The AUC for each curve is shown in the legend.



2B. ROC curves summarizing sensitivity and specificity of average NEWS, average MEWS, change in NEWS, and change in MEWS for the endpoints of 28-day mortality, recovery, and deterioration. The AUC for each curve is shown in the legend.



Supplemental Figure 3 Kaplan-Meier plots by arm and endpoint, with each plot stratified by a categorized baseline NEWS