Remdesivir for COVID-19

Review information

Authors

National COVID-19 Taskforce[1], [Empty name][1]

[1][Empty affiliation]

Citation example: NC-1T, [Empty name]. Remdesivir for COVID-19. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Characteristics of studies

Characteristics of included studies

Beigel 2020

Methods	RCT (n=1063)
Participants	Inclusion: Participants had to meet one of the following criteria suggestive of lower respiratory tract infection at the time of enrolment: radiographic infiltrates by imaging study, peripheral oxygen saturation (SpO2) <94% on room air, or requiring supplemental oxygen, mechanical ventilation, or extracorporeal membrane oxygenation (ECMO). There was no limit to the duration of symptoms prior to enrollment. Participants had to have a laboratory-confirmed SARS-CoV-2 infection as determined by a positive reverse transcription, polymerase-chain-reaction (RT-PCR) assay result from any respiratory specimen collected <72 hours prior to randomization. Exclusion: Having either an alanine aminotransferase (ALT) or an aspartate aminotransferase (AST) > 5 times the upper limit of the normal range; impaired renal function as determined by calculating an estiamted glomerular filtration rate (eGFR), or need for hemodialysis or hemofiltration; allergy to study product; pregnancy or breast-feeding; and anticipated discharge from the hospital or transfer to another hospital within 72 hours of enrollment. Mean age: 59 years Males: 684/1063 (64%) Severity: Mild (n=0); Moderate (n=541); Severe (n=197)
Interventions	(I) Remdesivir (200mg initial, 100mg maintenance) for 10 days; (C) Placebo for 10 days
Outcomes	Time to recovery (days); Recovery prevalence (n/N); All cause mortality at day 14 (n/N); Prevalence of mechanical ventilation (n/N); Serious adverse events (n/N); Adverse events (n/N); Discontinuation due to adverse events (n/N); Septic shock (n/N); Respiratory failure or ARDS (n/N)
Notes	Location: Multicentre - USA, Denmark, UK, Greece *Study characteristics and risk of bias analyses taken from COVID-NMA research group https://covid-nma.com/living_data/index.php **We have used version 2 of the Cochrane risk-of-bias tool for randomised trials (RoB 2) to assess the risk of bias for this study. Refer to Main text > Published notes for more details.**

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Quote from the protocol: ""The study will randomize participants 1:1 to placebo or investigational product. If additional arms are added to or dropped from the trial, randomization will proceed with an equal probability of assignment to each of the remaining arms. Randomization will be stratified by: Site; Severity of illness at enrollment (Severe disease: requiring mechanical ventilation or oxygen, a SpO2 ≤ 94% on room air, or tachypnea (respiratory rate ≥ 24 breaths/min); Mild-moderate disease: SpO2 > 94% and respiratory rate < 24 breaths/min without supplemental oxygen)."" ""Enrollment and randomization of subjects is done online using the enrollment module of Advantage eClinicalÂ®. Eligible subjects will be randomized and assigned in a 1:1 ratio to either remdesivir or placebo, with stratification by site and disease severity (Mild/Moderate disease or Severe disease). The randomization is based on a variable blocked scheme to provide an approximately balanced allocation to the treatment groups during the study. If arms are added or removed later in the study, randomization will continue in an equal allocation manner."""
Allocation concealment (selection bias)	Low risk	See Random sequence generation (selection bias)
Blinding of participants and personnel (performance bias)	High risk	Quote: "The treatment will be prepared by the licensed pharmacist and administered by an unblinded study nurse. All follow-up safety and efficacy evaluations will be performed by blinded clinic staff." Comment: Patients were blinded. The staff administering the intervention was not blinded. There inadequate information to assess whether co-intervention receipt was balanced between the two arms. Data were analyzed by using intent-to-treat analysis.
Blinding of outcome assessment (detection bias)	Low risk	Quote: "All follow-up safety and efficacy evaluations will be performed by blinded clinic staff". Risk assessed to be low for the outcomes: Time to clinical improvement. Clinical improvement. Mortality. Serious adverse events.
Incomplete outcome data (attrition bias)	Low risk	Comment: 1063 randomized/1059 analyzed. Four patients were excluded owing to no data after baseline (they did not fit eligibility the criteria). Risk assessed to be low for the outcomes: Time to clinical improvement. Clinical improvement. Mortality. Serious adverse events.
Selective reporting (reporting bias)	Low risk	Comment: the protocol was available. The statistical analysis plan was not available. Risk assessed to be low for the outcomes: Time to clinical improvement. Clinical improvement. Mortality. Serious adverse events.
Other bias	Unclear risk	

Beigel 2020 hi flow or NIV

Methods	
Participants	
Interventions	
Outcomes	
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	
Allocation concealment (selection bias)	Unclear risk	
Blinding of participants and personnel (performance bias)	Unclear risk	
Blinding of outcome assessment (detection bias)	Unclear risk	
Incomplete outcome data (attrition bias)	Unclear risk	
Selective reporting (reporting bias)	Unclear risk	
Other bias	Unclear risk	

