COVID-19: Remdesivir for Adults – A Living Review

Supplemental Materials

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Supplemental Table 1. Study Characteristics of the Included Trials

Author, Year Country Funding Risk of Bias	**Intervention Comparator Inclusion/exclusion criteria Study Period/Length of Follow-up**	**Demographics**
Beigel 2020[1] Adaptive Covid-19 Treatment Trial (ACTT-1) Multinational (60 sites and 13 subsites, 45 in the US) Design: RCT Funding: Primarily government, other Risk of Bias: Low	Intervention: Remdesivir (n=541) 200 mg on day 1 followed by 100 mg on days 2–10 (or until hospital discharge or death) in single daily infusions Comparator: Placebo (n=521) Inclusion criteria: 18 years or older and meeting 1 of the following criteria suggestive of lower respiratory tract infection at enrollment: radiographic infiltrates by imaging study, peripheral oxygen saturation (SpO2) ≤94% on room air, or requiring supplemental oxygen, mechanical ventilation, or ECMO; no limit to duration of symptoms prior to enrollment; laboratory-confirmed SARS-CoV-2 infection as determined by a positive RT-PCR assay result from any respiratory specimen collected <72 hours prior to randomization (during the study, this criterion was modified due to limitations in testing capacity to also allow a RT-PCR positive specimen that was collected ≥72 hours prior to randomization if the site was unable to obtain a repeat sample and if the participant had progressive disease consistent with ongoing SARS-CoV-2 infection) Exclusion criteria: ALT or AST >5 times the upper limit of the normal range, impaired renal function as determined by calculating an eGFR or need for hemodialysis or hemofiltration, allergy to study product, pregnancy or breast-feeding, and anticipated discharge from hospital or transfer to another hospital within 72 hours of enrollment **Study Period/Length of Follow-up:** 29 days	N=1062 **Age (years, mean):** 59 **Gender (male):** 64% **Race/Ethnicity:** White 53% Black/African American 21% Asian 13% Latino (of any race) 23% **Time from symptom onset to randomization** Overall, median [IQR] 9 days [6-12] Remdesivir median [IQR] 9 days [6-12] Placebo median [IQR] 9 days [7-13] **Oxygen status on admission:** Percent on no oxygen 13% Percent on supplemental oxygen 41% Percent on non-invasive ventilation 18% Percent on invasive ventilation 27%
Wang 2020[2] China Design: RCT	Intervention: Remdesivir (n=158; 2:1 ratio) 200 mg on day 1 followed by 100 mg on days 2–10 in single daily infusions Comparator: Placebo (n=79)	N=237 **Age (years, median):** Remdesivir 66 Placebo 64 **Gender (male):**

Author, Year Country Funding Risk of Bias	**Intervention Comparator Inclusion/exclusion criteria Study Period/Length of Follow-up**	**Demographics**
Funding: Government, other Risk of Bias: Low	Inclusion criteria: men and non-pregnant women with COVID-19, age at least 18 years, RT-PCR positive for SARS-CoV-2, pneumonia confirmed by chest imaging, oxygen saturation of 94% or lower on room air or a ratio of arterial oxygen partial pressure to fractional inspired oxygen of 300 mm Hg or less, within 12 days of symptom onset Exclusion criteria: pregnancy or breast feeding; hepatic cirrhosis; ALT or AST >5 times the upper limit of the normal range; known severe renal impairment (estimated eGFR<30 mL/min per 1·73 m²) or receipt of continuous renal replacement therapy, hemodialysis, or peritoneal dialysis; enrolment into an investigational treatment study for COVID-19 in the 30 days before screening **Study Period/Length of Follow-up:** 28 days	Remdesivir 56% Placebo 65% **Race:** East Asian **Time from symptom onset to drug** Remdesivir median [IQR] 11 days [9-12] Placebo median [IQR] 10 days [9-12] **Oxygen status on admission:** Percent on no oxygen Remdesivir 0% Placebo 4% Percent on supplemental O_2 Remdesivir 82% Placebo 83% Percent on non-invasive ventilation Remdesivir 18% Placebo 12% Percent on invasive ventilation Remdesivir 0% Placebo 1%
Goldman 2020[3] GS-US-540-5773 SIMPLE 1 55 hospitals around the world, including sites in the US, Italy, Spain, Germany,	Intervention 1: Remdesivir, 5-day course (n=200) 200 mg on day 1 followed by 100 mg on days 2–5 in single daily infusions Intervention 2: Remdesivir, 10-day course (n=197) 200 mg on day 1 followed by 100 mg on days 2–10 in single daily infusions	N=397 **Age (years, median):** 5-day group 61 10-day group 62 **Gender (male):** 5-day group 60%

Author, Year Country Funding Risk of Bias	**Intervention Comparator Inclusion/exclusion criteria Study Period/Length of Follow-up**	**Demographics**
Hong Kong, Singapore, South Korea, and Taiwan. Design: Randomized, open-label, multi-center Phase 3 clinical trial Funding: Industry Risk of Bias: Moderate	Inclusion criteria: patients ≥ 18 years (at all sites), or aged ≥ 12 and < 18 years of age weighing ≥ 40 kg (where permitted according to local law) currently hospitalized with SARS-CoV-2 infection confirmed by PCR test ≤ 4 days before randomization; radiographic evidence of pulmonary infiltrates and peripheral capillary oxygen saturation (SpO2) ≤ 94% or requiring supplemental oxygen at screening Exclusion criteria: Pregnant or women who were breast feeding infants, ALT or AST >5 times the upper limit of the normal range, creatinine clearance < 50 mL/min using the Cockcroft-Gault formula for participants ≥ 18 years of age and Schwartz Formula for participants < 18 years of age; mechanically ventilated (including V-V ECMO) ≥ 5 days, or any duration of V-A ECMO; evidence of multiorgan failure; concurrent treatment with other agents with actual or possible direct acting antiviral activity against SARS-CoV-2 < 24 hours prior to study drug dosing; participant in any other clinical trial of an experimental treatment for COVID-19 **Study Period/Length of Follow-up:** 14 days (up to 30 days for adverse events)	10-day group 68% **Race:** White 70% Black 11% Asian 11% Other 7% **Time from symptom onset to drug** Remdesivir 5-day median [IQR] 8 days [5-11] Remdesivir 10-day median [IQR] 9 days [6-12] **Oxygen status on admission:** Percent on no oxygen 14% Percent on supplemental oxygen 55% Percent on non-invasive ventilation 27% Percent on invasive ventilation 4%
Spinner 2020[4] GS-US-540-5774 SIMPLE 2 105 sites in the US, France, Germany, Hong Kong, Italy, Republic of Korea, The Netherlands, Singapore, Spain, Switzerland, Taiwan and the United Kingdom	Intervention 1: Remdesivir, 5-day course (n=199) 200 mg on day 1 followed by 100 mg on days 2–5 in single daily infusions Intervention 2: Remdesivir, 10-day course (n=197) 200 mg on day 1 followed by 100 mg on days 2–10 in single daily infusions Comparator: Standard care (n=200) Inclusion criteria: ≥ 18 years (at all sites), or aged ≥ 12 and < 18 years of age weighing ≥ 40 kg (where permitted according to local law and approved by relevant review boards) currently hospitalized and requiring medical care for COVID-19; SARS-CoV-2 infection confirmed by PCR test ≤ 4 days before randomization; moderate COVID-19 pneumonia (peripheral capillary oxygen	**N=596 randomized (584 analyzed)** **Age (years, median):** 5-day group 58 10-day group 56 Standard care 57 **Gender (male):** 61% **Race:** White 58% Black 18% Asian 18% Other 7% Latino (of any race) 18%

