Title: Antivirals in non-severe COVID-19 infection: a systematic review and network meta-analysis

Correspondence:
Dena Zeraatkar
Email: Dena_Zeraatkar@hms.harvard.edu

Appendix 1, as submitted by the authors. Appendix to: Pitre T Van Alstine R, Chick G, et al. Antiviral drugs in nonsevere COVID-19: a systematic review and network meta-analysis. CMAJ 2022. doi: 10.1503/cmaj.220471.

Table of contents

Appendix 1, as submitted by the authors. Appendix to: Pitre T Van Alstine R, Chick G, et al.
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Supplement 1. Search strategy

We leveraged our search strategy and search results from the Epistemonikos/World Health Organization COVID-19 L-OVE repository. Details on the search strategy are found here: but also presented below.

The COVID-19 L·OVE repository was built, and is maintained, by systematic searches in multiple databases, trial registries and preprint servers. Searches are not restricted by study design, language or publication status: The following sources are regularly searched:
Pubmed/medline (updated several times a day) EMBASE (updated weekly) CINAHL (updated weekly) PsycINFO (updated weekly) LILACS (Latin American & Caribbean Health Sciences Literature) (updated weekly) Wanfang Database (updated every 2 weeks) CBM - Chinese Biomedical Literature Database (updated every 2 weeks) CNKI - Chinese National Knowledge Infrastructure (updated every 2 weeks) VIP - Chinese Scientific Journal Database (updated every 2 weeks) IRIS (WHO Institutional Repository for Information Sharing) (updated weekly) IRIS PAHO (PAHO Institutional Repository for Information Sharing)) (updated weekly) IBECS - Índice Bibliográfico Español en Ciencias de la Salud (Spanish Bibliographic Index on Health Sciences) (updated weekly) Microsoft Academic (last searched: 23 August 2021) ICTRP Search Portal (updated daily) Clinicaltrials.gov (updated daily) ISRCTN registry (updated daily) Chinese Clinical Trial Registry (updated daily) IRCT - Iranian Registry of Clinical Trials (updated daily)

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EU Clinical Trials Register: Clinical trials for covid-19 (updated daily)
NIPH Clinical Trials Search (Japan) - Japan Primary Registries Network (JPRN) (JapicCTI, JMACCT CTR, jRCT, UMIN CTR) (updated daily, via ICTRP search portal)
UMIN-CTR - UMIN Clinical Trials Registry (updated daily, via ICTRP search portal)
JRCT - Japan Registry of Clinical Trials (updated daily, via ICTRP search portal)
JAPIC Clinical Trials Information (updated daily, via ICTRP search portal)
Clinical Research Information Service (CRiS), Republic of Korea (updated daily, via ICTRP search portal)
ANZCTR - Australian New Zealand Clinical Trials Registry (updated daily, via ICTRP search portal)
ReBec - Brazilian Clinical Trials Registry (updated daily, via ICTRP search portal)
CTRI - Clinical Trials Registry - India (updated daily, via ICTRP search portal)
RPCEC - Cuban Public Registry of Clinical Trials (updated daily, via ICTRP search portal)
DRKS - German Clinical Trials Register (updated daily, via ICTRP search portal)
LBCTR - Lebanese Clinical Trials Registry (updated daily, via ICTRP search portal)
TCTR - Thai Clinical Trials Registry (updated daily, via ICTRP search portal)
NTR - The Netherlands National Trial Register (updated daily, via ICTRP search portal)
PACTR - Pan African Clinical Trial Registry (updated daily, via ICTRP search portal)
REPEC - Peruvian Clinical Trial Registry (updated daily, via ICTRP search portal)
SLCTR - Sri Lanka Clinical Trials Registry (updated daily, via ICTRP search portal)
medRxiv (updated several times a day)
bioRxiv (updated several times a day)
SSRN Preprints (updated several times a day)
ChinaXiv (updated every 2 weeks)
SciELO Preprints (updated weekly)
Research Square (updated daily)

We adapted our main COVID-19 boolean strategy (see below) to the syntax of each source. The information is obtained from the sources using different technology solutions, such as querying publicly available APIs, subscribing to RSS feeds, parsing .csv files posted on

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websites and running traditional manual searches.
Box 1. Search strategy (version 1.0)
COVID OR *coronavir* OR *coronovir* OR *betacoronavir* OR *beta-coronavirus* OR "corona virus" OR "virus corona" OR "corono virus" OR "virus corono" OR *neocoronavir* OR hcov* OR *2019-ncov* OR *cv19* OR *cv-19* OR "cv 19" OR n-cov* OR ncov* OR (wuhan* AND (virus OR viruses OR viral)) OR *cv-19* OR sars* OR sari OR "severe acute respiratory syndrome" OR antisars* OR anti-sars* OR "corona patients" OR *pandemi*

The records are deduplicated and cleansed using proprietary software of Epistemonikos Foundation.

Other Search sources
In order to identify articles that an electronic search could potentially miss, we:
Manually check all the systematic reviews and other types of evidence syntheses (e.g. overviews of systematic reviews, scoping reviews, guidelines) and add all articles included in those.
Evaluate potentially eligible articles that users send by email and other means (e.g. twitter).
As randomised trials are particularly relevant for decision-making, we also:
Run a regular search for randomised trials on Twitter using the terms #COVID19 OR #COVID-19 OR #COVID_19 OR #COVID randomized OR randomised.
Scan relevant scientific conferences.
Manually review press release websites.
Check the websites of the main trials and companies relevant to COVID-19.

How articles in the interface works

Article selection
The details of the automated classification process and the classification workflow are described in the 'COVID-19 L·OVE classification platform' section. We describe here the specificities of the 'COVID-19 classification' process since it defines if a record becomes part of the 'COVID-19 L·OVE repository.

Automated classification
All the articles retrieved by the electronic searches are assessed by two automated classifiers specifically developed for this project. The first classifier is a binary exact-match classifier based on a continuously updated list of terms obtained by applying Word2vec technology with proprietary software developed by Epistemonikos to the corpus of documents available in the repository. The terms with more similar vectors are analyzed by a team of content and methods experts and are selected based on their incremental recall (i.e. their capacity to identify new 'positives' in the unclassified records). The second classifier combines a highly specific COVID-19 boolean strategy with the publication date of the articles (year 2020 or more recent).
Human classification

The articles included by the classifiers are screened by the COVID-19 L·OVE users, collaborators or methods team (e.g. during collective screening of the classification platform).

The articles excluded by the classifier are not checked. However, any time an article is identified by another means (e.g. a study included in a systematic review) the methods team checks for the presence of any term that can be added to the search strategy or the list of terms used by the exact-match classifier.

Eligibility criteria
Articles are only included if they directly address an issue concerning COVID-19 or the indirect consequences of COVID-19 (e.g. the consequences of lockdown). We do not include COVID-19 articles that might be relevant but were conducted in different contexts (e.g. telemedicine before the COVID-19 pandemic, facemasks for influenza).
Inclusion in the repository is not restricted by study design, language or publication status.

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Supplement 2. Risk of bias tool

Bias from the randomization process	
Issues to consider: Random sequence generation Allocation concealment	
Definitely low risk of bias	Trials that assign participants to alternative interventions using a randomly generated sequence and maintain allocation concealment. Examples of methods for developing a randomly generated allocation sequence include a random number generator, random number table, coin tossing, shuffling cards or envelopes, and throwing dice. If a trial is described as 'randomized' without any additional details related to how the allocation sequence was developed, we will assume that the allocation sequence was appropriately developed. Examples of methods for maintaining allocation concealment include using central allocation via a computer or phone system, pharmacy-controlled allocation, opaque sealed envelopes, and sequentially numbered drug containers. *Note that an explicit description of random sequence generation is not necessary for a rating of low risk of bias.*

Probably low risk of bias	Trials in which healthcare providers were blind to the intervention but which provide no information on allocation concealment and in which there are no major baseline imbalances. *Note that an explicit description of random sequence generation is not necessary for a rating of probably low risk of bias.*
Probably high risk of bias	Trials in which healthcare providers were not blind to the intervention and which provide no information on allocation concealment Trials in which there are substantial baseline differences between trial arms that suggest a problem with the randomization process but there are no other limitations related to randomization.
Definitely high risk of bias	Trials in which allocation is by judgment of the clinician, by preference of the participant, by availability of the intervention, based on the results of a laboratory test, or other non-random rules (e.g., birthdate, etc.). Trials in which investigators enrolling participants could possibly foresee the arm to which each subsequent patient would be randomized, such as allocation using an open allocation schedule (e.g. a list of random numbers), assignment envelopes used without appropriate safeguards (e.g. use of unsealed, non-opaque or not sequentially numbered envelopes), alternation between arms, case record number, or any other explicitly unconcealed procedure, rate as high risk.
Bias due to deviations from the intended intervention	
Issues to consider: Blinding of healthcare providers/clinicians and participants Imbalances in cointerventions or behaviors	

Definitely low risk of bias	Therapy trials in which healthcare providers are blind to the intervention administered and in which there are no significant differences in administered co-interventions. Therapy trials that are described as double or triple blind.
Probably low risk of bias	Therapy trials in which healthcare providers are not blind to the intervention administered. Therapy trials in which healthcare providers are blind to the intervention administered but there are significant differences in administered co-interventions that suggests that blinding may have been compromised. Therapy trials in which healthcare providers are described as being blind to the intervention but allocation concealment was inadequate.
Probably high risk of bias	
Definitely high risk of bias	Therapy trials in which healthcare providers are not blind to the intervention and in which there are significant differences in administered co-interventions.
Bias due to missing data	
Issues to consider: Missing outcome measures Loss to follow-up	
Definitely low risk of bias	Trials in which missing outcome data (including outcome data that has been imputed) < 10%. For in-patient trials, we will assume low risk of bias due to missing data unless otherwise specified.

Probably low risk of bias	Trials in which missing outcome data (including outcome data that has been imputed) is between 10% to 15% and missing outcome data is unlikely to be related to the true outcome and there is no imbalance in numbers of or reasons for missing data across intervention groups.
Probably high risk of bias	Trials in which missing outcome data (including outcome data that has been imputed) is between 10% to 15% and missing outcome data is likely to be related to the true outcome or there are imbalances in numbers of or reasons for missing data across intervention groups.
Definitely high risk of bias	Trials in which missing outcome data (including outcome data that has been imputed) > 15%.
Bias due to measurement of the outcome	
Issues to consider: Blinding of outcome adjudicators Objectivity of outcome *Note that the judgments may differ across outcomes.*	
Definitely low risk of bias	Trials in which patients are blind to the intervention and in which outcomes are patient-reported. Trials in which outcomes are measured by a third-party (investigator or clinician) and in which the third-party is blind to the intervention. Trials in which the outcomes are objective. Trials that are described as double or triple blind.
Probably low risk of bias	
Probably high risk of bias	

Definitely high risk of bias	Trials in which patients are not blind and in which outcomes are patient-reported (e.g., time to symptom resolution). Trials in which outcome adjudicators are not blind and the outcomes are not objective (e.g., adverse effects leading to discontinuation, transfusion-related acute lung injury, transfusion-associated circulatory overload, allergic reactions, infection with suspected/symptomatic COVID-19, venous thromboembolism, time to symptom resolution including fever, time to clinical improvement if the criteria for clinical improvement are not objective).
Bias in selection of the reported results	
Issues to consider: Selective reporting of timepoints Selective reporting of outcome measures *Note that we are only interested in selective reporting for the outcomes for which we are extracting data.* *Note that the judgments may differ across outcomes.*	
Definitely low risk of bias	Results for outcomes that were analyzed and reported according to a pre-specified statistical analysis plan or protocol (including the timepoint for the measurement of the outcome).
Probably low risk of bias	Results for outcomes that were analyzed and reported but that were not prespecified in a statistical analysis plan or protocol but the timepoint at which results are reported is consistent with the timepoint for other outcomes in the trial report or there is little reason to believe the outcome was selectively reported.