Beigel 2020 Inv vent

Methods	
Participants	
Interventions	
Outcomes	
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	
Allocation concealment (selection bias)	Unclear risk	
Blinding of participants and personnel (performance bias)	Unclear risk	
Blinding of outcome assessment (detection bias)	Unclear risk	
Incomplete outcome data (attrition bias)	Unclear risk	
Selective reporting (reporting bias)	Unclear risk	
Other bias	Unclear risk	

Beigel 2020 lo-flow

Methods	
Participants	
Interventions	
Outcomes	
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	
Allocation concealment (selection bias)	Unclear risk	
Blinding of participants and personnel (performance bias)	Unclear risk	
Blinding of outcome assessment (detection bias)	Unclear risk	
Incomplete outcome data (attrition bias)	Unclear risk	
Selective reporting (reporting bias)	Unclear risk	
Other bias	Unclear risk	

Beigel 2020 no O2

Methods	
Participants	
Interventions	
Outcomes	
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	
Allocation concealment (selection bias)	Unclear risk	
Blinding of participants and personnel (performance bias)	Unclear risk	
Blinding of outcome assessment (detection bias)	Unclear risk	
Incomplete outcome data (attrition bias)	Unclear risk	
Selective reporting (reporting bias)	Unclear risk	
Other bias	Unclear risk	

DisCoVeRy

Methods	
Participants	
Interventions	
Outcomes	
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	
Allocation concealment (selection bias)	Unclear risk	
Blinding of participants and personnel (performance bias)	Unclear risk	
Blinding of outcome assessment (detection bias)	Unclear risk	
Incomplete outcome data (attrition bias)	Unclear risk	
Selective reporting (reporting bias)	Unclear risk	
Other bias	Unclear risk	

DisCoVeRy moderate

Methods	
Participants	
Interventions	
Outcomes	
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	
Allocation concealment (selection bias)	Unclear risk	
Blinding of participants and personnel (performance bias)	Unclear risk	
Blinding of outcome assessment (detection bias)	Unclear risk	
Incomplete outcome data (attrition bias)	Unclear risk	
Selective reporting (reporting bias)	Unclear risk	
Other bias	Unclear risk	

DisCoVeRy severe

Methods	
Participants	
Interventions	
Outcomes	
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	
Allocation concealment (selection bias)	Unclear risk	
Blinding of participants and personnel (performance bias)	Unclear risk	
Blinding of outcome assessment (detection bias)	Unclear risk	
Incomplete outcome data (attrition bias)	Unclear risk	
Selective reporting (reporting bias)	Unclear risk	
Other bias	Unclear risk	

Mahajan 2021

Methods	
Participants	
Interventions	
Outcomes	
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	
Allocation concealment (selection bias)	Unclear risk	
Blinding of participants and personnel (performance bias)	Unclear risk	
Blinding of outcome assessment (detection bias)	Unclear risk	
Incomplete outcome data (attrition bias)	Unclear risk	
Selective reporting (reporting bias)	Unclear risk	
Other bias	Unclear risk	

SOLIDARITY 2020

Methods	RCT (n=5451)
Participants	Eligibility: consenting adults (age ≥18) hospitalised with definite COVID-19, not already receiving any of the study drugs, without known allergy or contra-indications to any of them (in the view of the physician responsible for their care), and without anticipated transfer within 72 hours to a non-study hospital. Patients invited to join the study will be those who are admitted to a collaborating hospital; no wider recruitment efforts are expected. A patient is not eligible for the trial if believed by their physician to have a significant contraindication to any one of the study drugs (eg, serious chronic liver or heart disease or pregnancy)
Interventions	remdesivir (intravenous) was 200 mg on day 0 and 100 mg on days 1 through 9.
Outcomes	primary objective was to assess effects on in-hospital mortality (i.e., death during the original hospitalization; follow-up ceased at discharge), regardless of whether death occurred before or after day 28. The only protocol-specified secondary outcomes were the initiation of mechanical ventilation and hospitalization duration.
Notes	Albania, Argentina, Canada, Colombia, Egypt, Finland, France, Honduras, India, Indonesia, Iran, Ireland, Italy, Kuwait, Lebanon, Lithuania, Luxembourg, Malaysia, North Macedonia, Norway, Pakistan, Peru, Philippines, Saudi Arabia, South Africa, Spain, Switzerland. **We have used version 2 of the Cochrane risk-of-bias tool for randomised trials (RoB 2) to assess the risk of bias for this study. Refer to Main text > Published notes for more details.**

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	
Allocation concealment (selection bias)	Unclear risk	
Blinding of participants and personnel (performance bias)	Unclear risk	
Blinding of outcome assessment (detection bias)	Unclear risk	
Incomplete outcome data (attrition bias)	Unclear risk	
Selective reporting (reporting bias)	Unclear risk	
Other bias	Unclear risk	

SOLIDARITY 2020 low/hi flow

Methods	
Participants	
Interventions	
Outcomes	
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	
Allocation concealment (selection bias)	Unclear risk	
Blinding of participants and personnel (performance bias)	Unclear risk	
Blinding of outcome assessment (detection bias)	Unclear risk	
Incomplete outcome data (attrition bias)	Unclear risk	
Selective reporting (reporting bias)	Unclear risk	
Other bias	Unclear risk	