Author, Year Country Funding Risk of Bias	**Intervention Comparator Inclusion/exclusion criteria Study Period/Length of Follow-up**	**Demographics**
Design: Randomized, open-label, multi-center Phase 3 clinical trial Funding: Industry Risk of Bias: Low	saturation (SpO_2) >94% on room air radiographic evidence of pulmonary infiltrates) Exclusion criteria: Women who were pregnant or breast feeding infants, ALT or AST >5 times the upper limit of the normal range; creatinine clearance < 50 mL/min using the Cockcroft-Gault formula for participants ≥ 18 years of age and Schwartz Formula for participants < 18 years of age; mechanically ventilated at screening; concurrent treatment or planned concurrent treatment with other agents with actual or possible direct acting antiviral activity against SARS-CoV-2; participation in any other clinical trial of an experimental treatment for COVID-19 **Study Period/Length of Follow-up:** 11 days (primary outcome); final assessment on day 28	**Time from symptom onset to drug** Remdesivir 5-day median [IQR] 8 days [5-11] Remdesivir 10-day median [IQR] 8 days [5-11] **Oxygen status on admission:** Percent on no oxygen: 84% Percent on supplemental oxygen: 15% Percent on non-invasive ventilation: NA Percent on invasive ventilation: NA
WHO Solidarity 2020[5] 30 countries: Europe (13), Canada, Latin America (5), Asia (9), Africa (2) Design: Open-label randomized trial Funding: No funders for main Solidarity trial Risk of Bias: Moderate	Intervention: Remdesivir, intravenous, (n=2750), 200 mg on day 0 followed by 100 mg on days 1-9 (treatment stopped at discharge or death) Comparator: No study drug (local standard of care) (n=2725) Inclusion criteria: ≥ 18 years, hospitalized with a diagnosis of COVID-19, not known to have received any study drug, without anticipated transfer elsewhere within 72 hours, no contraindication to any study drug (physician's view) Exclusion criteria: none reported **Study Period/Length of Follow-up:** 28 days (Note: mortality only during initial hospitalization; follow-up ceased at discharge)	**N=5475 randomized (5451 analyzed)** **Age (years):** <50: 35% 50-69: 47% 70+: 18% **Gender (male):** 63% **Race: NR** **Geographic Location** Europe or Canada: 26% Latin America: 18% Asia or Africa: 56% **Time from symptom onset to drug: NR** **Oxygen status on admission:** Percent on no oxygen: 24%

Author, Year Country Funding Risk of Bias	**Intervention Comparator Inclusion/exclusion criteria Study Period/Length of Follow-up**	**Demographics**
		Percent on oxygen: 67% Percent on ventilation: 9%
*DisCoVeRy 2021[6] ** *Sub-study of WHO Solidarity with additional newer recruited patients not included in WHO Solidarity study results. 53% (n=440) of the study population was included WHO Solidarity results and 47% (n=392) patients were unique* *5 countries with 48 sites: France, Belgium, Austria, Portugal, Luxembourg* *Design: Open-label randomized trial* *Funding: Institut National de la Santé et de la Recherche Médicale* *Risk of Bias: Low*	*Intervention: Remdesivir, intravenous, (n=429), 200 mg on day 0 followed by 100 mg on days 1-9 (treatment stopped after 5 days if the patient was discharged)* *Comparator: No study drug (local standard of care) (n=428)* *Inclusion criteria: (see WHO Solidarity)* *Exclusion criteria: Liver enzymes (ALT/AST) levels >5 times the upper limit of normal, stage 4 severe chronic kidney disease or requiring dialysis (ie, eGFR <30 mL/min), anticipated transfer to another hospital, which is not a study site within 72 hours, pregnant or breastfeeding, previously treated with 1 of the antivirals evaluated in the trial in the past 29 days, contraindication to any study medication including allergy* *Study Period/Length of Follow-up: 28 days*	*N=857 randomized (832 analyzed)* *Age (years, median): 64* *Gender (male): 70%* *Race:* *White 69%* *North African 15%* *Sub-Saharan African 7%* *Other 9%* *Time from symptom onset to drug: median [IQR] 9 days [7-12]* *Oxygen status on admission:* *Percent on no oxygen: 1%* *Percent on supplemental oxygen 77%* *Percent on non-invasive ventilation 4%* *Percent on invasive ventilation 18%* *Percent on ECMO <1%*
NOR-Solidarity 2021[7] *Sub-study of WHO Solidarity* *Norway* *Design: Open-label randomized trial*	*Intervention: Remdesivir, intravenous, (n=43), 200 mg on day 0 followed by 100 mg on days 1-9 (treatment stopped at discharge or death)* *Comparator: No study drug (local standard of care) (n=58 allocated versus remdesivir, 87 total in full analysis set)* *Inclusion criteria: (see WHO Solidarity)*	*N=101 randomized (83 completed 3-month follow-up).* *Age (years): 59* *Gender (male): 73%* *Race: NR*