	Please note that outcomes that were not prespecified in a protocol or statistical analysis plan and that are reported in the trial preprint or publication should be rated at probably low risk of bias unless there are other important reasons to suspect that results for those outcomes were selectively reported (e.g., results are presented at timepoints that don't match the timepoints reported for other outcomes).
Probably high risk of bias	Results for outcomes that were analyzed and reported but that were not prespecified in a statistical analysis plan or protocol but the timepoint at which results are reported is not consistent with the timepoint for other outcomes in the trial report or there are other reasons to believe that the outcome is selectively reported.
Definitely high risk of bias	Results for outcomes that were analyzed and reported for which there are inconsistencies with the statistical analysis plan or protocol. These inconsistencies may include outcome measures of interest or the timepoints for the measurement of outcomes.

Supplement 3. Meta-analysis and GRADE terminology

These are provided to help readers who are unfamiliar with network meta-analysis or GRADE.

Network meta-analysis	A type of meta-analysis that compares more than two treatments against one another using direct and indirect estimates to produce a network estimate. Normally, the network estimates are presented in the results, unless the certainty of the direct estimates are higher.
Frequentist network meta-analysis	This is one of the two methods of analysis for network meta-analysis. The other is a Bayesian network meta-analysis. They differ in the usual way that Bayesian and frequentist statistics differ, mainly that Bayesian methods use probabilities in the analysis whereas frequentists do not. The consequence of this is that Bayesian methods usually produce wider confidence intervals than frequentist estimates, as a result of assumed greater network wide heterogeneity. Both are valid methods of performing network analysis.
Node splitting	Network estimates that have indirect and direct evidence, these estimates are split into three components. The network estimate, indirect estimate and direct estimate are inspected for consistency. Consistency is assessed mainly by inspection of the point estimate and the confidence intervals (i.e., whether they overlap).
Heterogeneity estimators	Ae methods for calculating heterogeneity (differences between studies) in meta-analysis. Restricted Maximum Likelihood (REML) estimator is one such example. Simulation studies show that this method produces better error rates.
Meta-regression	Is similar to simple regression, where the outcome of interest is predicted on the basis of one or more explanatory variables.

Dose-response meta-analysis	Dose-response meta-analysis summarizes the quantitative relationship between doses of an exposure and an outcome across studies.
ICEMAN tool	Is a validated instrument designed to evaluate the credibility of a subgroup.
GRADE	GRADE is the most widely adopted tool for grading the quality of evidence and for making recommendations with over 100 organizations worldwide officially endorsing GRADE. The GRADE framework requires judgements to be made by the researchers and may not be reproducible [1-3]

Domains for evaluating evidence for network and dose-response meta-analysis [4-9].

All ratings start at high and may be downgraded due to issues in one or more domains below.

Risk of bias	Using a validated tool, researchers can assess the risk of bias of studies included in an estimate. They rate the certainty down once for studies at risk of bias. We rated studies using a modification of the risk of bias tool 2.0, which was used in two previous peer reviewed meta-analyses. For each estimate, we looked at the proportion of studies that were at risk of bias. We rated down for risk of bias once if removal of the risk of bias studies from the analysis significantly changed the results. We rated down for risk of bias also if all the studies were at risk of bias. We did not rate down more than once.

Imprecision	Using minimally important differences, we rated down the certainty of evidence by once, twice or three times, depending on how uncertain the result is. Using a minimally contextualized framework, we rated down once for imprecision if the confidence intervals included the MID. If the confidence interval included the MID in both directions we rated down twice. We did not rate down three times for any estimate. .
Indirectness	This is assessed whether the population and intervention of interest are congruent with the research question. If it is not, researchers may rate down the certainty of evidence. We assessed this by evaluating each trial and making judgements on the included trials, interventions (dose, route, duration) and how each outcome was measured.
Publication bias	In estimates with 10 more studies, publication bias can be assessed. If there is publication bias, investigators may rate down. We assessed publication bias by inspecting funnel plots and Egger's statistical test.
Inconsistency	The individual study estimates may be inconsistent with each other. If this is detected, we may further rate down the certainty of evidence.

	We assessed for inconsistency by reviewing forest plots for each estimate. Both the width and overlap of confidence intervals were measured. I^2 statistics were also assessed. If inconsistency was detected, we rated down if removal of that study changed the results.
Incoherence	Coherence refers to consistency between direct and indirect estimates We planned to rate down for incoherence when the indirect and direct estimates were different enough such that there was no overlap in confidence intervals. We rated down for incoherence in the duration of the hospitalization network. According to guidance, in the face of incoherence, one needs to base the certainty rating on the evidence that most contributes to the network estimate. When incoherence is present, however, we rated down the network evidence further.
Intransitivity	Intransitivity is the dissimilarity of important factors that may affect the outcome being investigated (i.e., effect modifiers) across comparisons. We looked at multiple possible effect modifiers across the network to determine whether there was intransitivity.

Related methodological clarifications

Point estimates and statistical significance

A common interpretation confusion is around statistical significance. GRADE does not include statistical significance in the rating of the certainty of the evidence. To illustrate why, take for example, a point estimate of drug X versus placebo may indicate a reduction in mortality by 1% and be statistically significant but the certainty of the estimate may be very low, based on the methods described above. Despite the result being statistically significant, you may not trust the result and limit its implications for practice. Furthermore, statistical significance does not translate into clinical significance. Therefore, the GRADE approach does not place emphasis on statistical significance. Rather, the focus is on the certainty around the point estimate using the validated methods described above. Further issues with interpretation of p-values and the importance of interpreting the effect size has been previously discussed [10-13].

Minimally contextualized approach

A minimally contextualized approach minimizes value judgments regarding the magnitude of intervention effects. It involves a multi-step process, including choosing a reference intervention (i.e placebo) and a decision threshold. A decision threshold can be determined by pre-existing analysis of minimally important differences or by researcher judgment (i.e. a 2% reduction in mortality or a 5% reduction in serious adverse events). The decision threshold is important in determining imprecision, as interventions with 95% credibility interval that cross the decision threshold may be labeled imprecise [4].

Simple language summary

The GRADE approach uses a standardized method for reporting the certainty of evidence in simple language [14]. The use of language will also depend on whether the researchers chose a partially or fully contextual approach. For our paper, we chose a partially contextualized approach. The simple language summary used in our paper is as follows:

High certainty evidence = Drug X reduces mortality
Moderate certainty evidence = Drug X likely reduces mortality
Low certainty evidence = Drug X may reduce mortality

Very low certainty evidence = The evidence of drug X on mortality is very uncertain

Summary of findings (Table 2)

We present the results of our NMA in table 2, which summarizes the network estimates of each treatment node versus placebo. Direct estimates were occasionally presented if the certainty of the evidence was higher. All head-to-head comparisons are presented in the supplementary files, but one can determine the relative effectiveness of one drug versus another by looking at how each drug compares against placebo. This is possible because the network estimates essentially standardize the results against placebo. This is the accepted method for presenting the summary of findings for NMA, which is elegantly demonstrated in the largest living network meta-analysis in the world [15].

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Supplement 4. Studies excluded from the systematic review and meta-analysis

Study	**Abd-Elsalam 2021 (NCT04345419)**
Intervention	Remdesivir
Exclusion reason	Only severe patients, average saturation <92% on room air.
Study	**Abbass 2021 (ISRCTN21085622)**
Intervention	Daclatasvir, sofosbuvir
Exclusion reason	Majority severe/critical, no subgroup data.
Study	**Ader 2021 (NCT04315948)**
Intervention	Remdesivir
Exclusion reason	Only severe patients based on exclusion criteria, no subgroup data.
Study	**Alavi-Moghaddam 2021 (IRCT20200328046882N1)**
Intervention	Sofosbuvir
Exclusion reason	100% severe disease.
Study	**Arabi 2021 (NCT02735707)**
Intervention	Lopinavir-ritonavir
Exclusion reason	Severe patients only, no subgroup data.
Study	**Cao 2020 (ChiCTR2000029308)**

Intervention	Lopinavir-ritonavir
Exclusion reason	Severe only, no subgroup data.
Study	**Darazam 2021 (NCT04350684)**
Intervention	umifenovir
Exclusion reason	Only severe patients (SpO2 <93% on room air), no subgroup data.
Study	**El-Bendary 2021 (NR)**
Intervention	sofosbuvir-daclatasvir
Exclusion reason	Only severe patients (SpO2 <90% on room air), no subgroup data.
Study	**Fitzgerald 2021 (NCT04746183)**
Intervention	Molnupiravir
Exclusion reason	No outcomes of interest.
Study	**Horby 2020 (NCT04381936)**
Intervention	Lopinavir-ritonavir
Exclusion reason	Only severe patients, no subgroup data.
Study	**Kalantari 2021 (NR)**
Intervention	Lopinavir-ritonavir

Exclusion reason	Only severe patients, no subgroup data.
Study	**Khodashahi 2020 (IRCT20200325046859N2)**
Intervention	Umifenovir
Exclusion reason	Only severe patients, no subgroup data.
Study	**Lou 2020 (ChiCTR2000029544)**
Intervention	Baloxavir marboxil
Exclusion reason	Mostly severe, no subgroup data.
Study	**Mahajan 2021 (NR)**
Intervention	Remdesivir
Exclusion reason	Only severe patients included, no subgroup data.
Study	**Nojomi 2020 (IRCT20180725040596N2)**
Intervention	Lopinavir-ritonavir
Exclusion reason	Only severe patients included with average SpO2 <90%. No subgroup data.
Study	**Ogbuagu 2021 (NCT04252664)**
Intervention	Remdesivir
Exclusion reason	No outcomes of interest.
Study	**Ramachandran 2021 (CTRI/2020/09/027535)**

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Intervention	Umifenovir
Exclusion reason	All patients on oxygen, no subgroup data.
Study	**SOLIDARITY 2020 (ISRCTN83971151, NCT04315948)**
Intervention	Lopinavir-ritonavir
Exclusion reason	Only severe patients, no subgroup data.
Study	**Sadeghi 2020 (IRCT20200128046294N2)**
Intervention	Sofosbuvir-daclatasvir
Exclusion reason	Only severe patients, no subgroup data.
Study	**Sayad 2021 (IRCT20130812014333N145)**
Intervention	Sofosbuvir, velpatasvir
Exclusion reason	Only severe patients, no subgroup data.
Study	**Solaymani-Dodaran 2021 (IRCT20200318046812N1)**
Intervention	Favipiravir
Exclusion reason	Only severe patients, no subgroup data.
Study	**Wang 2021 (NCT04257656)**
Intervention	Remdesivir
Exclusion reason	All patients on oxygen, no subgroup data.

Study	**Yadegarinia 2020 (NR)**
Intervention	Umifenovir
Exclusion reason	Only severe patients, no subgroup data.