SOLIDARITY 2020 no O2

Methods	
Participants	
Interventions	
Outcomes	
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	
Allocation concealment (selection bias)	Unclear risk	
Blinding of participants and personnel (performance bias)	Unclear risk	

Blinding of outcome assessment (detection bias)	Unclear risk	
Incomplete outcome data (attrition bias)	Unclear risk	
Selective reporting (reporting bias)	Unclear risk	
Other bias	Unclear risk	

SOLIDARITY 2020 ventilation

Methods	
Participants	
Interventions	
Outcomes	
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	
Allocation concealment (selection bias)	Unclear risk	
Blinding of participants and personnel (performance bias)	Unclear risk	
Blinding of outcome assessment (detection bias)	Unclear risk	
Incomplete outcome data (attrition bias)	Unclear risk	
Selective reporting (reporting bias)	Unclear risk	
Other bias	Unclear risk	

Spinner 2020

Methods	RCT (N=595)
Participants	Hospitalized patients with SARS-CoV-2 infection confirmed by polymerase chain reaction assay within 4 days of randomization and moderate COVID-19 pneumonia (defined as any radiographic evidence of pulmonary infiltrates and oxygen saturation >94% on room air) were enrolled. Excluding: Patients with alanine aminotransferase or aspartate aminotransferase greater than 5 times the upper limit of normal or creatinine clearance of less than 50 mL/min.
Interventions	All patients randomized to a remdesivir group received 200 mg of remdesivir intravenously on day 1, followed by 100 mg of remdesivir once daily for the subsequent days, infused over 30 to 60 minutes

Outcomes	The primary efficacy end point was the distribution of clinical status assessed on the 7-point ordinal scale on study day 11. Secondary end point was the proportion of patients with adverse events throughout the duration of the study.
Notes	France, Germany, Hong Kong, Italy, The Netherlands, Republic of Korea, Singapore, Spain, Switzerland, Taiwan, United Kingdom, United States. **We have used version 2 of the Cochrane risk-of-bias tool for randomised trials (RoB 2) to assess the risk of bias for this study. Refer to Main text > Published notes for more details.**

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	
Allocation concealment (selection bias)	Unclear risk	
Blinding of participants and personnel (performance bias)	Unclear risk	
Blinding of outcome assessment (detection bias)	Unclear risk	
Incomplete outcome data (attrition bias)	Unclear risk	
Selective reporting (reporting bias)	Unclear risk	
Other bias	Unclear risk	

Wang 2020

Methods	RCT (n=237)
Participants	Inclusion criteria: Men and non-pregnant women with COVID-19 who were aged at least 18 years and were RT-PCR positive for SARS-CoV-2, had pneumonia confirmed by chest imaging, had 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, and were within 12 days of symptom onset. Exclusion criteria: Pregnancy or breast feeding; hepatic cirrhosis; alanine aminogransferase or aspartate aminotransferase > 5 times the upper limit of normal; known severe renal impairment (eGFR < 30 mL/min per 1.73m^2) or receipt of continuous renal replacement therapy, haemodialysis, or peritoneal dialysis; possibility of transfer to a non-study hospital within 72 hours; enrolment into an investigational treatment study for COVID-19 in the 30 days before screening. The use of other treatments, including lopinavir-ritonavir, was permitted. Mean age: NR Males: 140/237 (59%) Severity: Mild (n=0); Moderate (n=0); Severe (n=235)
Interventions	(I) Remdesivir (200mg initial, 100mg maintenance) for 10 days; (C) Placebo for 10 days
Outcomes	Clinical improvement (n/N); Time to improvement (days); All cause mortality at day 14 (n/N); All cause mortality at day 28 (n/N); Duration of mechanical ventilation (days); Duration of supplemental oxygen (days); Serious adverse events (n/N); Adverse events (n/N); Discontinuation due to adverse events (n/N); Septic shock (n/N); Respiratory failure or ARDS (n/N); Duration of hospital stay (days); Pulmonary embolism (n/N); Time from randomisation to death (days)

Notes	Location: Multicentre - China *Study characteristics and risk of bias analyses taken from COVID-NMA research group https://covid-nma.com/living_data/index.php **We have used version 2 of the Cochrane risk-of-bias tool for randomised trials (RoB 2) to assess the risk of bias for this study. Refer to Main text > Published notes for more details.**