Author, Year Country Funding Risk of Bias	**Intervention Comparator Inclusion/exclusion criteria Study Period/Length of Follow-up**	**Demographics**
Funding: National Clinical Therapy Research in the Specialist Health Services, Norway	*Exclusion criteria: severe comorbid conditions with life expectancy <3 months, level of aspartate aminotransferase or ALT > 5 times the upper limit of normal, rate-corrected QT interval greater >470 ms, pregnancy, breastfeeding, acute occurrence of a comorbid condition in a 7-day period before inclusion, known intolerance to study drugs, participation in a potentially confounding trial, or concomitant medications interfering with the study drugs* *Study Period/Length of Follow-up: 90 days (3 months)*	*Time from symptom onset to drug: mean 7 days* *Oxygen status on admission: NR* *Patients with respiratory failure (Po_2–FIo_2 <40 kPa): 44%*
Mahajan 2021[8] India Design: Open-label randomized trial Funding: No funders Risk of Bias: High	Intervention: Remdesivir, intravenous, (n=41) 200 mg on day 1 followed by 100 mg once daily on days 2-5. Both treatment groups continued supportive therapy Comparator: No study drug (local standard of care) (n=41) Inclusion criteria: 18 to 60 years of age hospitalized with a diagnosis of COVID-19 by PCR, radiographic evidence of pneumonia, respiratory rate >24/min, oxygen saturation ≤94%, creatine clearance >40 mL/min Exclusion criteria: receiving mechanical ventilation, multi organ failure, AST/ALT >3 times the upper limit of normal **Study Period/Length of Follow-up:** 24 days or until discharge or death	**N=82 randomized (70 analyzed)** **Age (years):** 58 **Gender (male):** 66% **Race: NR** **Time from symptom onset to drug:** mean 7 days **Oxygen status on admission:** Percent on no oxygen: 0% Percent on low-flow oxygen: 76% Percent on high-flow oxygen /non-invasive ventilation: 24% Percent on invasive mechanical ventilation: 0%
Abd-Elsalam 2021[9] Egypt Design: Open-label randomized trial	Intervention: Remdesivir, intravenous, (n=105), 200 mg on day 0 followed by 100 mg on days 1-9 Comparator: No study drug (local standard of care) (n=104) Inclusion criteria: 18 to 80 years of age hospitalized with COVID-19 infection confirmed by PCR test and had mild to moderate symptoms	**N=209 randomized (200 analyzed)** **Age (years): 53.5** **Gender (male): 60%** **Race: NR** **Time from symptom onset to drug: Unclear**

Author, Year Country **Funding** **Risk of Bias**	**Intervention** **Comparator** **Inclusion/exclusion criteria** **Study Period/Length of Follow-up**	**Demographics**
Funding: Not reported Risk of Bias: Low	Exclusion criteria: History of renal impairment or those with ALT and/or AST levels >5 times the upper limit of normal, pregnant or breastfeeding, allergy or contraindication to remdesivir **Study Period/Length of Follow-up:** 6 months	**Oxygen status on admission:** Not reported

Abbreviations. ALT = alanine aminotransferase; AST = aspartate aminotransferase; ECMO = extracorporeal membrane oxygenation; eGFR = estimated glomerular filtration rate; IQR = interquartile range; RT-PCR = reverse transcription, polymerase-chain-reaction; SARS-CoV = Severe Acute Respiratory Syndrome Coronavirus-2 infection

* Indicates newly identified sub-study

Supplemental Table 2. Search Strategies

Source	Strategy
MEDLINE and CENTRAL (Cochrane Central Trials Register)	1. exp Coronavirus/ or exp Coronavirus Infections/ 2. (nCoV or 2019-nCoV or ((new or novel or wuhan) adj3 coronavirus) or covid19 or covid-19 or SARS-CoV-2 or "Severe Acute Respiratory Syndrome Coronavirus 2").ti,ab,kw. 3. 1 or 2 4. (remdesivir or Veklury or GS-5734).ti,ab,kw. 5. 3 and 4
WHO Database	1. remdesivir or Veklury or GS-5734
NIH COVID-19 iSearch Portfolio	1. remdesivir or Veklury or GS-5734 Title/Abstract fields only, medRxiv
Journal Tables of Contents (New England Journal of Medicine, JAMA Network, The Lancet)	Keyword search: (remdesivir or Veklury or GS-5734)
Gilead Sciences, Inc. https://www.gilead.com/science-and-medicine/research	

Supplemental Table 3. GRADE Approach to Rating the Certainty of Evidence

The GRADE approach to rating the certainty of evidence for randomized controlled trials is based on 5 reasons to possibly rate down the quality of evidence.[10]

Reason	Consequence
Limitations in study design or execution (risk of bias)	↓ 1 or 2 levels
Inconsistency of results	↓ 1 or 2 levels
Indirectness of evidence	↓ 1 or 2 levels
Imprecision	↓ 1 or 2 levels
Publication bias	↓ 1 or 2 levels

Supplemental Table 4. Study Outcomes A

Author, Year (ref)	Length of hospital stay		Time to recovery		Mortality		Recovery or Combined endpoint "Clinical Improvement"	
	Remdesivir	**Placebo**	**Remdesivir**	**Placebo**	**Remdesivir**	**Placebo**	**Remdesivir**	**Placebo**
Beigel 2020[1] ACTT-1	Median [IQR] 12 [6 to 28] Difference -5.0 days [95% CI, -7.7 to -2.3] Median [IQR] for those who did not die 10 [5 to 21] Difference -4.0 days [95% CI, -6.0 to -2.0]	Median [IQR] 17 [8 to 28] Median [IQR] for those who did not die 14 [7 to 27]	Median [95% CI] 10 days [9 to 11]	Median [95% CI] 15 days [13 to 18]	14-day 6.5% (35/541) HR 0.55 [95% CI, 0.36 to 0.83] (through day 15) 29-day 10.9% (59/541) HR 0.73 [95% CI, 0.52 to 1.03]	14-day 11.7% (61/521) 29-day 14.8% (77/521)	Day 29 Recovery * 73.8% (399/541) Recovery Rate Ratio 1.29 [95% CI, 1.12 to 1.49] *Recovery Mild/mod. Disease* † *98.2% (54/55)* *Severe Disease* ‡ *71.0% (345/486)*	Day 29 Recovery * 67.6% (352/521) *Recovery Mild/mod. Disease* † *92.0% (46/50)* *Severe Disease* ‡ *65.0% (306/471)*
Wang 2020[2]	Median [IQR] 25 days [16 to 38] Difference 0.0 days [95% CI, -4.0 to 4.0]	Median [IQR] 24 days [18 to 36]	Time to Clinical Improvement Median [IQR] 21 days [13 to 28]	Time to Clinical Improvement Median [IQR] 23 days [15 to 28]	28-day 13.9% (22/158) ARD 1.1% [95% CI, -8.1 to 10.3]	28-day 12.8% (10/78)	Day 28 Recovery ‖ 70.7% (106/150) Day 28 Clinical improvement § 65.2% (103/158) ARD 7.5% [95% CI, -5.7 to 20.7] HR 1·23 [95% CI, 0·87 to 1·75]	Day 28 Recovery ‖ 63.6% (49/77) Day 28 Clinical improvement § 57.7% (45/78)