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Supplement 5. Trial characteristics

Study	Year	Country	N	Age	Male %	Inpatient %	Mild %	Moderate %	Severe %	Critical %	Respiratory condition %	Cardiovascular disease %	Diabetes %	Hypertension %
Ader	2021	France, Luxembourg	300	63	71.7	100	0	63.81	36.19	NR	15.09	25.9	21.95	NR
Ali	2022	Canada	1282	65.51	59.8	100	0	NR	NR	NR	18.42	19.91	26.78	NR
Arruda	2021	Brazil	150	38.04	35.4	0	NR	NR	0	0	6.28	3.15	9.76	17.04
Balykova_1	2020	Russia	39	47.33	NR	100	0	100	0	0	NR	0	NR	NR
Balykova_2	2020	Russia	206	49.68	48.54	100	0	NR	NR	NR	4.85	5.83	8.74	27.67
Barratt-Due	2021	Norway	94	59.8	65.75	100	NR	NR	NR	NR	5.52	15.47	17.13	30.39
Beigel	2020	United States, Denmark, United Kingdom, Greece, Germany, Korea, Mexico, Spain, Japan, Singapore	1062	58.9	64.41	100	NA	NR	90.11	NR	21.2	17.42	31.57	50.71
Bernal	2021	Multicontinental	1433	44.85	48.71	0	54.78	44.52	0.28	0	3.98	11.65	15.91	NR
Chen	2020	China	240	NR	46.61	NR	0	88.55	10.17	1.27	NR	NR	11.44	27.97
Criner	2020	China	384	57	61	100	0	100	0	0	11	NR	NR	39
Doi	2020	Japan	89	50	61.36	100	NR	NR	NR	NR	NR	NR	NR	NR

Study	Year	Country	N	Age	Male %	Inpatient %	Mild %	Moderate %	Severe %	Critical %	Respiratory condition %	Cardiovascular disease %	Diabetes %	Hypertension %
EPIC-HR	2021	Argentina, Brazil, Bulgaria, Colombia, Czechia, Hungary, India, Japan, Korea, Malaysia, Mexico, Peru, Puerto Rico, Poland, Russia, South Africa, Spain, Taiwan, Thailand, Turkey, Ukraine, United States	2085	NR	NR	0	NR	NR	NR	NR	NR	NR	NR	NR
EPIC-SR	2021	North America, South America, Europe, Africa, Asia,	854	NR	NR	0	NR	NR	0	0	NR	NR	NR	NR

Study	Year	Country	N	Age	Male %	Inpatient %	Mild %	Moderate %	Severe %	Critical %	Respiratory condition %	Cardiovascular disease %	Diabetes %	Hypertension %
		United States												
Fischer	2021	United States	85	40.09	48.51	0	NR	NR	0	0	NR	NR	NR	NR
Gaitain-Duarte	2021	Colombia	324	55.39	67.61	100	NR	NR	NR	NR	4.42	2.68	12	27.8
Ghaderkhani	2020	Iran	56	44.38	60.38	3.77	NR	NR	0	0	NR	NR	NR	NR
Gottlieb	2021	United States, Spain, Denmark, United Kingdom	584	50.5	52.14	0	NR	NR	0	0	24.02	7.83	61.57	47.69
Huang	2020	China	69	42.5	45.54	100	NR	NR	0	0	0	0	NR	NR
Ivashchenko	2020	Russia	40	50.73	50	100	0	100	0	0	NR	NR	NR	NR
Kasgari	2020	Iran	48	52.5	37.5	100	0	100	0	0	2.08	22.92	37.5	35.42
Khoo	2021	United Kingdom	8	56	27.78	0	NR	NR	0	0	NR	NR	NR	NR
Li	2020	China	69	49.4	46.51	100	12.79	87.21	0	0	0	2.33	2.32	10.47
McCreary	2021	United States	105	56	40.95	0	NR	NR	0	0	NR	NR	NR	NR
Mobarak	2021	Iran	1083	58	54.02	100	0	100	0	0	6.92	9.14	27.61	33.98
Nourian	2020	Iran	90	62.23	NR	100	56.1	43.9	0	0	4.88	31.71	45.12	45.12
Ogbuagu	2021	China	1005	NR	NR	100	0	NR	NR	0	NR	NR	NR	NR

Study	Year	Country	N	Age	Male %	Inpatient %	Mild %	Moderate %	Severe %	Critical %	Respiratory condition %	Cardiovascular disease %	Diabetes %	Hypertension %
Pan	2020	Albania, Argentina, Austria, Belgium, Brazil, Canada, Colombia, Egypt, Finland, France, Honduras, India, Indonesia, Iran, Ireland, Italy, Kuwait, Lebanon, Lithuania, Luxembourg, Macedonia, Malaysia, Norway, Pakistan, Phillippines, Peru, Saudi Arabia, South Africa, Spain,	5475	NR	62.94	100	NR	NR	NR	NR	10.53	20.88	25.19	NR

Study	Year	Country	N	Age	Male %	Inpatient %	Mild %	Moderate %	Severe %	Critical %	Respiratory condition %	Cardiovascular disease %	Diabetes %	Hypertension %
		Switzerland												
Parienti	2021	France	60	45.25	43.33	0	95	5	0	0	NR	NR	3.33	5
Ren	2020	China	20	52	60	100	100	0	0	0	0	5	5	5

Study	Year	Country	N	Age	Male %	Inpatient %	Mild %	Moderate %	Severe %	Critical %	Respiratory condition %	Cardiovascular disease %	Diabetes %	Hypertension %
Roozbeh	2020	Iran	60	43	47.27	0	100	0	0	0	NR	0	NR	NR
Ruzhentsova	2020	Russia	168	41.8	47.02	24.4	25.6	74.4	0	0	0	0	0	NR
Shinkai	2021	Japan	156	45.34	66.67	100	0	100	0	0	NR	NR	NR	NR
Udwadia	2020	India	150	43.29	73.47	100	60.54	39.46	0	0	0	0	NR	NR
Wang_1	2020	China	237	65	59.32	100	0	0	100	0	NR	7.2	23.73	43.22
Wang_2	2020	China	60	NR	38.3	100	0	100	0	0	NR	NR	NR	NR
Wu	2020	China	52	58	50	100	NR	NR	NR	NR	5.8	23.1	15.4	28.8
Yadollahzadeh	2021	Iran	112	57.56	44.64	100	NR	NR	0	0	3.57	15.18	21.43	25
Yakoot	2020	Egypt	89	49.01	42.7	100	13.48	68.54	17.98	0	1.12	8.99	19.1	25.84
Yethindra	2020	Kyrgyzstan	30	36.5	60	100	NR	NR	0	0	NR	0	NR	NR
Zhao	2021	China	55	55.7	45.45	0	1.82	96.36	1.82	NR	NR	7.27	14.55	30.91
Zheng	2020	China	60	46.73	47.19	100	0	94.38	5.62	NR	2.02	3.03	8.08	6.06

[a]N = number randomized

[b]Mild = Symptomatic but no dyspnea or abnormal chest imaging

[c]Moderate = Evidence of lower respiratory disease but whose spO2 is >=94% on room air

[d]Severe = spO2 is <94% on room air

[e]Critical = respiratory failure, shock or multiorgan dysfunction

[f]Respiratory condition = any chronic lung disease

[g]Cardiovascular disease = any chronic cardiac or vascular disease

[h]Diabetes = either type I or II

NR = not reported

Supplement 6. Risk of bias judgements

Study	Outcome	Bias arising from the randomization process	Bias due to deviations from the intended intervention	Bias due to missing outcome data	Bias in measurement of the outcome	Bias in selection of the reported results
Ader	Adverse events leading to drug discontinuation	Low risk	Probably low risk	Low risk	High risk	Low risk
Balykova_1	Adverse events leading to drug discontinuation	Low risk	Probably low risk	Low risk	High risk	Low risk
Gaitan-Duarte	Adverse events leading to drug discontinuation	Low risk	Probably low risk	Low risk	High risk	Low risk
Parienti	Adverse events leading to drug discontinuation	Low risk	Probably low risk	Low risk	High risk	Low risk
Yakoot	Adverse events leading to drug discontinuation	Low risk	Probably low risk	Low risk	High risk	Low risk
Huang	Adverse events leading to drug discontinuation	Probably high risk	Probably low risk	Low risk	High risk	Low risk

Khoo	Adverse events leading to drug discontinuation	Probably high risk	Probably low risk	Low risk	High risk	Low risk
Ruzhentsova	Adverse events leading to drug discontinuation	Probably high risk	Probably low risk	Low risk	High risk	Low risk
Udwadia	Adverse events leading to drug discontinuation	Probably high risk	Probably low risk	Low risk	High risk	Low risk
Beigel	Adverse events leading to drug discontinuation	Low risk	Low risk	Low risk	Low risk	Low risk
Bernal	Adverse events leading to drug discontinuation	Low risk	Low risk	Low risk	Low risk	Low risk
Fischer	Adverse events leading to drug discontinuation	Low risk	Low risk	Low risk	Low risk	Low risk
Wang_1	Adverse events leading to drug discontinuation	Low risk	Low risk	Low risk	Low risk	Low risk
EPIC-HR	Adverse events leading to drug discontinuation	Probably low risk	Low risk	Low risk	Low risk	Low risk
Gottlieb	Adverse events leading to drug discontinuation	Probably low risk	Low risk	Low risk	Low risk	Low risk

Bernal	Hospital admission	Low risk	Low risk	Low risk	Low risk	Low risk
McCreary	Hospital admission	Low risk	Low risk	Low risk	Low risk	Low risk
Roozbeh	Hospital admission	Low risk	Low risk	Low risk	Low risk	Low risk
EPIC-HR	Hospital admission	Probably low risk	Low risk	Low risk	Low risk	Low risk
EPIC-SR	Hospital admission	Probably low risk	Low risk	Low risk	Low risk	Low risk
Gottlieb	Hospital admission	Probably low risk	Low risk	Low risk	Low risk	Low risk
Arruda	Hospital admission	Probably high risk	Probably low risk	Low risk	Low risk	Low risk
Ader	Mechanical ventilation	Low risk	Probably low risk	Low risk	Low risk	Low risk
Balykova_2	Mechanical ventilation	Low risk	Probably low risk	Low risk	Low risk	Low risk
Beigel	Mechanical ventilation	Low risk	Low risk	Low risk	Low risk	Low risk
Bernal	Mechanical ventilation	Low risk	Low risk	Low risk	Low risk	Low risk
Gaitan-Duarte	Mechanical ventilation	Low risk	Probably low risk	Low risk	Low risk	Low risk
McCreary	Mechanical ventilation	Low risk	Low risk	Low risk	Low risk	Low risk
Pan_remdesivir	Mechanical ventilation	Low risk	Probably low risk	Low risk	Low risk	Low risk

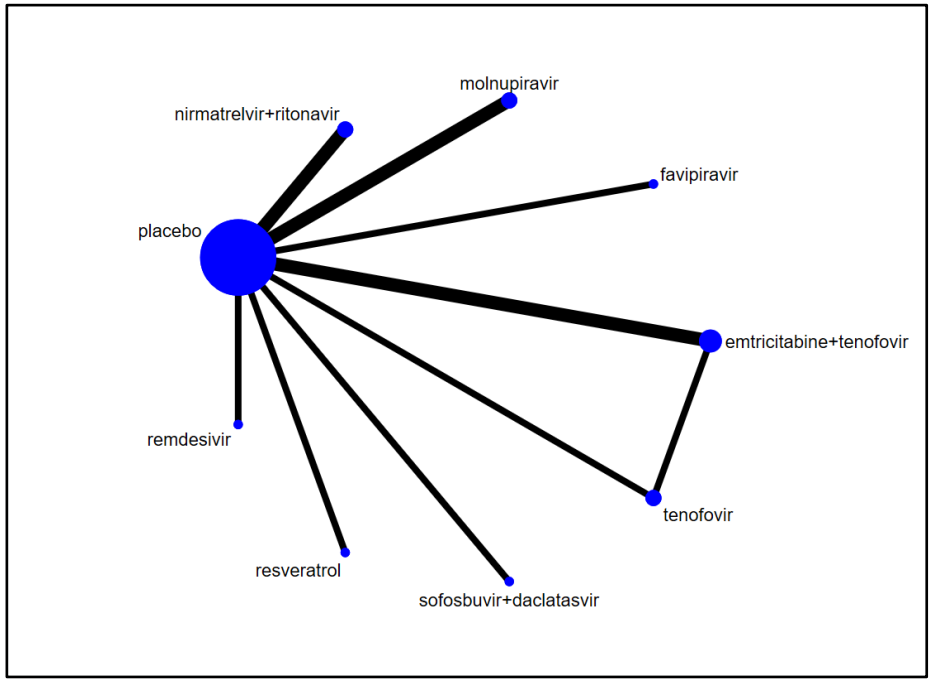
Yakoot	Mechanical ventilation	Low risk	Probably low risk	Low risk	Low risk	Low risk
Ghandehari	Mechanical ventilation	Probably high risk	Probably low risk	Low risk	Low risk	Low risk
Ivashchenko	Mechanical ventilation	Probably high risk	Probably high risk	Low risk	Low risk	Low risk
Criner	Adverse events leading to drug discontinuation	Probably high risk	Probably low risk	Low risk	High risk	Probably high risk
Barratt-Due	Adverse events leading to drug discontinuation	Low risk	Probably low risk	Low risk	High risk	Probably low risk
Kasgari	Adverse events leading to drug discontinuation	Low risk	Probably low risk	Low risk	High risk	Probably low risk
Nourian	Adverse events leading to drug discontinuation	Low risk	Probably high risk	Low risk	High risk	Probably low risk
Shinkai	Adverse events leading to drug discontinuation	Low risk	Probably low risk	Low risk	High risk	Probably low risk
Ivashchenko	Adverse events leading to drug discontinuation	Probably high risk	Probably high risk	Low risk	High risk	Probably low risk
Ren	Adverse events leading to drug discontinuation	Probably high risk	Probably low risk	Low risk	High risk	Probably low risk