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote from the protocol: "The allocation sequence is generated according to computer-generated random numbers. Patient randomisation is stratified based on respiratory support methods at the time of enrolment: (1) no oxygen support, oxygen support with nasal duct or mask; (2) high-flow oxygen, non-invasive ventilation, invasive ventilation/ECMO. Concealment mechanism {16b} The allocation sequences are kept in sealed, opaque envelopes. Remdesivir and placebo are preblinded and stored in a secure area in the pharmacy at a temperature strictly controlled according to the protocol. An independent pharmacist is assigned to dispense the study drug in water-proof, sealed, opaque bags. Participants are enrolled by the investigators of each study site. A pharmacist in the central pharmacy assigns participants to interventions." Comment: Few baseline imbalances between groups are noted in Table 1 (e.g., more participants with comorbidities in the remdesivir arm).
Allocation concealment (selection bias)	Low risk	See Random sequence generation (selection bias)
Blinding of participants and personnel (performance bias)	Low risk	Quote from the protocol: "This is a double-blind trial. Trial participants, investigators, care providers, outcome assessors, and data analysts are all blinded. Treatment allocation will only be unblinded after database lock." Risk assessed to be low for the outcomes: Negative viral conversion incidence. Time to clinical improvement. Time to death. Mortality. Length of hospital stay. WHO clinical progression scale Score 6 and above. WHO clinical progression scale Score 7 and above. Total intubation time. Adverse events. Serious adverse events. Clinical improvement incidence.
Blinding of outcome assessment (detection bias)	Low risk	See Blinding of participants and personnel (performance bias)
Incomplete outcome data (attrition bias)	Low risk	Comment: 237 randomized/237 analyzed for all outcomes except negative viral conversion incidence. For this outcome, respiratory specimens were not collected at one study site (n=27 participants with missing data in remdesivir group and n=13 in control group), in which the safety of medical care workers during aerosol generating procedures could not be guaranteed. Risk assessed to be low for the outcomes: Time to clinical improvement. Time to death. Mortality. Length of hospital stay. WHO clinical progression scale Score 6 and above. WHO clinical progression scale Score 7 and above. Total intubation time. Adverse events. Serious adverse events. Clinical improvement incidence. Risk assessed to be "some concerns" for the outcomes: Negative viral conversion incidence.
Selective reporting (reporting bias)	Low risk	Comment: the protocol was available. The statistical analysis plan was not available. Participant recuitment was terminated early, therefore the study was underpowered, which may be the reason why some of the analyses specified in the protocol (e.g., supporting analyses by gender) are not reported in the paper. For dichotomous outcomes, data were collected at 7, 14, 21 and 28 days, but are reported only for 7, 14 and 21 days. However, these reported comparisons are not statistically significant, so it is unlikely that the outcomes were selected on the basis of the result. Risk assessed to be low for the outcomes: Negative viral conversion incidence. Time to clinical improvement. Time to death. Mortality. Length of hospital stay. WHO clinical progression scale Score 6 and above. WHO clinical progression scale Score 7 and above. Total intubation time.

		Adverse events. Serious adverse events. Clinical improvement incidence.
Other bias	High risk	Comment: Blinded study (participants and personnel). Efficacy outcome data were analyzed by using modified intention-to-treat analysis (1 participant withdrew consent post-randomization in the control arm). Safety outcome data (adverse events) were analyzed by using "naÃ¯ve" per protocol analysis for participants who received no doses of the treatment in the intervention arm (3 participants who did not receive remdesivir were excluded from analysis).

Footnotes

Characteristics of excluded studies

Footnotes

References to studies

Included studies

Beigel 2020

* Biegel J.H., Tomashek K.M., Dodd, L.E. et al. Remdesivir for the Treatment of Covid-19 - Preliminary Report. The New England Journal of Medicine 2020.

Beigel 2020 hi flow or NIV

[Empty]

Beigel 2020 Inv vent

[Empty]

Beigel 2020 lo-flow

[Empty]

Beigel 2020 no O2

[Empty]

DisCoVeRy

[Empty]

DisCoVeRy moderate

[Empty]

DisCoVeRy severe

[Empty]

Mahajan 2021

[Empty]

SOLIDARITY 2020

[Empty]

SOLIDARITY 2020 low/hi flow

[Empty]

SOLIDARITY 2020 no O2

[Empty]

SOLIDARITY 2020 ventilation

[Empty]

Spinner 2020

Christoph D. Spinner, MD; Robert L. Gottlieb,MD, PhD; Gerard J. Criner, MD; JosÃ© RamÃ³n Arribas LÃ³pez, MD; Anna Maria Cattelan, MD;Alex Soriano Viladomiu, MD; Onyema Ogbuagu, MD; Prashant Malhotra, MD; Kathleen M. Mullane, DO; Antonella Castagna, MD;Louis Yi Ann Chai, MD; Meta Roestenberg, MD; Owen Tak Yin Tsang, MD; Enos Bernasconi, MD; Paul Le Turnier, MD; Shan-Chwen Chang, MD;Devi SenGupta, MD; Robert H. Hyland, DPhil; Anu O. Osinusi, MD; Huyen Cao, MD; Christiana Blair, MS; HongyuanWang, PhD;Anuj Gaggar,MD, PhD; Diana M. Brainard, MD; Mark J. McPhail, MD; Sanjay Bhagani, MD; Mi Young Ahn, MD; Arun J. Sanyal, MD;Gregory Huhn, MD; Francisco M. Marty, MD; for the GS-US-540-5774 Investigators. Effect of Remdesivir vs Standard Care on Clinical Status at 11 Daysin Patients With Moderate COVID-19A Randomized Clinical Trial. JAMA August 21, 2020.. [DOI: 10.1001/jama.2020.16349]

Wang 2020

Wang, Y., Zhang, D., Du, G. et al. Remdesivir in adults with severe COVID-19: a randomised, double-blind, placebo-controlled, multicentre trial. The Lancet 29 April 2020.