Goldman 2020[3] GS-US-540-5773 SIMPLE 1	**Remdesivir 5-day**	**Remdesivir 10-day**	**Remdesivir 5-day**	**Remdesivir 10-day**	**Remdesivir 5-day**	**Remdesivir 10-day**	**Remdesivir 5-day**	**Remdesivir 10-day**
	NR	NR	Median [IQR] 10 days [6 to 18] HR 0.81 [95% CI, 0.64 to 1.04]	Median [IQR] 11 days [7 to not possible to estimate]	14-day 8.0% (16/200) P=.70	14-day 10.7% (21/197)	Day 14 Clinical recovery ‖ 64.5% (129/200) Baseline-adjusted ARD and p-value -6.3% [95% CI, -15.4 to 2.8]; P=.17 Clinical (≥2-point) improvement ¶ 64.5% (129/200) Baseline-adjusted ARD and P-value -6.5% [95% CI, -15.7 to 2.8]; P=.16	Day 14 Clinical recovery ‖ 53.8% (106/197) Clinical (≥2-point) improvement ¶ 54.3% (107/197)
Spinner 2020[4] GS-US-540-5774 SIMPLE 2 with standard care	**Remdesivir**	**Standard Care**	**Remdesivir**	**Standard Care**	**Remdesivir**	**Standard Care**	**Remdesivir**	**Standard Care**
	NR	NR	Median [IQR] 5 day 6 (5-10) 10 day 8 (4-13)	Median [IQR] 7 (4-14)	11-day 5-day 0% (0/191) 10-day 1.0% (2/193) HR for 5-day vs standard care 0.51 [95% CI, 0.09 to 2.80] HR for 10-day vs standard care	11-day 2.0% (4/200)	Day 11 Recovery ‖ 5-day 73.8% (141/191) 10-day 68.4% (132/193) HR for 5-day vs standard care 1.18 [95% CI, 0.96 to 1.45] HR for 10-day vs standard care	Day 11 Recovery ‖ 64.0% (128/200)

					0.76 [95% CI, 0.17 to 3.40]		1.11 [95% CI, 0.90 to 1.36] Clinical (≥2-point) improvement ¶ 5-day 70.2% (134/191) 10-day 65.3% (126/193) HR for 5-day vs standard care 1.15 [95% CI, 0.93 to 1.42] HR for 10-day vs standard care 1.16 [95% CI, 0.93 to 1.43]	Clinical (≥2-point) improvement ¶ 60.5% (121/200)
WHO Solidarity 2020[5]	Still hospitalized at day 7 69%	Still hospitalized at day 7 59%	NR	NR	12.5% (301/2743) Rate Ratio: 0.95 [95% CI, 0.81 to 1.11]	12.7% (303/2708)	NR	NR
*DisCoVeRy 2021[6] ** *	*Still hospitalized at day 15* *49.0% (203/414)* *Still hospitalized at day 29* *27.8% (115/414)*	*Still hospitalized at day 15* *45.2% (189/418)* *Still hospitalized at day 29* *33.3% (139/418)*	*Days to Improvement of 2 categories of the 7-point ordinal scale or hospital discharge within 29 days* *Median [IQR]* *12 [8 to 24]*	*Days to Improvement of 2 categories of the 7-point ordinal scale or hospital discharge within 29 days* *Median [IQR]* *11 [7 to 26]*	*Overall* *At day 29* *8.2% (34/414)* *Moderate disease* *5.9% (15/253)* *Severe disease* *11.8% (19/161)* *Unique patients*	*Overall* *At day 29* *8.9% (37/418)* *Moderate disease* *6.0% (15/251)* *Severe disease* *13.2% (22/167)*	*Day 29 Recovery ††* *64% (265/414)*	*Day 29 Recovery ††* *57.7% (241/418)*

					(no overlap with Solidarity) *At day 29* *8.2%* *(16/195)* *Moderate disease* *3.6% (4/112)* *Severe disease* *14.5% (12/83)*	*Unique patients (no overlap with Solidarity)* *At day 29* *10.2%* *(20/197)* *Moderate disease* *8.1% (9/111)* *Severe disease* *12.8% (11/86)*		
NOR-Solidarity 2021[7] *Sub-study of WHO Solidarity*	*NR*	*NR*	*NR*	*NR*	*In-hospital* *7.1%* *RR 1.0 [95% CI, 0.2 to 4.6]* *HR 1.0 [95% CI, 0.4 to 2.9]* *28 day* *2.4%* *Estimated Marginal Risk Difference vs SC* *-2.9% [95% CI, -10.3 to 4.5]* *60 day* *7.1%* *Estimated Marginal Risk Difference vs SC* *1.9% [95% CI,*	*In-hospital* *7.0%* *28 day* *5.3%* *60 day* *5.3%*	*NR*	*NR*

				-7.8 to 11.6]			
Mahajan 2021[8]	NR	NR	Patients in the remdesivir group and standard of care group had an equal time to recovery between 10 and 20 days (no other data reported)	All patients 14.6% (6/41) Per protocol Day 12-24 14.7% (5/34)	All patients 12.2% (5/41) Per Protocol Day 12-24 8.3% (3/36)	NR	NR
Abd-Elsalam 2021[9]	Mean 12.4 days Median [IQR] 10 days [8 to 14]	Mean 16.7 days Median [IQR] 16 days [12 to 21]	NR	NR	9% (9/100)	7% (7/100)	NR	NR

Abbreviations. ARD = absolute risk difference; CI =confidence intervals; HR = Hazard ratio; IQR = interquartile range; NR = not reported; OR = odds ratio; RR = relative risk; SC = standard care

* Defined by either discharge from the hospital or hospitalization extended for purposes of infection-control only with no medical needs.

† Mild/moderate disease was defined by a SpO2 >94% and respiratory rate <24 breaths per minute without supplemental oxygen requirement.

‡ Severe disease was defined as participants meeting 1 or more of the following criteria: requiring invasive or non-invasive mechanical ventilation, requiring supplemental oxygen, an SpO2 ≤94% on room air, or respiratory rate ≥24 breaths per minute.