Wang_2	Adverse events leading to drug discontinuation	Probably high risk	Probably low risk	Low risk	High risk	Probably low risk
Mobarak	Adverse events leading to drug discontinuation	Low risk	Low risk	Low risk	Low risk	Probably low risk
Wu	Adverse events leading to drug discontinuation	High risk	Probably low risk	Low risk	Low risk	Probably low risk
Fischer	Hospital admission	Low risk	Low risk	Low risk	Low risk	Probably low risk
Parienti	Hospital admission	Low risk	Probably low risk	Low risk	Low risk	Probably low risk
Ruzhentsova	Hospital admission	Probably high risk	Probably low risk	Low risk	Low risk	Probably low risk
Kasgari	Mechanical ventilation	Low risk	Probably low risk	Low risk	Low risk	Probably low risk
Mobarak	Mechanical ventilation	Low risk	Low risk	Low risk	Low risk	Probably low risk
Nourian	Mechanical ventilation	Low risk	Probably high risk	Low risk	Low risk	Probably low risk
Shinkai	Mechanical ventilation	Low risk	Probably low risk	Low risk	Low risk	Probably low risk
Wang_1	Mechanical ventilation	Low risk	Low risk	Low risk	Low risk	Probably low risk
Balykova_1	Mechanical ventilation	Probably high risk	Probably high risk	Low risk	Low risk	Probably low risk

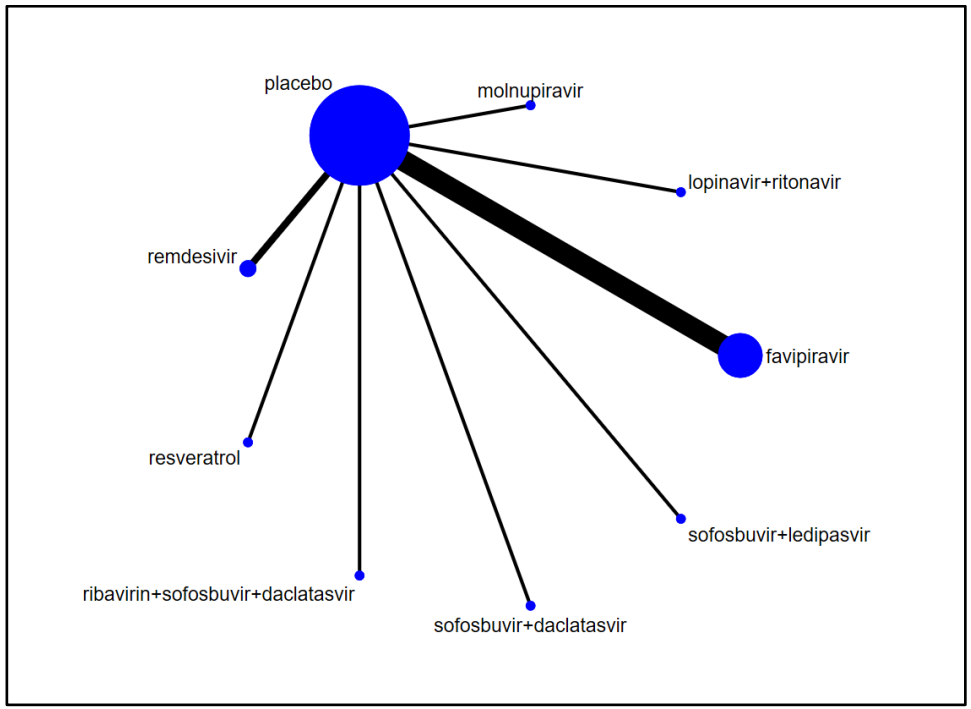
Doi	Mechanical ventilation	Probably high risk	Probably low risk	Low risk	Low risk	Probably low risk
Ruzhentsova	Mechanical ventilation	Probably high risk	Probably low risk	Low risk	Low risk	Probably low risk
Udwadia	Mechanical ventilation	Probably high risk	Probably low risk	Low risk	Low risk	Probably low risk
Ghandehari	Adverse events leading to drug discontinuation	Probably high risk	Probably low risk	Low risk	Probably high risk	Probably low risk
Li	Adverse events leading to drug discontinuation	Low risk	Probably low risk	Low risk	Probably low risk	Probably low risk

Supplement 7. Network diagrams

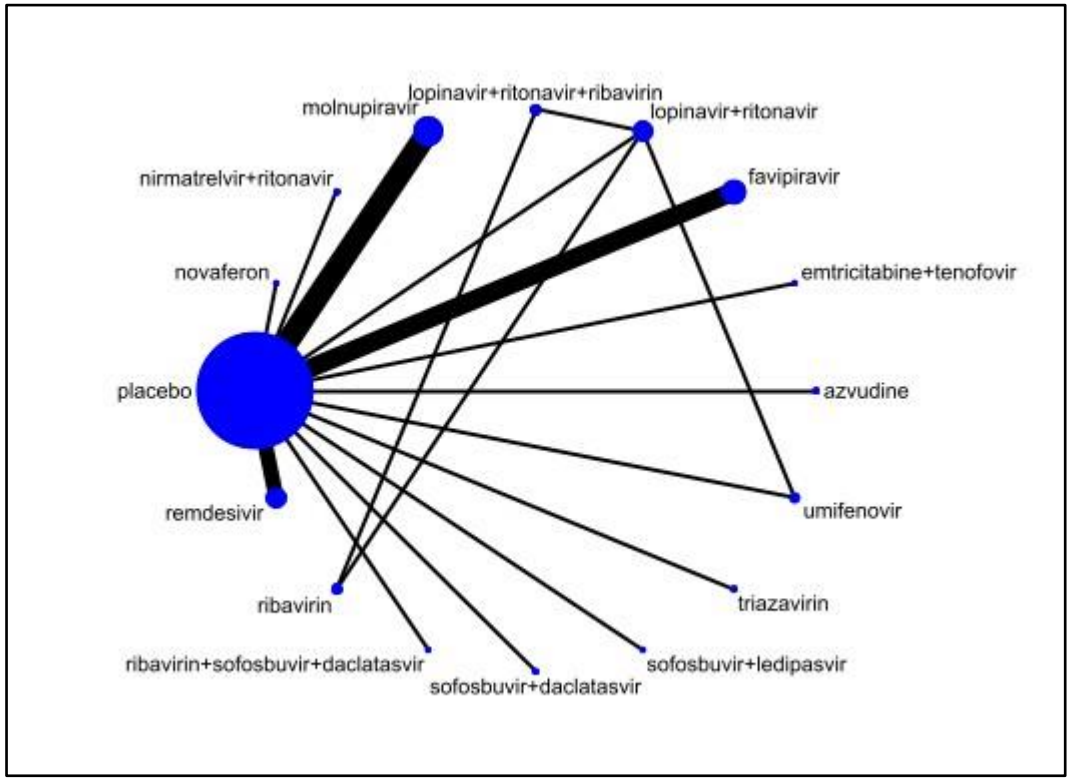
Hospitalizations:



Mechanical ventilation:



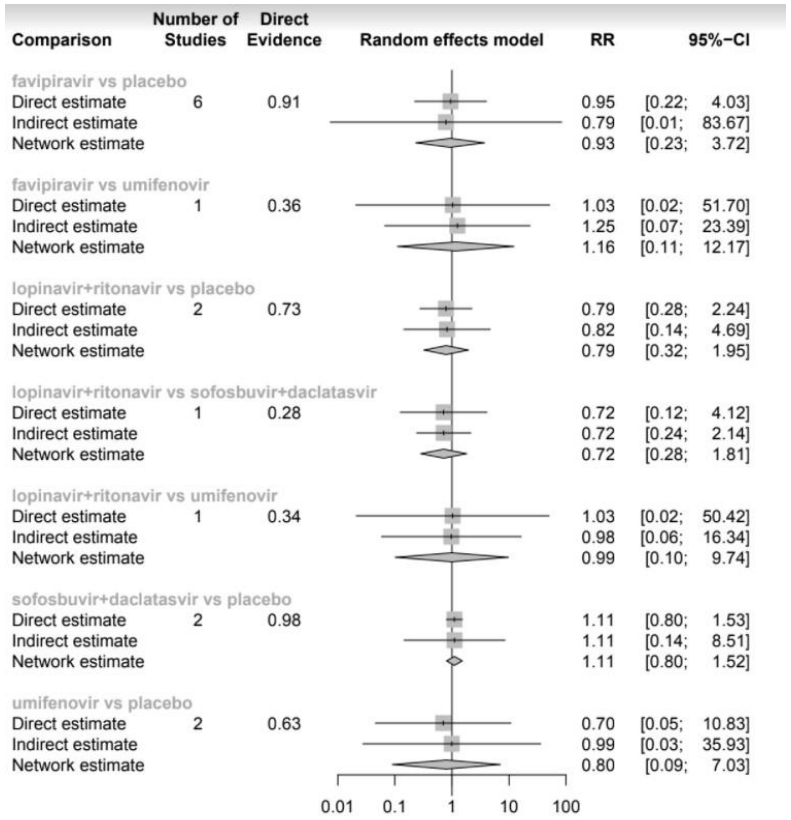
Adverse events lead to drug discontinuation:



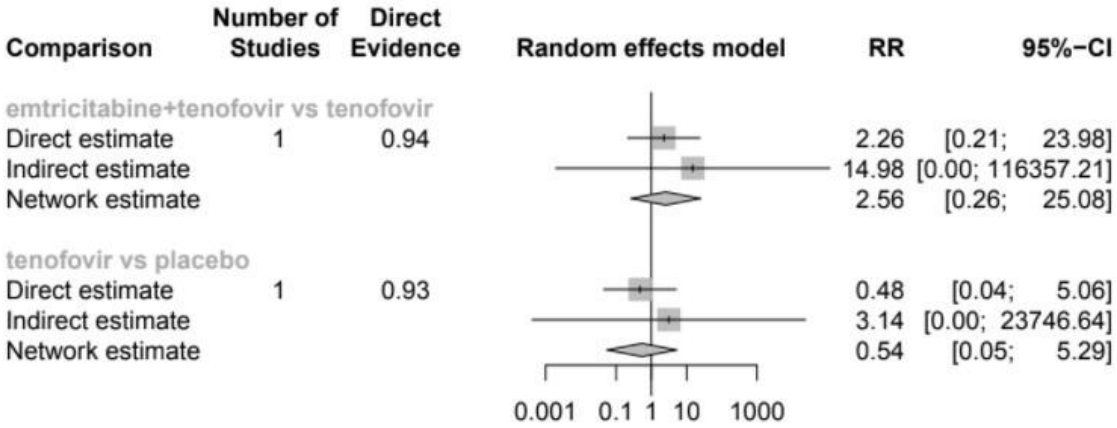
Supplement 8. Node splitting models

No node splitting plots available for mechanical ventilation or adverse events due to no indirect evidence comparisons. The number of the direct evidence column is the P-value to test for differences between groups.