Excluded studies

Data and analyses

1 Remdesivir vs control

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
1.1 All cause mortality (day 28)	5	7333	Risk Ratio (M-H, Random, 95% CI)	0.93 [0.82, 1.06]
1.2 All-cause mortality (day 28; ventilation)	5	1332	Risk Ratio (M-H, Random, 95% CI)	1.16 [0.96, 1.41]

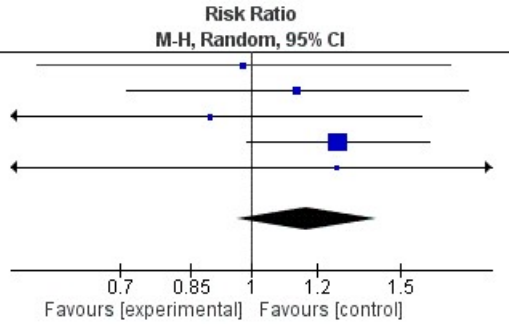
1.3 All-cause mortality (day 28; hospital no ventilation)	8	6904	Risk Ratio (M-H, Random, 95% CI)	0.81 [0.65, 1.01]
1.4 All cause mortality (day 14)	3	1877	Risk Ratio (M-H, Random, 95% CI)	0.61 [0.43, 0.86]
1.5 All-cause mortality (day 28; subgroups v1)	9	7322	Risk Ratio (M-H, Random, 95% CI)	0.92 [0.73, 1.16]
1.5.1 No, low/hi	6	6318	Risk Ratio (M-H, Random, 95% CI)	0.72 [0.52, 1.01]
1.5.2 Ventilation	4	1004	Risk Ratio (M-H, Random, 95% CI)	1.20 [0.98, 1.47]
1.6 All-cause mortality (day 28; subgroups v2 in EP)	12	8236	Risk Ratio (M-H, Random, 95% CI)	0.95 [0.79, 1.13]
1.6.1 No, low/hi, Beigel NIV	8	6904	Risk Ratio (M-H, Random, 95% CI)	0.81 [0.65, 1.01]
1.6.2 Ventilation	5	1332	Risk Ratio (M-H, Random, 95% CI)	1.16 [0.96, 1.41]
1.7 Adverse events	4	2704	Risk Ratio (M-H, Random, 95% CI)	1.03 [0.92, 1.16]
1.8 Discontinuation due to adverse events	3	1880	Risk Ratio (M-H, Random, 95% CI)	1.73 [0.57, 5.28]
1.9 Septic shock	2	1296	Risk Ratio (M-H, Random, 95% CI)	1.02 [0.34, 3.01]
1.10 Clinical recovery (day 28)	3	1876	Risk Ratio (M-H, Random, 95% CI)	0.99 [0.86, 1.14]
1.11 Time to recovery	2	1643	Hazard Ratio (IV, Random, 95% CI)	1.24 [1.08, 1.42]
1.12 Time to improvement (2 points on scale)	2	810	Hazard Ratio (IV, Random, 95% CI)	1.17 [1.00, 1.38]
1.13 Respiratory failure or ARDS	3	2120	Risk Ratio (M-H, Random, 95% CI)	0.82 [0.50, 1.33]
1.14 Mechanical ventilation or ECMO	1	766	Risk Ratio (M-H, Random, 95% CI)	0.57 [0.42, 0.79]
1.15 Discharge from hospital	3	6365	Risk Ratio (M-H, Random, 95% CI)	1.03 [0.94, 1.13]
1.16 Duration of hospital stay (days)	0	0	Mean Difference (IV, Fixed, 95% CI)	Not estimable
1.17 Serious adverse events	4	2689	Risk Ratio (M-H, Random, 95% CI)	0.82 [0.65, 1.04]
1.20 Patients requiring ventilation	2	5034	Risk Ratio (M-H, Random, 95% CI)	1.04 [0.89, 1.21]

Figures

Figure 1 (Analysis 1.2)

Study or Subgroup	Remdesivir Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Beigel 2020 hi flow or NIV	19	95	20	98	11.4%	0.98 [0.56, 1.72]
Beigel 2020 Inv vent	28	131	29	154	16.6%	1.14 [0.71, 1.81]
DisCoVeRy severe	19	161	22	167	10.8%	0.90 [0.50, 1.59]
SOLIDARITY 2020 ventilation	98	254	71	233	58.0%	1.27 [0.99, 1.62]
Wang 2020	11	29	3	10	3.2%	1.26 [0.44, 3.63]
Total (95% CI)		**670**		**662**	**100.0%**	**1.16 [0.96, 1.41]**
Total events	175		145			

Heterogeneity: Tau² = 0.00; Chi² = 1.65, df = 4 (P = 0.80); I² = 0%
Test for overall effect: Z = 1.57 (P = 0.12)

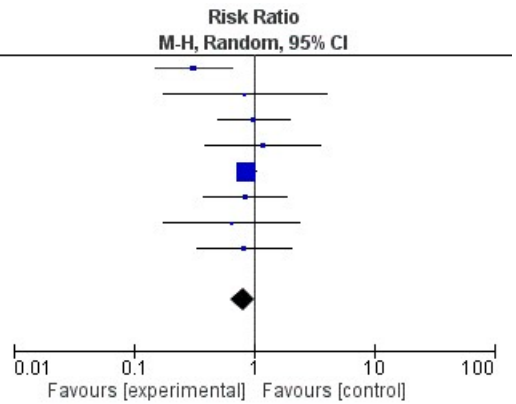


Forest plot of comparison: 1 Remdesivir vs control, outcome: 1.2 All-cause mortality (day 28; ventilation).