§ Defined as a 2-point reduction in patients' admission status on a 6-point ordinal scale, or live discharge from the hospital, whichever came first within 28 days after randomization. The 6-point scale was as follows: death=6; hospital admission for extracorporeal membrane oxygenation or mechanical ventilation=5; hospital admission for noninvasive ventilation or high-flow oxygen therapy=4; hospital admission for oxygen therapy (but not requiring high-flow or non-invasive ventilation)=3; hospital admission but not requiring oxygen therapy=2; and discharged or having reached discharge criteria (defined as clinical recovery - *ie*, normalization of pyrexia, respiratory rate <24 breaths per minute, saturation of peripheral oxygen >94% on room air, and relief of cough, all maintained for at least 72 h)=1

‖ Patients achieved clinical recovery if they no longer required oxygen support and medical care or were discharged from the hospital (improvement from a baseline score of 2 to 5 to a score of 6 or 7).

¶ Clinical improvement was defined as an improvement of 2 or more points from baseline on a predefined 7-point scale consisting of the following categories: 1, death; 2, hospitalized, receiving invasive mechanical ventilation or ECMO; 3, hospitalized, receiving noninvasive ventilation or high-flow oxygen devices; 4, hospitalized, requiring low-flow supplemental oxygen; 5, hospitalized, not requiring supplemental oxygen but receiving ongoing medical care (related or not related to Covid-19); 6, hospitalized, requiring neither supplemental oxygen nor ongoing medical care (other than that specified in the protocol for remdesivir administration); and 7, not hospitalized.

** Sub-study of WHO Solidarity with additional newer recruited patients not included in WHO Solidarity study results.

†† Defined by review authors as items 1 and 2 on a 7-point ordinal scale: 1=not hospitalized, no limitations on activities; and 2= not hospitalized, limitation on activities.

Supplemental Table 5. Study Outcomes B

Author, Year (ref)	Required invasive mechanical ventilation; Duration of invasive mechanical ventilation, days		Required oxygen; Duration of oxygen support, days	
	Remdesivir	**Placebo**	**Remdesivir**	**Placebo**
Beigel 2020[1] ACTT-1	17.6% (95/541) at Day 15 visit; Length of use if receiving at baseline, Median [IQR] 17 days [9 to 28] Difference -3.0 days [95% CI, -9.3 to 3.3] Length of new use during study, Median [IQR] 21.5 days [9 to 28] Difference 1.0 days [95% CI, -6.0 to 8.0]	23.2% (121/521) at Day 15 visit; Length of use if receiving at baseline, Median [IQR] 20 days [8 to 28] Length of new use during study, Median [IQR] 23 days [12 to 28]	10.7% (58/541) at Day 15 visit: Length of use if receiving at baseline, Median [IQR] 13 days [5 to 28] Difference -8.0 days [95% CI, -11.8 to -4.2] Length of new use during study, Median [IQR] 4 days [2 to 12] Difference -1.0 days [95% CI, -7.6 to 5.6]	11.5% (60/521) at Day 15 visit; Length of use if receiving at baseline, Median [IQR] 21 days [8 to 28] Length of new use during study, Median [IQR] 5.5 days [1 to 15]
Wang 2020[2]	8.2% (13/158) Median [IQR] 7.0 days [4 to 16] Difference -4.0 days [95% CI, -14.0 to 2.0]	12.8% (10/78) Median [IQR] 15.5 days [6 to 21]	Median [IQR] 19.0 days [11 to 30] Difference -2.0 days [95% CI, -6.0 to 1.0]	Median [IQR] 21.0 days [14 to 30.5]
Goldman 2020[3] GS-US-540-5773 SIMPLE 1	**Remdesivir 5-day**	**Remdesivir 10-day**	**Remdesivir 5-day**	**Remdesivir 10-day**
	8.0% (16/200); Duration NR	16.8% (33/197); Duration NR	NR	NR
Spinner 2020[4] GS-US-540-5774 SIMPLE 2 with standard care	**Remdesivir**	**Standard Care**	**Remdesivir**	**Standard Care**
	5-day 0% (0/191) 10-day 0.5% (1/193)	2.0% (4/200)	Time to Room Air Median [IQR] 5-day 5 (3-7) 10-day	6 (4-14)

			4 (2-6) 6.3% (12/191) and 6.7% (13/193) required oxygen support on Day 1	11% (22/200) required oxygen support on Day 1
WHO Solidarity 2020[5]	**Remdesivir**	**Standard Care**	**Remdesivir**	**Standard Care**
	Initiation of ventilation in those not already ventilated 11.9% (295/2489)	Initiation of ventilation in those not already ventilated 11.5% (284/2475)	NR	NR
*DisCoVeRy 2021[6] **	*6.3% (26/414) at Day 29* *15.0% (62/414) at Day 15* Initiation of ventilation in those not already ventilated *Unique patients* *(no overlap with Solidarity)* *Within 29 days* *15.7% (27/172)*	*9.8% (41/418) at Day 29* *18.9% (79/418) at Day 15* Initiation of ventilation in those not already ventilated *Unique patients* *(no overlap with Solidarity)* *Within 29 days* *29.9% (52/174)*	*Required supplemental oxygen or non-invasive ventilation or HFNO* *10.1% (42/414) at Day 29* *22.0% (91/414) at Day 15*	*Required supplemental oxygen or non-invasive ventilation or HFNO* *11.5% (48/418) at Day 29* *19.4% (81/418) at Day 15*
NOR-Solidarity 2021[7] Sub-study of WHO Solidarity	*9.5%* *Estimated Marginal Risk Difference vs SC* *2.5% [95% CI, -8.6 to 13.6]*	*7.0%*	*NR*	*NR*
Mahajan 2021[8]	Day 12-24 11.8% (4/34)	Day 12-24 5.6% (2/36)	Day 12-24 Supplemental O_2 11.8% (4/34) Day 12-24 High-flow O_2 or/ non-invasive ventilation 55.9% (19/34)	Day 12-24 Supplemental O_2 16.7% (6/36) Day 12-24 High-flow O_2 or/ non-invasive ventilation 61.1% (22/36)
Abd-Elsalam 2021[9]	Initiation of mechanical ventilation in those not already ventilated 11% (11/100)	Initiation of mechanical ventilation in those not already ventilated 8% (8/100)	NR	NR

Abbreviations. ECMO = extracorporeal membrane oxygenation; HFNO = high flow nasal oxygen; IQR = interquartile range; NR = not reported; SC = standard care
* Sub-study of WHO Solidarity with additional newer recruited patients not included in WHO Solidarity study results