Mortality



Hospitalizations



Supplement 9. Network estimates with GRADE ratings

Mortality network

Mortality network	Comparison	Network estimate			Network estimate			
		Relative estimate			Absolute risk per 1000			
Treatment 1	Treatment 2	Point estimate	CI Lower limit	CI upper limit	Point estimate	CI Lower limit	CI upper limit	GRADE rating
azvudine	emtricitabine+tenofovir	1.39	0.03	74.77	3.73	-9.2	981.85	Very low
azvudine	favipiravir	1.08	0.02	66.65	0.95	-12.43	830.3	Very low
emtricitabine+tenofovir	favipiravir	0.77	0.15	3.94	-2.9	-10.74	37.2	Very low
azvudine	lopinavir+ritonavir	1.26	0.02	68.06	2.72	-10.27	705.17	Very low
emtricitabine+tenofovir	lopinavir+ritonavir	0.9	0.26	3.14	-1.02	-7.78	22.47	Moderate
favipiravir	lopinavir+ritonavir	1.17	0.23	6.03	1.8	-8.12	52.91	Very low
azvudine	lopinavir+ritonavir+ribavirin	1.12	0	295.21	1.49	-12.3	3634.37	Very low
emtricitabine+tenofovir	lopinavir+ritonavir+ribavirin	0.8	0.01	47.82	-2.42	-12.19	578.4	Very low
favipiravir	lopinavir+ritonavir+ribavirin	1.04	0.02	71.11	0.53	-12.16	866.07	Very low
lopinavir+ritonavir	lopinavir+ritonavir+ribavirin	0.89	0.02	43.61	-1.35	-12.13	526.34	Very low
azvudine	molnupiravir	5.43	0.09	324.79	16.62	-3.41	1214.21	Very low

emtricitabine+tenofovir	molnupiravir	3.89	0.84	18.14	10.86	-0.61	64.26	Moderate
favipiravir	molnupiravir	5.05	0.77	33.17	15.19	-0.87	120.65	Low
lopinavir+ritonavir	molnupiravir	4.31	0.91	20.51	12.43	-0.35	73.18	Moderate
lopinavir+ritonavir+ribavirin	molnupiravir	4.84	0.07	320.55	14.42	-3.48	1198.3	Very low
azvudine	nirmatrelvir+ritonavir	8.29	0.09	755.58	13.4	-1.67	1387.1	Very low
emtricitabine+tenofovir	nirmatrelvir+ritonavir	5.94	0.51	68.76	9.09	-0.89	124.56	Low
favipiravir	nirmatrelvir+ritonavir	7.71	0.53	112.18	12.33	-0.86	204.37	very low
lopinavir+ritonavir	nirmatrelvir+ritonavir	6.58	0.56	77.18	10.26	-0.81	140.03	Low
lopinavir+ritonavir+ribavirin	nirmatrelvir+ritonavir	7.39	0.07	738.85	11.75	-1.7	1356.35	Very low
molnupiravir	nirmatrelvir+ritonavir	1.53	0.11	21	0.97	-1.63	36.77	Low
azvudine	placebo	1	0.02	48.8	0	-13.04	636.12	Very low
emtricitabine+tenofovir	placebo	0.72	0.3	1.7	-3.76	-9.28	9.29	Moderate
favipiravir	placebo	0.93	0.23	3.72	-0.93	-10.21	36.16	Very low
lopinavir+ritonavir	placebo	0.79	0.32	1.95	-2.74	-9.01	12.67	Low
lopinavir+ritonavir+ribavirin	placebo	0.89	0.02	48.41	-1.44	-13.09	630.94	Very low
molnupiravir	placebo	0.18	0.05	0.66	-10.86	-12.62	-4.55	Moderate
nirmatrelvir+ritonavir	placebo	0.12	0.01	1.19	-11.7	-13.15	2.58	Moderate
remdesivir	placebo	0.82	0.54	1.26	-2.38	-6.17	3.43	High
resveratrol	placebo	1	0.02	49.5	0	-13.04	645.54	Low
ribavirin	placebo	0.87	0.02	46.95	-1.79	-13.1	611.52	Very low

ribavirin+sofosbuvir+daclatasvir	placebo	0.14	0.01	2.62	-11.41	-13.21	21.59	Low
sofosbuvir+daclatasvir	placebo	1.11	0.8	1.52	1.41	-2.61	6.93	High
sofosbuvir+ledipasvir	placebo	0.95	0.2	4.44	-0.63	-10.59	45.84	Very low
triazavirin	placebo	0.33	0.01	7.82	-8.87	-13.12	90.75	Very low
umifenovir	placebo	0.8	0.09	7.03	-2.68	-12.1	80.22	Very low
azvudine	remdesivir	1.22	0.02	60.82	2.37	-10.62	651.02	Very low
emtricitabine+tenofovir	remdesivir	0.87	0.33	2.28	-1.38	-7.25	13.98	Moderate
favipiravir	remdesivir	1.13	0.27	4.83	1.44	-7.99	41.63	very low
lopinavir+ritonavir	remdesivir	0.97	0.36	2.62	-0.36	-6.99	17.59	Moderate
lopinavir+ritonavir+ribavirin	remdesivir	1.09	0.02	60.3	0.94	-10.67	645.34	Very low
molnupiravir	remdesivir	0.22	0.06	0.86	-8.44	-10.25	-1.53	Moderate
nirmatrelvir+ritonavir	remdesivir	0.15	0.01	1.51	-9.28	-10.73	5.57	Moderate
azvudine	resveratrol	1	0	246.42	0	-13.47	3320.44	Very low
emtricitabine+tenofovir	resveratrol	0.72	0.01	38.95	-3.83	-13.35	513.39	Low
favipiravir	resveratrol	0.93	0.01	58.37	-0.94	-13.33	776.17	Very low
lopinavir+ritonavir	resveratrol	0.79	0.01	43.49	-2.78	-13.33	574.85	Low
lopinavir+ritonavir+ribavirin	resveratrol	0.89	0	237.07	-1.46	-13.48	3193.85	Very low
molnupiravir	resveratrol	0.18	0	11.15	-11.04	-13.49	137.29	Very low
nirmatrelvir+ritonavir	resveratrol	0.12	0	11.12	-11.9	-13.51	136.98	Very low
remdesivir	resveratrol	0.82	0.02	41.54	-2.42	-13.31	548.49	Very low

azvudine	ribavirin	1.16	0	304.39	1.77	-11.35	3457.77	Very low
emtricitabine+tenofovir	ribavirin	0.83	0.01	49.32	-1.95	-11.24	550.66	Very low
favipiravir	ribavirin	1.07	0.02	73.33	0.85	-11.22	824.34	Very low
lopinavir+ritonavir	ribavirin	0.92	0.02	44.97	-0.94	-11.18	501.14	Very low
lopinavir+ritonavir+ribavirin	ribavirin	1.03	0.02	50.42	0.35	-11.16	563.26	Very low
molnupiravir	ribavirin	0.21	0	14.08	-8.97	-11.36	149.1	Low
nirmatrelvir+ritonavir	ribavirin	0.14	0	13.94	-9.81	-11.38	147.47	Low
remdesivir	ribavirin	0.95	0.02	52.69	-0.58	-11.2	589.07	Very low
resveratrol	ribavirin	1.16	0	307.13	1.77	-11.35	3488.93	Very low
azvudine	ribavirin+sofosbuvir+daclatasvir	7	0.05	899.57	11.03	-1.74	1651.79	Very low
emtricitabine+tenofovir	ribavirin+sofosbuvir+daclatasvir	5.02	0.24	104.41	7.39	-1.39	190.08	Very low
favipiravir	ribavirin+sofosbuvir+daclatasvir	6.51	0.26	163.41	10.13	-1.36	298.54	Very low
lopinavir+ritonavir	ribavirin+sofosbuvir+daclatasvir	5.56	0.26	116.88	8.38	-1.35	213.02	very low
lopinavir+ritonavir+ribavirin	ribavirin+sofosbuvir+daclatasvir	6.24	0.04	874.07	9.64	-1.76	1604.91	Very low
molnupiravir	ribavirin+sofosbuvir+daclatasvir	1.29	0.05	30.89	0.53	-1.74	54.94	Low
nirmatrelvir+ritonavir	ribavirin+sofosbuvir+daclatasvir	0.84	0.02	34.3	-0.29	-1.8	61.21	Low
remdesivir	ribavirin+sofosbuvir+daclatasvir	5.75	0.3	108.82	8.73	-1.28	198.21	Very low
resveratrol	ribavirin+sofosbuvir+daclatasvir	7	0.05	908.85	11.03	-1.74	1668.84	Very low
ribavirin	ribavirin+sofosbuvir+daclatasvir	6.06	0.04	848.28	9.3	-1.76	1557.5	Very low
azvudine	sofosbuvir+daclatasvir	0.9	0.02	44.71	-1.37	-14.08	626.68	Very low

emtricitabine+tenofovir	sofosbuvir+daclatasvir	0.65	0.26	1.63	-5.04	-10.63	8.97	Low
favipiravir	sofosbuvir+daclatasvir	0.84	0.2	3.48	-2.28	-11.43	35.61	Very low
lopinavir+ritonavir	sofosbuvir+daclatasvir	0.72	0.28	1.81	-4.04	-10.26	11.65	Low
lopinavir+ritonavir+ribavirin	sofosbuvir+daclatasvir	0.81	0.01	44.04	-2.77	-14.13	617.15	Very low
molnupiravir	sofosbuvir+daclatasvir	0.17	0.04	0.62	-11.95	-13.7	-5.46	Moderate
nirmatrelvir+ritonavir	sofosbuvir+daclatasvir	0.11	0.01	1.1	-12.77	-14.18	1.48	Low
remdesivir	sofosbuvir+daclatasvir	0.74	0.44	1.26	-3.69	-8.08	3.79	Low
resveratrol	sofosbuvir+daclatasvir	0.9	0.02	45.28	-1.37	-14.08	634.92	Very low
ribavirin	sofosbuvir+daclatasvir	0.78	0.01	42.75	-3.12	-14.13	598.57	Very low
ribavirin+sofosbuvir+daclatasvir	sofosbuvir+daclatasvir	0.13	0.01	2.41	-12.49	-14.24	20.25	Very low
azvudine	sofosbuvir+ledipasvir	1.05	0.02	68.76	0.63	-12.44	856.93	Very low
emtricitabine+tenofovir	sofosbuvir+ledipasvir	0.75	0.13	4.4	-3.12	-11.02	43.01	Very low
favipiravir	sofosbuvir+ledipasvir	0.98	0.12	7.75	-0.29	-11.09	85.42	Very low
lopinavir+ritonavir	sofosbuvir+ledipasvir	0.83	0.14	4.96	-2.1	-10.88	50.14	Very low
lopinavir+ritonavir+ribavirin	sofosbuvir+ledipasvir	0.94	0.01	67.71	-0.8	-12.48	843.74	Very low
molnupiravir	sofosbuvir+ledipasvir	0.19	0.03	1.43	-10.2	-12.32	5.41	Low
nirmatrelvir+ritonavir	sofosbuvir+ledipasvir	0.13	0.01	2	-11.04	-12.55	12.71	Low
remdesivir	sofosbuvir+ledipasvir	0.86	0.17	4.26	-1.74	-10.44	41.28	very low
resveratrol	sofosbuvir+ledipasvir	1.05	0.02	69.58	0.63	-12.45	867.35	Very low
ribavirin	sofosbuvir+ledipasvir	0.91	0.01	65.72	-1.15	-12.49	818.52	Very low

ribavirin+sofosbuvir+daclatasvir	sofosbuvir+ledipasvir	0.15	0.01	4.04	-10.75	-12.58	38.4	Very low
sofosbuvir+daclatasvir	sofosbuvir+ledipasvir	1.16	0.24	5.6	2.04	-9.6	58.16	Very low
azvudine	triazavirin	3	0.02	448.27	8.68	-4.25	1940.37	Very low
emtricitabine+tenofovir	triazavirin	2.15	0.08	56.65	5	-3.98	241.41	Very low
favipiravir	triazavirin	2.79	0.09	87.53	7.77	-3.95	375.37	Very low
lopinavir+ritonavir	triazavirin	2.38	0.09	63.37	6	-3.95	270.57	Very low
lopinavir+ritonavir+ribavirin	triazavirin	2.68	0.02	434.46	7.27	-4.27	1880.46	Very low
molnupiravir	triazavirin	0.55	0.02	16.59	-1.94	-4.26	67.65	Very low
nirmatrelvir+ritonavir	triazavirin	0.36	0.01	17.87	-2.77	-4.31	73.2	Low
remdesivir	triazavirin	2.46	0.1	59.46	6.35	-3.9	253.6	Very low
resveratrol	triazavirin	3	0.02	452.75	8.68	-4.25	1959.82	Very low
ribavirin	triazavirin	2.6	0.02	421.64	6.93	-4.27	1824.83	Very low
ribavirin+sofosbuvir+daclatasvir	triazavirin	0.43	0.01	31.33	-2.48	-4.31	131.59	Very low
sofosbuvir+daclatasvir	triazavirin	3.32	0.14	79.06	10.05	-3.73	338.65	Very low
sofosbuvir+ledipasvir	triazavirin	2.86	0.09	95.67	8.06	-3.97	410.69	Very low
azvudine	umifenovir	1.25	0.01	107.74	2.38	-9.27	1004.65	Very low
emtricitabine+tenofovir	umifenovir	0.9	0.09	9.32	-0.96	-8.6	78.31	Very low
favipiravir	umifenovir	1.17	0.11	12.17	1.55	-8.36	105.14	Very low
lopinavir+ritonavir	umifenovir	0.99	0.1	9.74	-0.05	-8.46	82.28	Low
lopinavir+ritonavir+ribavirin	umifenovir	1.12	0.01	101.68	1.1	-9.3	947.58	Very low

molnupiravir	umifenovir	0.23	0.02	2.87	-7.24	-9.24	17.58	Low
nirmatrelvir+ritonavir	umifenovir	0.15	0.01	3.56	-7.99	-9.35	24.1	Very low
remdesivir	umifenovir	1.03	0.11	9.43	0.27	-8.36	79.38	Very low
resveratrol	umifenovir	1.25	0.01	108.96	2.38	-9.28	1016.05	Very low
ribavirin	umifenovir	1.08	0.01	98.68	0.79	-9.3	919.38	Very low
ribavirin+sofosbuvir+daclatasvir	umifenovir	0.18	0	6.77	-7.73	-9.37	54.27	Very low
sofosbuvir+daclatasvir	umifenovir	1.38	0.15	12.44	3.62	-7.96	107.72	Very low
sofosbuvir+ledipasvir	umifenovir	1.19	0.08	17.14	1.81	-8.63	151.93	Very low
triazavirin	umifenovir	0.42	0.01	19.27	-5.48	-9.33	171.94	Very low