Figure 2 (Analysis 1.3)

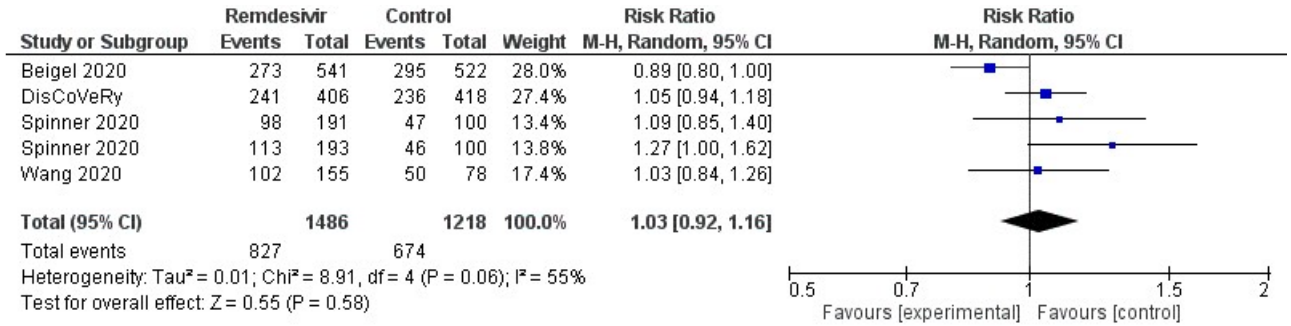
Study or Subgroup	Remdesivir Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Beigel 2020 lo-flow	9	232	25	203	8.2%	0.32 [0.15, 0.66]
Beigel 2020 no O2	3	75	3	63	1.9%	0.84 [0.18, 4.02]
DisCoVeRy moderate	15	253	15	251	9.2%	0.99 [0.50, 1.99]
Mahajan 2021	6	41	5	41	3.8%	1.20 [0.40, 3.62]
SOLIDARITY 2020 low/hi flow	192	1828	219	1811	61.2%	0.87 [0.72, 1.04]
SOLIDARITY 2020 no O2	11	661	13	664	7.2%	0.85 [0.38, 1.88]
Spinner 2020	5	384	4	200	2.8%	0.65 [0.18, 2.40]
Wang 2020	11	129	7	68	5.7%	0.83 [0.34, 2.04]
Total (95% CI)		**3603**		**3301**	**100.0%**	**0.81 [0.65, 1.01]**
Total events	252		291			

Heterogeneity: Tau² = 0.01; Chi² = 7.69, df = 7 (P = 0.36); I² = 9%
Test for overall effect: Z = 1.89 (P = 0.06)



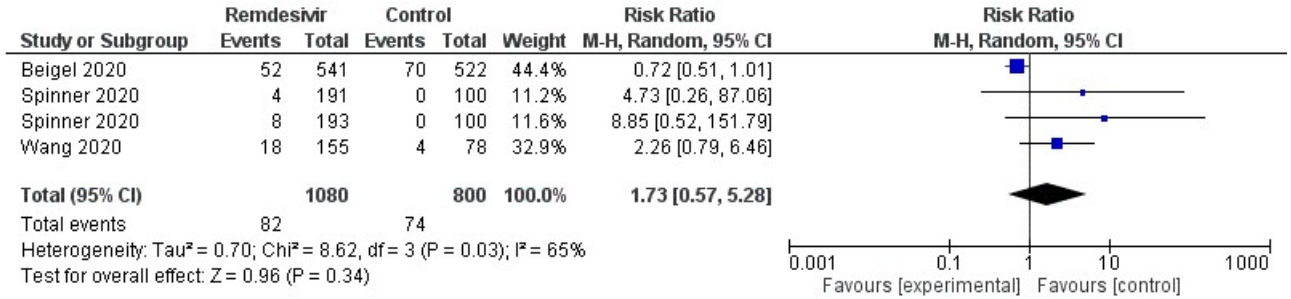
Forest plot of comparison: 1 Remdesivir vs control, outcome: 1.3 All-cause mortality (day 28; hospital no ventilation).