Supplemental Table 6. Viral Load

Author, Year (ref) Viral load definition	Pre		Post	
	Remdesivir	**Placebo**	**Remdesivir**	**Placebo**
Beigel 2020[1] ACTT-1	NR	NR	NR	NR
Wang 2020[2] ***Mean baseline viral load of nasopharyngeal and oropharyngeal swabs***	4.7 log_{10} copies/mL	4.7 log_{10} copies per mL	NR	NR
Upper respiratory tract specimens	*Estimated from graph* 3.7 log_{10} copies/mL	*Estimated from graph* 3.6 log_{10} copies/mL	*Estimated from graph* 0.6 log_{10} copies/mL	*Estimated from graph* 0.1 log_{10} copies/mL
Lower respiratory tract specimens	*Estimated from graph* 7.3 log_{10} copies/mL	*Estimated from graph* 6.4 log_{10} copies/mL	*Estimated from graph* 1.4 log_{10} copies/mL	*Estimated from graph* 0.0 log_{10} copies/mL
Goldman 2020[3] GS-US-540-5773 SIMPLE 1	**Remdesivir 5-day**	**Remdesivir 10-day**	**Remdesivir 5-day**	**Remdesivir 10-day**
	NR	NR	NR	NR
Spinner 2020[4] GS-US-540-5774 SIMPLE 2 with standard care	**Remdesivir**	**Standard Care**	**Remdesivir**	**Standard Care**
	NR	NR	NR	NR
WHO Solidarity 2020[5]	**Remdesivir**	**Standard Care**	**Remdesivir**	**Standard Care**
	NR	NR	NR	NR
*DisCoVeRy 2021[6] ** *nasopharyngeal swab*	*Median* 3.2 log_{10} copies/ 10,000 cells	*Median* 3.2 log_{10} copies/ 10,000 cells	*Least mean square difference in viral load at day 14, -0.004 log_{10} copies/10,000 cells [95% CI, -0.031 to 0.022] P=.75*	
NOR-Solidarity 2021[7] *Sub-study of WHO Solidarity* *oropharynx*	*1.6 (1.6) log_{10} copies/1000 cells*	*2.3 (1.8) log_{10} copies/1000 cells*	*Difference in viral level at day 10, 0.203 log_{10} copies/1000 cells [95% CI, -0.348 to 0.754]* *Difference in daily viral decrease rate, 0.113 log_{10} copies/1000 cells*	

			[95% CI, -0.001 to 0.227]	
Mahajan 2021[8]	NR	NR	NR	NR
Abd-Elsalam 2021[9]	NR	NR	NR	NR

Abbreviations. NR = not reported

* Sub-study of WHO Solidarity with additional newer recruited patients not included in WHO Solidarity study results

Supplemental Table 7. Harms A (Number of Subjects Reporting at Least 1 Event)

Author, Year (ref)	Serious AE		AE leading to drug withdrawal		Any AE	
	Remdesivir	**Placebo**	**Remdesivir**	**Placebo**	**Remdesivir**	**Placebo**
Beigel 2020[1] ACTT-1	24.6% (131/532) * *Study-related* 2 events Grade 3 or 4 51.3% (273/532)	31.6% (163/516) * *Study-related* 3 events Grade 3 or 4 57.2% (295/516)	10.7% (57/532) *	14.9% (77/516) *	57.3% (305/532)[a]	62.6% (323/516)[a]
Wang 2020[2]	18.1% (28/155)	25.6% (20/78)	11.6% (18/155)	5.1% (4/78)	65.8% (102/155) Grade 3 or 4 8.4% (13/155)	64.1% (50/78) Grade 3 or 4 14.1% (11/78)
Goldman 2020[3] GS-US-540-5773 SIMPLE 1	**Remdesivir 5-day**	**Remdesivir 10-day**	**Remdesivir 5-day**	**Remdesivir 10-day**	**Remdesivir 5-day**	**Remdesivir 10-day**
	21.0% (42/200)	34.5% (68/197)	4.5% (9/200) P=.07	10.2% (20/197)	70.5% (141/200) P=.86 Grade ≥3 30% (60/200)	73.6% (145/197) Grade ≥3 43% (85/197)
Spinner 2020[4] GS-US-540-5774 SIMPLE 2 with standard care	**Remdesivir**	**Standard Care**	**Remdesivir**	**Standard Care**	**Remdesivir**	**Standard Care**
	5-day 4.7% (9/191) 10-day 5.2% (10/193)	9.0% (18/200)	5-day 2.1% (4/191) 10-day 4.1% (8/193)	NA	5-day 51.3% (98/191) 10-day 58.5% (113/193) Grade ≥3	46.5% (93/200) Grade ≥3

					5-day 10.5% (20/191) 10-day 12% (24/193)	12.0% (24/200)
WHO Solidarity 2020[5]	**Remdesivir**	**Standard Care**	**Remdesivir**	**Standard Care**	**Remdesivir**	**Standard Care**
	NR	NR	NR	NR	NR	NR
DisCoVeRy 2021[6] †	*33.3% (135/406)*	*31.1% (130/418)*	*NR*	*NR*	*59.4% (241/406)*	*56.5% (236/418)*
NOR-Solidarity 2021[7] Sub-study of WHO Solidarity	*19.0% (8/42) P=.56 ‡*	*14.9% (13/87)*	*0% (0/42)*	*0% (0/87)*	*38.5% (20/42)*	*25.3% (22/87)*
Mahajan 2021[8]	NR	NR	7.3% (3/41) due to abnormal ALT and AST values	0/41	NR	NR
Abd-Elsalam 2021[9]	0% (0/100)	0% (0/100)	0% (0/100)	0% (0/100)	NR	NR

Abbreviations. AE = adverse event; ALT = alanine aminotransferase; AST = aspartate aminotransferase; NR = not reported

* Data for the treated population

† Sub-study of WHO Solidarity with additional newer recruited patients not included in published WHO Solidarity study results

‡ P-value calculated by review team

Supplemental Table 8. Harms B (Number of Subjects Reporting at Least 1 Event)