Hospitalization network

Hospitalization network	Comparison	Network estimate			Network estimate			
		Relative estimate			Absolute risk per 1000			
Treatment 1	Treatment 2	Point estimate	CI Lower limit	CI upper limit	Point estimate	CI Lower limit	CI upper limit	GRADE rating
emtricitabine+tenofovir	favipiravir	1.74	0.18	17.2	32.2	-35.68	705.02	Very low
emtricitabine+tenofovir	molnupiravir	2.28	0.5	10.31	48.76	-19.05	354.71	Very low
emtricitabine+tenofovir	nirmatrelvir+ritonavir	1.38	0.31	6.07	3.116	-5.658	41.574	Moderate

emtricitabine+tenofovir	placebo	1.38	0.31	6.07	20.67	-37.54	275.81	Very low
emtricitabine+tenofovir	remdesivir	4.9	0.83	28.87	59.397	-2.5891	424.4601	Very low
emtricitabine+tenofovir	resveratrol	4.14	0.28	60.14	56.206	-12.888	1058.606	Very low
emtricitabine+tenofovir	sofosbuvir+daclatasvir	5.32	0.4	71.05	61.0848	-8.484	990.507	Low
emtricitabine+tenofovir	tenofovir	2.56	0.26	25.08	45.864	-21.756	707.952	Very low
favipiravir	molnupiravir	1.31	0.22	7.75	11.81	-29.72	257.17	Low
favipiravir	nirmatrelvir+ritonavir	5.24	0.81	33.74	34.768	-1.558	268.468	Moderate
favipiravir	placebo	0.8	0.14	4.58	-10.88	-46.78	194.75	Very low
favipiravir	remdesivir	2.82	0.38	20.97	27.7186	-9.4426	304.1431	Low
favipiravir	resveratrol	2.39	0.14	40.62	24.881	-15.394	709.198	Low
favipiravir	sofosbuvir+daclatasvir	3.07	0.2	48.22	29.2698	-11.312	667.6908	Low
favipiravir	tenofovir	1.47	0.08	26.21	13.818	-27.048	741.174	Very low
molnupiravir	nirmatrelvir+ritonavir	4.66	2.26	9.61	30.012	10.332	70.602	High
molnupiravir	placebo	0.7	0.5	1	-16.32	-27.2	0	High
molnupiravir	remdesivir	2.15	0.77	5.98	17.5145	-3.5029	75.8454	Low
molnupiravir	resveratrol	1.82	0.19	17.24	14.678	-14.499	290.696	Low
molnupiravir	sofosbuvir+daclatasvir	2.34	0.27	20.02	18.9476	-10.3222	268.9428	Low
molnupiravir	tenofovir	1.12	0.11	11.25	3.528	-26.166	301.35	Very low
nirmatrelvir+ritonavir	molnupiravir	0.27	0.14	0.52	-27.8	-32.77	-18.29	Moderate
nirmatrelvir+ritonavir	placebo	0.15	0.08	0.29	-46.24	-50.05	-38.62	High

nirmatrelvir+ritonavir	remdesivir	0.54	0.17	1.73	-7.0058	-12.6409	11.1179	Low
nirmatrelvir+ritonavir	resveratrol	0.46	0.04	4.62	-9.666	-17.184	64.798	Low
nirmatrelvir+ritonavir	sofosbuvir+daclatasvir	0.59	0.06	5.39	-5.7974	-13.2916	62.0746	Low
nirmatrelvir+ritonavir	tenofovir	0.28	0.03	3.01	-21.168	-28.518	59.094	Very low
remdesivir	placebo	0.28	0.11	0.75	-39.17	-48.42	-13.6	Low
remdesivir	resveratrol	0.85	0.07	9.64	-2.685	-16.647	154.656	Low
remdesivir	sofosbuvir+daclatasvir	1.09	0.1	11.28	1.2726	-12.726	145.3592	Low
remdesivir	tenofovir	0.52	0.04	6.26	-14.112	-28.224	154.644	Very low
resveratrol	placebo	0.33	0.04	3.1	-36.45	-52.22	114.24	Low
resveratrol	sofosbuvir+daclatasvir	1.29	0.06	27.99	4.1006	-13.2916	381.6386	Low
resveratrol	tenofovir	0.62	0.03	15.03	-11.172	-28.518	412.482	Very low
sofosbuvir+daclatasvir	placebo	0.26	0.03	2.17	-40.26	-52.77	63.65	Low
sofosbuvir+daclatasvir	tenofovir	0.48	0.02	10.89	-15.288	-28.812	290.766	Very low
tenofovir	placebo	0.54	0.05	5.29	-25.02	-51.68	233.38	Very low

Mechanical ventilation network

Mechanical ventilation network	Comparison	Network estimate			Network estimate			
		Relative estimate			Absolute risk			

Treatment 1	Treatment 2	Point estimate	CI Lower limit	CI upper limit	Point estimate	CI Lower limit	CI upper limit	GRADE rating
favipiravir	lopinavir+ritonavir	2.1366	0.605	7.545	16.25338	-5.6485	93.5935	Low
favipiravir	molnupiravir	3.2502	0.9934	10.6342	21.286892	-0.062436	91.139532	Low
favipiravir	placebo	1.3958	0.6127	3.1797	8.7076	-8.5206	47.9534	Low
favipiravir	remdesivir	3.0125	0.6991	12.9818	20.3665	-3.06918	122.21436	Low
favipiravir	resveratrol	1.3958	0.0259	75.1791	8.7076	-21.4302	1631.9402	Very low
favipiravir	ribavirin+sofosbuvir+daclatasvir	12.562	0.6359	248.1677	27.7488	-0.87384	593.20248	Very low
favipiravir	sofosbuvir+daclatasvir	0.9288	0.311	2.7741	-2.3496	-22.737	58.5453	Very low
favipiravir	sofosbuvir+ledipasvir	1.9541	0.3743	10.2018	14.88396	-9.76092	143.54808	Very low
lopinavir+ritonavir	molnupiravir	1.5212	0.4225	5.4773	4.930552	-5.46315	42.355258	Low
lopinavir+ritonavir	placebo	0.6533	0.2511	1.6994	-7.6274	-16.4758	15.3868	Low
lopinavir+ritonavir	remdesivir	1.41	0.3024	6.5735	4.1492	-7.11552	56.8497	Moderate
lopinavir+ritonavir	resveratrol	0.6533	0.0118	36.2406	-7.6274	-21.7404	775.2932	Low
lopinavir+ritonavir	ribavirin+sofosbuvir+daclatasvir	5.8795	0.2861	120.81	11.7108	-1.71336	287.544	Low
lopinavir+ritonavir	sofosbuvir+daclatasvir	0.4347	0.1313	1.4393	-18.6549	-28.6671	14.4969	Low
lopinavir+ritonavir	sofosbuvir+ledipasvir	0.9146	0.1633	5.1208	-1.33224	-13.05252	64.28448	Very low
molnupiravir	placebo	0.4118	0.1719	0.9865	-12.9404	-18.2182	-0.297	Moderate
molnupiravir	remdesivir	2.1583	0.6457	7.2136	11.721996	-3.61386	63.37872	Moderate

molnupiravir	resveratrol	0.4633	0.0078	27.4824	-11.8074	-21.8284	582.6128	Low
molnupiravir	ribavirin+sofosbuvir+daclatasvir	3.8649	0.194	76.9865	6.87576	-1.9344	182.3676	Low
molnupiravir	sofosbuvir+daclatasvir	0.2858	0.0936	0.8727	-23.5686	-29.9112	-4.2009	High
molnupiravir	sofosbuvir+ledipasvir	0.6012	0.1135	3.1857	-6.22128	-13.8294	34.09692	Very low
remdesivir	placebo	0.463327619	0.1386270378	1.54870683	-11.80679238	-18.95020517	12.07155026	Low
remdesivir	resveratrol	0.4633	0.0078	27.4824	-11.8074	-21.8284	582.6128	Low
remdesivir	ribavirin+sofosbuvir+daclatasvir	4.17	0.1858	93.5995	7.608	-1.95408	222.2388	Low
remdesivir	sofosbuvir+daclatasvir	0.3083	0.0756	1.2572	-22.8261	-30.5052	8.4876	Moderate
remdesivir	sofosbuvir+ledipasvir	0.6487	0.0996	4.2228	-5.48028	-14.04624	50.27568	Very low
resveratrol	placebo	1	0.02023230735	49.5049505	0	-21.55488924	1067.108911	Very low
resveratrol	ribavirin+sofosbuvir+daclatasvir	9	0.0711	1139.5282	19.2	-2.22936	2732.46768	Low
resveratrol	sofosbuvir+daclatasvir	0.6654	0.0126	35.1343	-11.0418	-32.5842	1126.4319	Low
resveratrol	sofosbuvir+ledipasvir	1.4	0.022	89.2852	6.24	-15.2568	1377.24912	Very low
ribavirin+sofosbuvir+daclatasvir	placebo	0.1111111111	0.006315176569	1.955034213	-19.55555556	-21.86106612	21.01075269	Low
ribavirin+sofosbuvir+daclatasvir	sofosbuvir+daclatasvir	0.0739	0.0038	1.4222	-30.5613	-32.8746	13.9326	Low
ribavirin+sofosbuvir+daclatasvir	sofosbuvir+ledipasvir	0.1556	0.0063	3.8379	-13.17264	-15.50172	44.27124	Very low
sofosbuvir+daclatasvir	placebo	1.502855425	0.730994152	3.089280198	11.06281936	-5.918128655	45.96416435	Moderate
sofosbuvir+daclatasvir	sofosbuvir+ledipasvir	2.1039	0.4231	10.462	17.22084	-8.99964	147.6072	Low

sofosbuvir+ledipasvir	placebo	0.7142857143	0.1704303366	2.994011976	-6.285714286	-18.25053259	43.86826347	Very low