Figure 3 (Analysis 1.7)



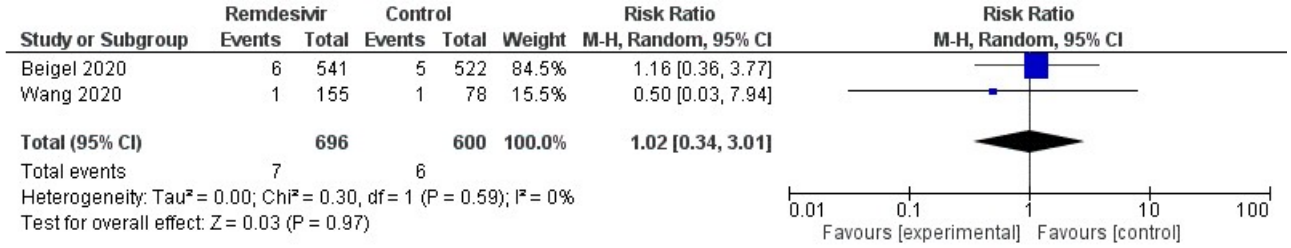
Forest plot of comparison: 1 Remdesivir vs control, outcome: 1.7 Adverse events.

Figure 4 (Analysis 1.8)



Forest plot of comparison: 1 Remdesivir vs control, outcome: 1.8 Discontinuation due to adverse events.

Figure 5 (Analysis 1.9)

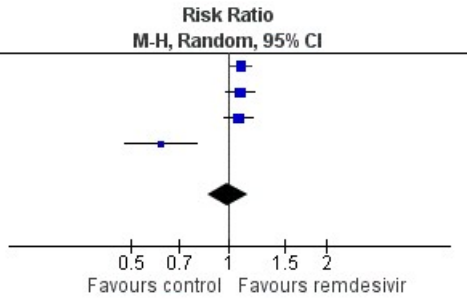


Forest plot of comparison: 1 Remdesivir vs control, outcome: 1.9 Septic shock.

Figure 6 (Analysis 1.10)

Study or Subgroup	Remdesivir Events	Remdesivir Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Beigel 2020	399	541	352	521	29.4%	1.09 [1.01, 1.18]
Spinner 2020	174	193	83	100	27.7%	1.09 [0.98, 1.20]
Spinner 2020	170	191	83	100	27.6%	1.07 [0.97, 1.19]
Wang 2020	60	153	49	77	15.3%	0.62 [0.48, 0.80]
Total (95% CI)		**1078**		**798**	**100.0%**	**0.99 [0.86, 1.14]**
Total events	803		567			

Heterogeneity: Tau² = 0.02; Chi² = 18.21, df = 3 (P = 0.0004); I² = 84%
Test for overall effect: Z = 0.08 (P = 0.93)

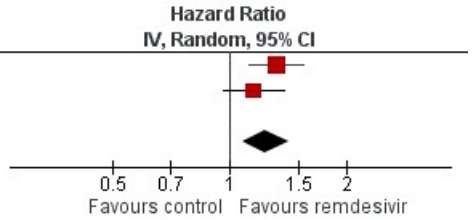


Forest plot of comparison: 1 Remdesivir vs control, outcome: 1.10 Clinical recovery (day 28).

Figure 7 (Analysis 1.11)

Study or Subgroup	log[Hazard Ratio]	SE	Remdesivir Total	Control Total	Weight	Hazard Ratio IV, Random, 95% CI
Beigel 2020	0.2776	0.0838	538	521	53.8%	1.32 [1.12, 1.56]
Spinner 2020	0.1398	0.0921	384	200	46.2%	1.15 [0.96, 1.38]
Total (95% CI)			**922**	**721**	**100.0%**	**1.24 [1.08, 1.42]**

Heterogeneity: Tau² = 0.00; Chi² = 1.22, df = 1 (P = 0.27); I² = 18%
Test for overall effect: Z = 3.12 (P = 0.002)

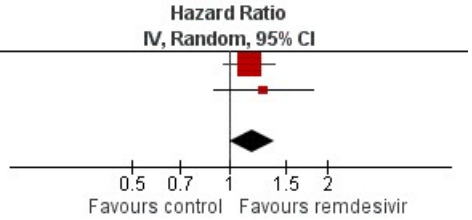


Forest plot of comparison: 1 Remdesivir vs control, outcome: 1.11 Time to recovery.

Figure 8 (Analysis 1.12)

Study or Subgroup	log[Hazard Ratio]	SE	Remdesivir Total	Control Total	Weight	Hazard Ratio IV, Random, 95% CI
Spinner 2020	0.1398	0.0921	384	200	79.5%	1.15 [0.96, 1.38]
Wang 2020	0.239	0.1814	150	76	20.5%	1.27 [0.89, 1.81]
Total (95% CI)			**534**	**276**	**100.0%**	**1.17 [1.00, 1.38]**

Heterogeneity: Tau² = 0.00; Chi² = 0.24, df = 1 (P = 0.63); I² = 0%
Test for overall effect: Z = 1.95 (P = 0.05)

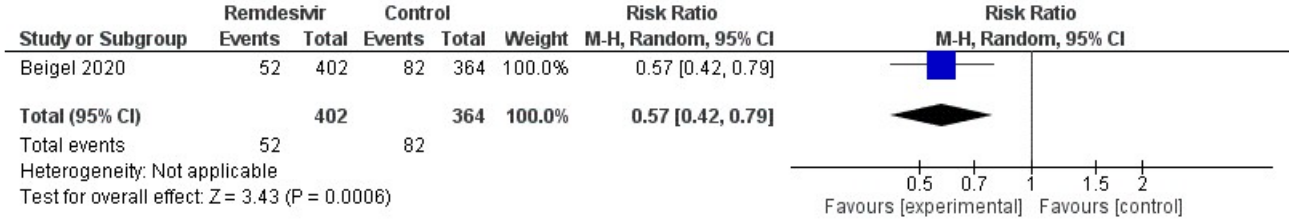


Forest plot of comparison: 1 Remdesivir vs control, outcome: 1.12 Time to improvement (2 points on scale).