Author, Year (Ref)	Respiratory failure or acute respiratory distress syndrome		Cardiopulmonary failure	
	Remdesivir	**Placebo**	**Remdesivir**	**Placebo**
Beigel 2020[1] ACTT-1	Serious respiratory failure 7.3% (39/532) * Respiratory distress 1.1% (6/532) *	Serious respiratory failure 8.0% (66/516) * Respiratory distress 2.1% (11/516) *	NR	NR
Wang 2020[2]	Respiratory failure or acute respiratory distress syndrome 10.3% (16/155) Grade 3 or 4 2.6% (4/155)	Respiratory failure or acute respiratory distress syndrome 7.7% (6/78) Grade 3 or 4 5.1% (4/78)	5.2% (8/155)	9.0% (7/78)
Goldman 2020[3] GS-US-540-5773 SIMPLE 1	**Remdesivir 5-day**	**Remdesivir 10-day**	**Remdesivir 5-day**	**Remdesivir 10-day**
	6.0% (12/200)	10.7% (21/197)	NR	NR
Spinner 2020[4] GS-US-540-5774 SIMPLE 2 with standard care	**Remdesivir**	**Standard Care**	**Remdesivir**	**Standard Care**
	NR	NR	NR	NR
Pan 2020[5] WHO Solidarity *Interim results*	**Remdesivir**	**Standard Care**	**Remdesivir**	**Standard Care**
	NR	NR	NR	NR
DisCoVeRy 2021[6] †	*Acute respiratory distress syndrome* *8.6%* *(35/406)*	*Acute respiratory distress syndrome* *8.9%* *(37/418)*	*NR*	*NR*

	Acute respiratory failure 7.4% (30/406)	*Acute respiratory failure 11.2% (47/418)*		
NOR-Solidarity 2021[7] *Sub-study of WHO Solidarity*	*NR*	*NR*	*NR*	*NR*
Mahajan 2021[8]	NR	NR	NR	NR
Abd-Elsalam 2021[9]	NR	NR	NR	NR

Abbreviations. AE = adverse event; NR = not reported
*Data for the treated population

Supplemental Table 9. Risk of Bias of Studies

Author, Year (ref)	Random sequence generation	Allocation concealment	Blinding *	Incomplete outcome data †	Selective outcome reporting ‡	Overall Risk of Bias §
Beigel 2020[1] ACTT-1	Low, adequate, permuted randomization sequence	Low, adequate, web-based	Low, patient, provider Follow-up safety and efficacy evaluations performed by blinded clinic staff	Low, 1 placebo patient and 3 remdesivir patients excluded due to no data after baseline.	No	Low
Wang 2020[2] Note: trial stopped early	Low, adequate, permuted block randomization sequence	Low, adequate, centralized	Low, patient, provider	Low, 1 placebo patient withdrew consent, not in ITT analyses. Three remdesivir patients did not take drug and are not in the safety analyses.	No	Low
Goldman 2020[3] GS-US-540-5773 SIMPLE 1	Low, adequate, computer generated	Low, adequate, web-based	Open-label Outcome assessors were not blinded.	Low,2 patients in the 5-day group and 3 in the 10-day group not included in analyses (withdrawn or randomized in error)	No	Moderate based on imbalance between groups (patients randomly assigned to the 10-day group had significantly worse clinical status than those assigned to the 5-day group (P = 0.02)) and open label nature of study.
Spinner 2020[4] GS-US-540-5774 SIMPLE 2 with	Low, adequate, computer generated	Low, adequate, web-based	Open-label Outcome assessors were not blinded.	Low, 8 patients in the 5-day group and 4 in the 10-day group not included in analyses (did not start treatment)	No	Low

Author, Year (ref)	Random sequence generation	Allocation concealment	Blinding *	Incomplete outcome data †	Selective outcome reporting ‡	Overall Risk of Bias §
standard care						
WHO Solidarity 2020[5]	WHO: Unclear, not reported;	WHO: Low, adequate, cloud-based;	Open-label Blinded analyses of all relevant data	WHO: Low, 7 patients in remdesivir and 17 patients in control group not included in analyses (no or uncertain consent to follow-up)	WHO: Yes – limited reporting of hospitalization duration; no adverse event reporting	Moderate based on unclear sequence generation and selective outcomes reporting
Sub-studies of WHO Solidarity						
DisCoVeRy 2021[6] ‖	*Low, computer randomization procedures*	*Low, electronic case report form*	*Open-label* *Blinded analyses of all relevant data*	*Low, 12 patients in remdesivir and 10 patients in control group not included in analyses (no or uncertain informed consent or no confirmed positive PCR ≤9 days before randomization)*	*No*	*Low*
(NOR-Solidarity – sub-study)[7]	*Low, computer randomization procedures*	*Low, allocation sequence was prepared by an independent statistician*	*Open-label* *Blinded analyses of all relevant data*	*2% patients not included in full analysis set, 18% did not complete 3-month follow-up*	*No*	*Low*
Mahajan 2021[8]	Low, adequate, computer generated	Unclear, not reported	Open-label	High, 8 patients in remdesivir and 5 patients in control group not included in analyses (Patients who were discharged when symptom-free, withdrawn from treatment, for had treatment stopped due to elevated ALT or AST levels were excluded). 16% were excluded from analyses	No	High based on not using ITT analysis, attrition, and absence of information on allocation concealment

Author, Year (ref)	Random sequence generation	Allocation concealment	Blinding *	Incomplete outcome data †	Selective outcome reporting ‡	Overall Risk of Bias §
Abd-Elsalam 2021[9]	Low, adequate, computer generated	Low, adequate, sequentially numbered opaque sealed envelopes kept by the hospital pharmacist	Open-label	Low, 5 patients in remdesivir and 4 patients in control group not included in analyses (transferred to another hospital)	Yes, did not report viral load data (noted as	Low

Abbreviations. ALT = alanine aminotransferase; AST = aspartate aminotransferase; ITT = intent-to-treat

* For the open-label trial, blinding of study participants and study personnel was not feasible. This element was not considered in rating overall risk of bias.

† Incomplete outcome data was rated high if more than 10% of participants randomized were not included in the analyses.

‡ Selective reporting was determined by comparing reported outcomes with outcomes specified in the Methods section. If a protocol paper was available, reported outcomes were compared with outcomes specified in the protocol.

§ Studies were rated low risk of bias if at least 3 elements were rated low and no additional elements were rated high. Studies were rated High risk of bias if at least 2 elements were rated high risk of bias. All other studies were rated Moderate risk of bias.