Adverse events leading to drug discontinuation

Adverse events leading to drug discontinuation	Comparison	Network estimate			Network estimate			
		Relative estimate			Absolute risk			
Treatment 1	Treatment 2	Point estimate	CI Lower limit	CI upper limit	Point estimate	CI Lower limit	CI upper limit	GRADE rating
azvudine	placebo	0	-3.8255	3.8255	0	-38.255	38.255	Low
azvudine	emtricitabine+tenofovir	-1.9459	-6.7587	2.8669	-19.459	-67.587	28.669	very low
azvudine	favipiravir	-0.6381	-4.662	3.3858	-6.381	-46.62	33.858	very low
azvudine	lopinavir+ritonavir	-0.029	-5.1109	5.0529	-0.29	-51.109	50.529	very low
azvudine	lopinavir+ritonavir+ribavirin	-0.5522	-5.7162	4.6117	-5.522	-57.162	46.117	very low
azvudine	molnupiravir	0.4456	-3.4365	4.3277	4.456	-34.365	43.277	very low
azvudine	nirmatrelvir+ritonavir	0.9535	-2.9012	4.8081	9.535	-29.012	48.081	very low
azvudine	novaferon	0.7183	-4.7413	6.1778	7.183	-47.413	61.778	very low
azvudine	remdesivir	-0.2829	-4.275	3.7092	-2.829	-42.75	37.092	very low
azvudine	ribavirin	0.0663	-5.1309	5.2636	0.663	-51.309	52.636	very low
azvudine	ribavirin+sofosbuvir+daclatasvir	0	-5.4485	5.4485	0	-54.485	54.485	very low
azvudine	sofosbuvir+daclatasvir	-0.0018	-4.1468	4.1431	-0.018	-41.468	41.431	very low
azvudine	sofosbuvir+ledipasvir	0.0482	-5.4121	5.5085	0.482	-54.121	55.085	very low
azvudine	triazavirin	-1.0986	-6.0573	3.86	-10.986	-60.573	38.6	very low

azvudine	umifenovir	0.7073	-4.7399	6.1546	7.073	-47.399	61.546	very low
emtricitabine+tenofovir	favipiravir	1.3078	-1.8681	4.4837	13.078	-18.681	44.837	Low
emtricitabine+tenofovir	lopinavir+ritonavir	1.9169	-2.5238	6.3577	19.169	-25.238	63.577	very low
emtricitabine+tenofovir	lopinavir+ritonavir+ribavirin	1.3937	-3.1407	5.9281	13.937	-31.407	59.281	very low
emtricitabine+tenofovir	molnupiravir	2.3916	-0.6026	5.3857	23.916	-6.026	53.857	Low
emtricitabine+tenofovir	nirmatrelvir+ritonavir	2.8994	-0.0591	5.8579	28.994	-0.591	58.579	Low
emtricitabine+tenofovir	novaferon	2.6642	-2.2042	7.5325	26.642	-22.042	75.325	very low
emtricitabine+tenofovir	placebo	1.9459	-0.9745	4.8663	19.459	-9.745	48.663	Low
emtricitabine+tenofovir	remdesivir	1.663	-1.4725	4.7985	16.63	-14.725	47.985	Low
emtricitabine+tenofovir	ribavirin	2.0122	-2.5601	6.5845	20.122	-25.601	65.845	very low
emtricitabine+tenofovir	ribavirin+sofosbuvir+daclatasvir	1.9459	-2.9101	6.8019	19.459	-29.101	68.019	very low
emtricitabine+tenofovir	sofosbuvir+daclatasvir	1.9441	-1.3839	5.272	19.441	-13.839	52.72	Low
emtricitabine+tenofovir	sofosbuvir+ledipasvir	1.9941	-2.8751	6.8633	19.941	-28.751	68.633	very low
emtricitabine+tenofovir	triazavirin	0.8473	-3.4518	5.1464	8.473	-34.518	51.464	very low
emtricitabine+tenofovir	umifenovir	2.6532	-2.2013	7.5078	26.532	-22.013	75.078	very low
favipiravir	placebo	0.6381	-0.61	1.8863	6.381	-6.1	18.863	Low
favipiravir	lopinavir+ritonavir	0.6091	-2.9616	4.1798	6.091	-29.616	41.798	very low
favipiravir	lopinavir+ritonavir+ribavirin	0.0859	-3.6006	3.7723	0.859	-36.006	37.723	very low
favipiravir	molnupiravir	1.0838	-0.3285	2.496	10.838	-3.285	24.96	very low
favipiravir	nirmatrelvir+ritonavir	1.5916	0.2566	2.9265	15.916	2.566	29.265	Low

favipiravir	novaferon	1.3564	-2.7339	5.4466	13.564	-27.339	54.466	very low
favipiravir	remdesivir	0.3552	-1.3362	2.0465	3.552	-13.362	20.465	Very low
favipiravir	ribavirin	0.7044	-3.0286	4.4374	7.044	-30.286	44.374	very low
favipiravir	ribavirin+sofosbuvir+daclatasvir	0.6381	-3.4374	4.7137	6.381	-34.374	47.137	very low
favipiravir	sofosbuvir+daclatasvir	0.6363	-1.3897	2.6623	6.363	-13.897	26.623	Very low
favipiravir	sofosbuvir+ledipasvir	0.6863	-3.405	4.7776	6.863	-34.05	47.776	very low
favipiravir	triazavirin	-0.4605	-3.8534	2.9324	-4.605	-38.534	29.324	very low
favipiravir	umifenovir	1.3454	-2.7284	5.4193	13.454	-27.284	54.193	very low
lopinavir+ritonavir	lopinavir+ritonavir+ribavirin	-0.5232	-1.4399	0.3934	-5.232	-14.399	3.934	Moderate
lopinavir+ritonavir	ribavirin	0.0953	-0.9935	1.1841	0.953	-9.935	11.841	Moderate
lopinavir+ritonavir	umifenovir	0.7363	-2.6257	4.0983	7.363	-26.257	40.983	Low
lopinavir+ritonavir	molnupiravir	0.4746	-2.9354	3.8847	4.746	-29.354	38.847	very low
lopinavir+ritonavir	nirmatrelvir+ritonavir	0.9824	-2.3963	4.3612	9.824	-23.963	43.612	very low
lopinavir+ritonavir	novaferon	0.7472	-4.3873	5.8818	7.472	-43.873	58.818	very low
lopinavir+ritonavir	placebo	0.029	-3.3164	3.3744	0.29	-33.164	33.744	very low
lopinavir+ritonavir	remdesivir	-0.254	-3.7887	3.2808	-2.54	-37.887	32.808	very low
lopinavir+ritonavir	ribavirin+sofosbuvir+daclatasvir	0.029	-5.0939	5.1519	0.29	-50.939	51.519	very low
lopinavir+ritonavir	sofosbuvir+daclatasvir	0.0271	-3.6794	3.7337	0.271	-36.794	37.337	very low
lopinavir+ritonavir	sofosbuvir+ledipasvir	0.0772	-5.0582	5.2126	0.772	-50.582	52.126	very low
lopinavir+ritonavir	triazavirin	-1.0696	-5.6681	3.5288	-10.696	-56.681	35.288	very low

lopinavir+ritonavir+ribavirin	ribavirin	0.6186	-0.3606	1.5977	6.186	-3.606	15.977	Moderate
lopinavir+ritonavir+ribavirin	molnupiravir	0.9979	-2.5332	4.529	9.979	-25.332	45.29	very low
lopinavir+ritonavir+ribavirin	nirmatrelvir+ritonavir	1.5057	-1.9952	5.0066	15.057	-19.952	50.066	Low
lopinavir+ritonavir+ribavirin	novaferon	1.2705	-3.9453	6.4863	12.705	-39.453	64.863	very low
lopinavir+ritonavir+ribavirin	placebo	0.5522	-2.9165	4.021	5.522	-29.165	40.21	very low
lopinavir+ritonavir+ribavirin	remdesivir	0.2693	-3.3824	3.921	2.693	-33.824	39.21	very low
lopinavir+ritonavir+ribavirin	ribavirin+sofosbuvir+daclatasvir	0.5522	-4.652	5.7565	5.522	-46.52	57.565	very low
lopinavir+ritonavir+ribavirin	sofosbuvir+daclatasvir	0.5504	-3.2679	4.3686	5.504	-32.679	43.686	very low
lopinavir+ritonavir+ribavirin	sofosbuvir+ledipasvir	0.6004	-4.6162	5.817	6.004	-46.162	58.17	very low
lopinavir+ritonavir+ribavirin	triazavirin	-0.5464	-5.2353	4.1426	-5.464	-52.353	41.426	very low
lopinavir+ritonavir+ribavirin	umifenovir	1.2596	-2.2252	4.7443	12.596	-22.252	47.443	very low
molnupiravir	placebo	-0.5835	-1.2816	0.1147	-5.835	-12.816	1.147	Moderate
molnupiravir	nirmatrelvir+ritonavir	0.3687	-0.4746	1.2119	3.687	-4.746	12.119	Moderate
molnupiravir	novaferon	0.2726	-3.6782	4.2234	2.726	-36.782	42.234	very low
molnupiravir	remdesivir	-0.7286	-2.0474	0.5902	-7.286	-20.474	5.902	Low
molnupiravir	ribavirin	-0.3793	-3.959	3.2003	-3.793	-39.59	32.003	very low
molnupiravir	ribavirin+sofosbuvir+daclatasvir	-0.4456	-4.3812	3.4899	-4.456	-43.812	34.899	very low
molnupiravir	sofosbuvir+daclatasvir	-0.4475	-2.1747	1.2797	-4.475	-21.747	12.797	Low
molnupiravir	sofosbuvir+ledipasvir	-0.3974	-4.3493	3.5544	-3.974	-43.493	35.544	very low
molnupiravir	triazavirin	-1.5443	-4.7677	1.6792	-15.443	-47.677	16.792	Low

molnupiravir	umifenovir	0.2617	-3.6721	4.1955	2.617	-36.721	41.955	very low
nirmatrelvir+ritonavir	novaferon	-0.2352	-4.159	3.6886	-2.352	-41.59	36.886	very low
nirmatrelvir+ritonavir	placebo	-0.9535	-1.4269	-0.48	-9.535	-14.269	-4.8	Moderate
nirmatrelvir+ritonavir	remdesivir	-1.2364	-2.4721	-0.0007	-12.364	-24.721	-0.007	Moderate
nirmatrelvir+ritonavir	ribavirin	-0.8871	-4.437	2.6627	-8.871	-44.37	26.627	very low
nirmatrelvir+ritonavir	ribavirin+sofosbuvir+daclatasvir	-0.9535	-4.862	2.955	-9.535	-48.62	29.55	very low
nirmatrelvir+ritonavir	sofosbuvir+daclatasvir	-0.9553	-2.6199	0.7093	-9.553	-26.199	7.093	Low
nirmatrelvir+ritonavir	sofosbuvir+ledipasvir	-0.9053	-4.8301	3.0196	-9.053	-48.301	30.196	very low
nirmatrelvir+ritonavir	triazavirin	-2.0521	-5.2424	1.1382	-20.521	-52.424	11.382	Low
nirmatrelvir+ritonavir	umifenovir	-0.2461	-4.1528	3.6606	-2.461	-41.528	36.606	very low
novaferon	placebo	-0.7183	-4.6134	3.1769	-7.183	-46.134	31.769	very low
novaferon	remdesivir	-1.0012	-5.0601	3.0577	-10.012	-50.601	30.577	very low
novaferon	ribavirin	-0.6519	-5.9007	4.5968	-6.519	-59.007	45.968	very low
novaferon	ribavirin+sofosbuvir+daclatasvir	-0.7183	-6.2159	4.7794	-7.183	-62.159	47.794	very low
novaferon	sofosbuvir+daclatasvir	-0.7201	-4.9295	3.4893	-7.201	-49.295	34.893	very low
novaferon	sofosbuvir+ledipasvir	-0.6701	-6.1794	4.8393	-6.701	-61.794	48.393	very low
novaferon	triazavirin	-1.8169	-6.8295	3.1957	-18.169	-68.295	31.957	very low
novaferon	umifenovir	-0.0109	-5.5073	5.4855	-0.109	-55.073	54.855	very low
remdesivir	placebo	2.829	-8.584	14.243	28.29	-85.84	142.43	very low
remdesivir	ribavirin	0.3493	-3.3494	4.0479	3.493	-33.494	40.479	very low