Figure 9 (Analysis 1.13)

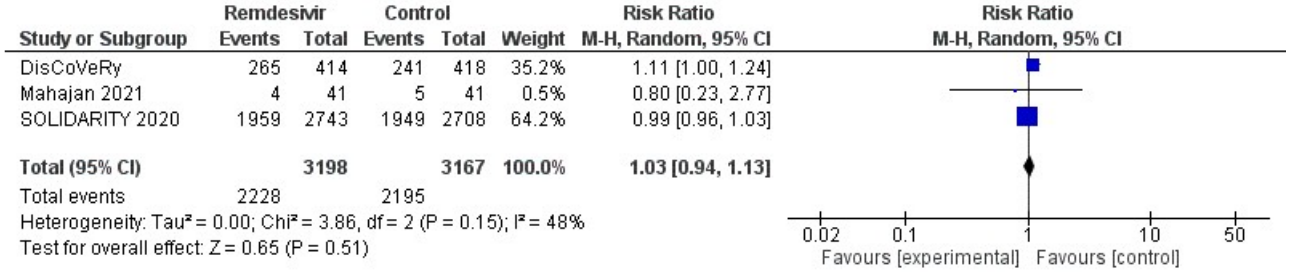
Forest plot of comparison: 1 Remdesivir vs control, outcome: 1.13 Respiratory failure or ARDS.

Figure 10 (Analysis 1.14)



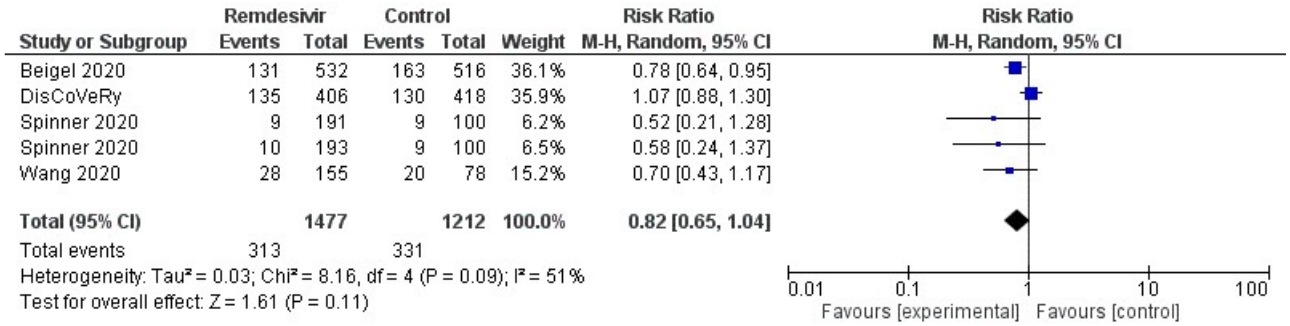
Forest plot of comparison: 1 Remdesivir vs control, outcome: 1.14 Mechanical ventilation or ECMO.

Figure 11 (Analysis 1.15)



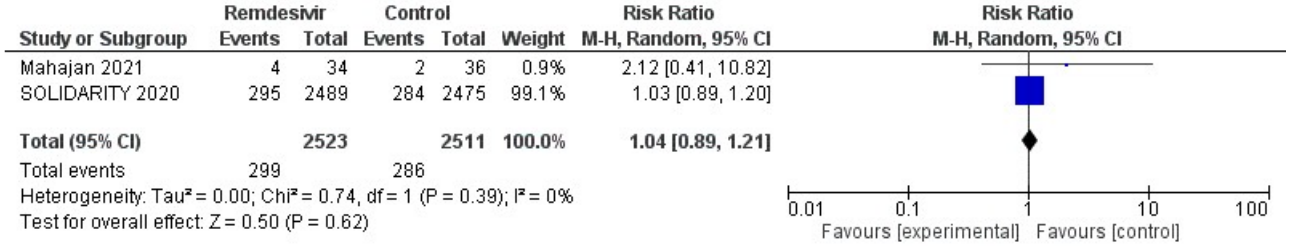
Forest plot of comparison: 1 Remdesivir vs control, outcome: 1.15 Discharge from hospital.

Figure 12 (Analysis 1.17)



Forest plot of comparison: 1 Remdesivir vs control, outcome: 1.17 Serious adverse events.

Figure 13 (Analysis 1.20)



Forest plot of comparison: 1 Remdesivir vs control, outcome: 1.20 Patients requiring ventilation.