‖ Sub-study of WHO Solidarity with additional newer recruited patients not included in WHO Solidarity study results

Supplemental Table 10. COVID-19 Disease Severity

COVID-19 Disease Severity	NIH COVID-19 Treatment Guidelines[11]	WHO Clinical Management of COVID-19[12]	Food and Drug Administration (FDA)[13]	Included Studies in Evidence Report
Asymptomatic or Pre-symptomatic	Individuals who test positive for SARS-CoV-2 by virologic testing using a molecular diagnostic (*eg*, polymerase chain reaction) or antigen test, but have no symptoms.	**NA**	Positive testing by standard reverse transcription polymerase chain reaction (RT-PCR) assay or equivalent test; no symptoms.	**NA**
Mild	Individuals who have any of the various signs and symptoms of COVID 19 (*eg*, fever, cough, sore throat, malaise, headache, muscle pain) without shortness of breath, dyspnea, or abnormal chest imaging.	Symptomatic patients meeting the case definition for COVID-19 without evidence of viral pneumonia or hypoxia.	Positive testing by standard RT-PCR assay or equivalent test; symptoms of mild illness with COVID-19 that could include fever, cough, sore throat, malaise, headache, muscle pain, gastrointestinal symptoms, without shortness of breath or dyspnea; no clinical signs indicative of Moderate, Severe, or Critical Severity	**ACTT-1[1]:** Mild/Moderate disease: confirmed COVID-19 positive and hospitalized with radiographic infiltrates by imaging, SpO_2 >94% and respiratory rate <24 breaths per minute without supplemental oxygen. Mild not defined. Results for Mild not provided.
Moderate	Individuals who have evidence of lower respiratory disease by clinical assessment or imaging and a saturation of oxygen (SpO2) ≥94% on room air at sea level.	Adolescent or adult with clinical signs of pneumonia (fever, cough, dyspnoea, fast breathing) but no signs of severe pneumonia, including SpO_2 ≥90% on room air OR Child with clinical signs of non-severe pneumonia (cough or difficulty breathing + fast breathing and/or chest indrawing) and no signs of severe pneumonia.	Positive testing by standard RT-PCR assay or equivalent testing; symptoms of moderate illness with COVID-19, which could include any symptom of mild illness or shortness of breath with exertion; clinical signs suggestive of moderate illness with COVID-19, such as respiratory rate ≥20 breaths per minute, saturation of oxygen (SpO_2) >93% on room air at sea level, heart rate ≥90 beats per minute; no clinical signs indicative of Severe or Critical Illness	**ACTT-1[1]:** Mild/Moderate disease: confirmed COVID-19 positive and hospitalized with radiographic infiltrates by imaging, SpO_2 >94% and respiratory rate <24 breaths per minute without supplemental oxygen. Moderate not further defined. Results for Moderate not provided. **SIMPLE 2[4]:** Moderate disease: confirmed COVID-19 positive and hospitalized with radiographic evidence of

COVID-19 Disease Severity	NIH COVID-19 Treatment Guidelines[11]	WHO Clinical Management of COVID-19[12]	Food and Drug Administration (FDA)[13]	Included Studies in Evidence Report
				pulmonary infiltrates and oxygen saturation >94% on room air. **WHO[5]:** Not defined as "moderate" but SOLIDARITY included and provided mortality data for hospitalized patients without supplemental oxygen on study entry.
Severe	Individuals who have respiratory frequency >30 breaths per minute, SpO_2 <94% on room air at sea level, ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO_2/FiO_2) <300 mmHg, or lung infiltrates >50%.	Adolescent or adult with clinical signs of pneumonia (fever, cough, dyspnoea, fast breathing) plus 1 of the following: respiratory rate >30 breaths/min; severe respiratory distress; or SpO_2 <90% on room air OR Child with clinical signs of pneumonia (cough or difficulty in breathing) + at least 1 of the following: 1) Central cyanosis or SpO_2 <90%; severe respiratory distress (*eg,* fast breathing, grunting, very severe chest indrawing); general danger sign: inability to breastfeed or drink, lethargy or unconsciousness, or convulsions. 2) Fast breathing (in breaths/min): <2 months: ≥60; 2–11 months: ≥50; 1–5 years: ≥40.	Positive testing by standard RT-PCR assay or an equivalent test; symptoms suggestive of severe systemic illness with COVID-19, which could include: any symptom of moderate illness or shortness of breath at rest, or respiratory distress; clinical signs indicative of severe systemic illness with COVID-19, such as respiratory rate ≥30 per minute, heart rate ≥125 per minute, SpO_2 ≤93% on room air at sea level or PaO_2/FiO_2 <300; no criteria for Critical Severity. Remdesivir Emergency Use Authorization Criteria: Hospitalized with severe disease defined as patients with an oxygen saturation ≤94% on room air or requiring supplemental oxygen or mechanical ventilation or requiring extracorporeal membrane oxygenation (ECMO).	**Wang,[2] ACTT-1,[1] SIMPLE-1[3]:** Hospitalized patients meeting 1 of more of the following criteria: radiographic infiltrates by imaging or clinical assessment and an oxygen saturation ≤94% on room air or tachypnea (respiratory rate >24 breaths per minute without supplemental oxygen) or requiring supplemental oxygen or mechanical ventilation **WHO[5-7]**: Not defined as "severe" but SOLIDARITY included and provided mortality data for hospitalized patients with supplemental oxygen on study entry.
Critical	Individuals who have respiratory failure, septic	Individuals who have respiratory failure, septic	Positive testing by standard RT-PCR assay or equivalent test; evidence of critical illness,	**ACTT-1[1]**: Not defined as "critical" but ACTT-1 included

COVID-19 Disease Severity	NIH COVID-19 Treatment Guidelines[11]	WHO Clinical Management of COVID-19[12]	Food and Drug Administration (FDA)[13]	Included Studies in Evidence Report
	shock, and/or multiple organ dysfunction.	shock, and/or multiple organ dysfunction	defined by at least 1 of the following: respiratory failure defined based on resource utilization requiring at least 1 of the following: endotracheal intubation and mechanical ventilation, oxygen delivered by high flow nasal cannula (heated, humidified, oxygen delivered via reinforced nasal cannula at flow rates >20 L/min with fraction of delivered oxygen ≥0.5), noninvasive positive pressure ventilation, ECMO, or clinical diagnosis of respiratory failure (*ie*, clinical need for 1 of the preceding therapies, but preceding therapies not able to be administered in setting of resource limitation); shock (defined by systolic blood pressure <90 mm Hg, or diastolic blood pressure <60 mm Hg or requiring vasopressors); multi-organ dysfunction/failure.	and provided recovery outcomes for patients requiring invasive mechanical ventilation or ECMO. **WHO[5-7]:** Not defined as "critical" but SOLIDARITY included and provided mortality data for hospitalized patients requiring invasive mechanical ventilation or ECMO on study entry.

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