remdesivir	ribavirin+sofosbuvir+daclatasvir	0.2829	-3.7612	4.3271	2.829	-37.612	43.271	very low
remdesivir	sofosbuvir+daclatasvir	0.2811	-1.6809	2.2431	2.811	-16.809	22.431	Low
remdesivir	sofosbuvir+ledipasvir	0.3311	-3.7288	4.3911	3.311	-37.288	43.911	very low
remdesivir	triazavirin	-0.8157	-4.1708	2.5394	-8.157	-41.708	25.394	very low
remdesivir	umifenovir	0.9903	-3.0521	5.0327	9.903	-30.521	50.327	very low
ribavirin	placebo	-0.663	-35.845	34.518	-6.63	-358.45	345.18	very low
ribavirin	ribavirin+sofosbuvir+daclatasvir	-0.0663	-5.3036	5.171	-0.663	-53.036	51.71	very low
ribavirin	sofosbuvir+daclatasvir	-0.0682	-3.9313	3.795	-0.682	-39.313	37.95	very low
ribavirin	sofosbuvir+ledipasvir	-0.0181	-5.2677	5.2314	-0.181	-52.677	52.314	very low
ribavirin	triazavirin	-1.1649	-5.8905	3.5607	-11.649	-58.905	35.607	very low
ribavirin	umifenovir	0.641	-2.8929	4.1749	6.41	-28.929	41.749	very low
ribavirin+sofosbuvir+daclatasvir	placebo	0	-38.797	38.797	0	-387.97	387.97	very low
ribavirin+sofosbuvir+daclatasvir	sofosbuvir+daclatasvir	-0.0018	-4.197	4.1933	-0.018	-41.97	41.933	very low
ribavirin+sofosbuvir+daclatasvir	sofosbuvir+ledipasvir	0.0482	-5.4502	5.5466	0.482	-54.502	55.466	very low
ribavirin+sofosbuvir+daclatasvir	triazavirin	-1.0986	-6.0992	3.902	-10.986	-60.992	39.02	very low
ribavirin+sofosbuvir+daclatasvir	umifenovir	0.7073	-4.7781	6.1928	7.073	-47.781	61.928	very low
sofosbuvir+daclatasvir	placebo	0.018	-15.94	15.977	0.18	-159.4	159.77	Low
sofosbuvir+daclatasvir	sofosbuvir+ledipasvir	0.05	-4.1603	4.2604	0.5	-41.603	42.604	very low
sofosbuvir+daclatasvir	triazavirin	-1.0968	-4.6324	2.4389	-10.968	-46.324	24.389	very low

sofosbuvir+daclatasvir	umifenovir	0.7092	-3.4843	4.9026	7.092	-34.843	49.026	very low
sofosbuvir+ledipasvir	placebo	-0.482	-39.444	38.48	-4.82	-394.44	384.8	very low
sofosbuvir+ledipasvir	triazavirin	-1.1468	-6.1603	3.8666	-11.468	-61.603	38.666	very low
sofosbuvir+ledipasvir	umifenovir	0.6591	-4.838	6.1563	6.591	-48.38	61.563	very low
triazavirin	placebo	10.986	-20.564	42.536	109.86	-205.64	425.36	very low
triazavirin	umifenovir	1.8059	-3.1933	6.8052	18.059	-31.933	68.052	very low
umifenovir	placebo	-7.073	-45.852	31.706	-70.73	-458.52	317.06	very low

Supplement 10. Heterogeneity estimates

Mortality

Number of studies: k = 32
Number of pairwise comparisons: m = 36
Number of treatments: n = 16
Number of designs: d = 17

Random effects model

Quantifying heterogeneity / inconsistency:
tau^2 = 0; tau = 0; I^2 = 0% [0.0%; 48.0%]

Tests of heterogeneity (within designs) and inconsistency (between designs):

	Q	d.f.	p-value
Total	6.07	19	0.9978
Within designs	5.97	15	0.9802
Between designs	0.10	4	0.9988

Hospitalizations

Number of studies: k = 10
Number of pairwise comparisons: m = 12
Number of treatments: n = 9
Number of designs: d = 8

Random effects model

Quantifying heterogeneity / inconsistency:
tau^2 = 0; tau = 0; I^2 = 0% [0.0%; 84.7%]

Tests of heterogeneity (within designs) and inconsistency (between designs):

	Q	d.f.	p-value
Total	1.61	3	0.6572
Within designs	1.45	2	0.4843
Between designs	0.16	1	0.6893

Mechanical ventilation

Number of studies: k = 14
Number of pairwise comparisons: m = 14
Number of treatments: n = 9
Number of designs: d = 8

Random effects model

Quantifying heterogeneity / inconsistency:
tau^2 = 0; tau = 0; I^2 = 0% [0.0%; 70.8%]

Tests of heterogeneity (within designs) and inconsistency (between designs):

	Q	d.f.	p-value
Total	3.2	6	0.7836
Within designs	3.2	6	0.7836

Between designs 0.0 0 --

Adverse events leading to drug discontinuation

Number of studies: k = 22
Number of pairwise comparisons: m = 26
Number of treatments: n = 16
Number of designs: d = 13

Random effects model

Quantifying heterogeneity / inconsistency:
tau^2 = 0; tau = 0; I^2 = 0% [0.0%; 62.4%]

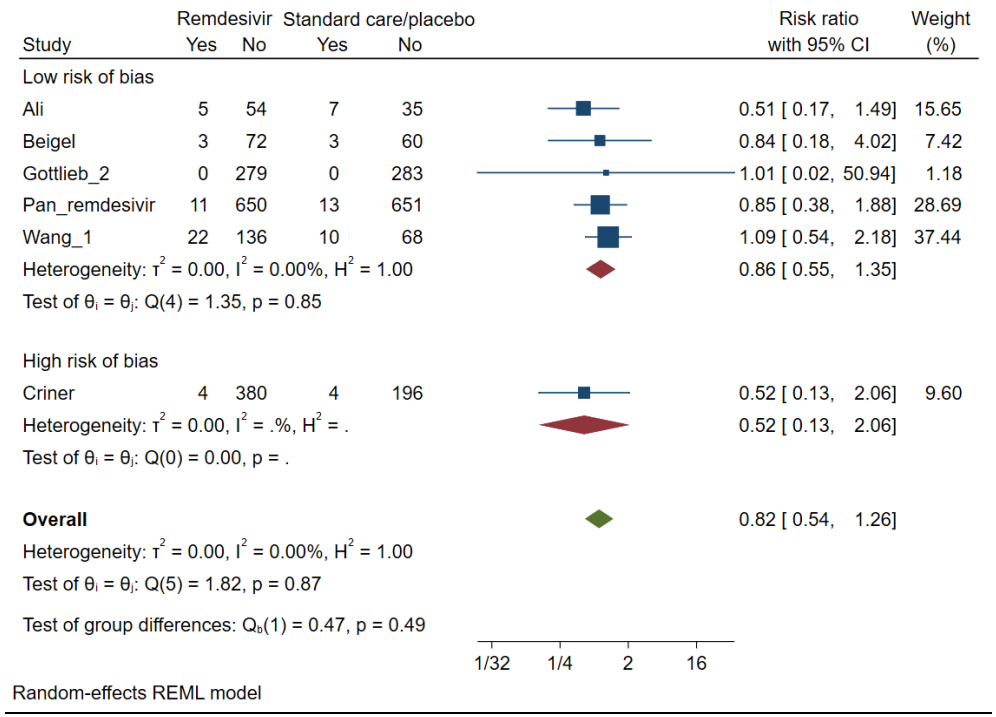
Tests of heterogeneity (within designs) and inconsistency (between designs):

	Q	d.f.	p-value
Total	7.68	9	0.5671
Within designs	7.68	9	0.5671
Between designs	0.00	0	--

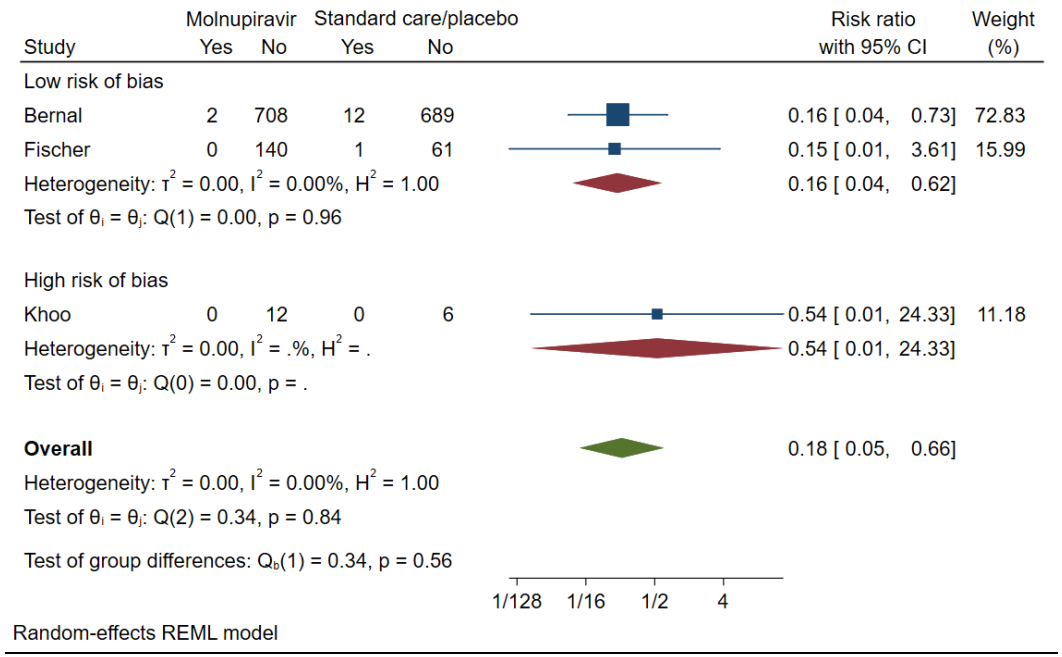
Supplement 11. Subgroup analysis

Mortality subgroups

Remdesivir - risk of bias

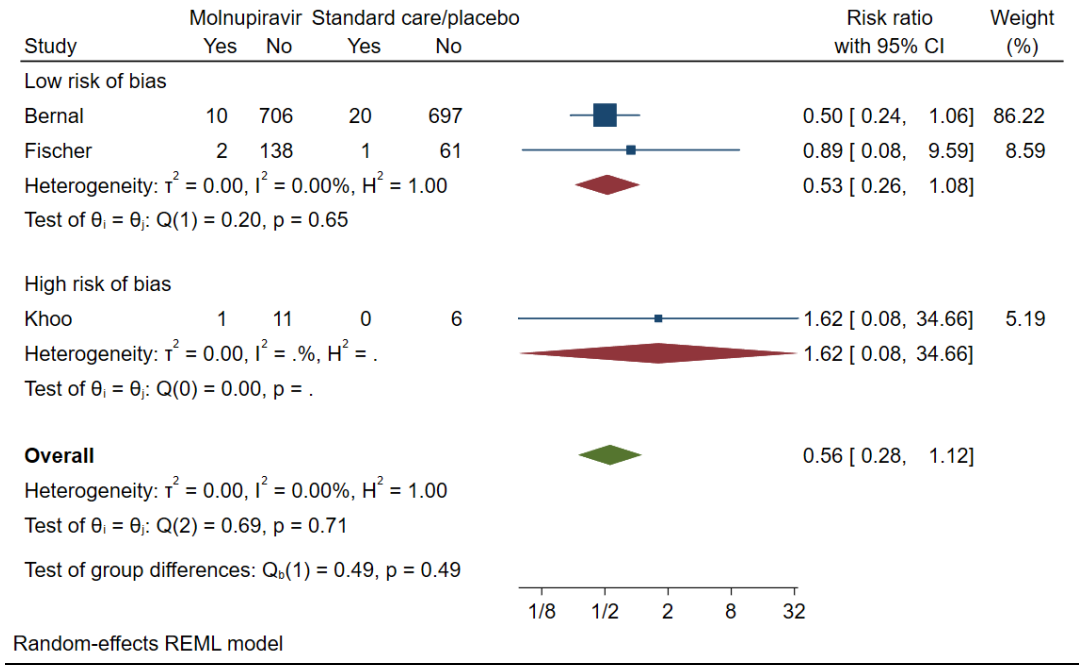


Molnupiravir - risk of bias

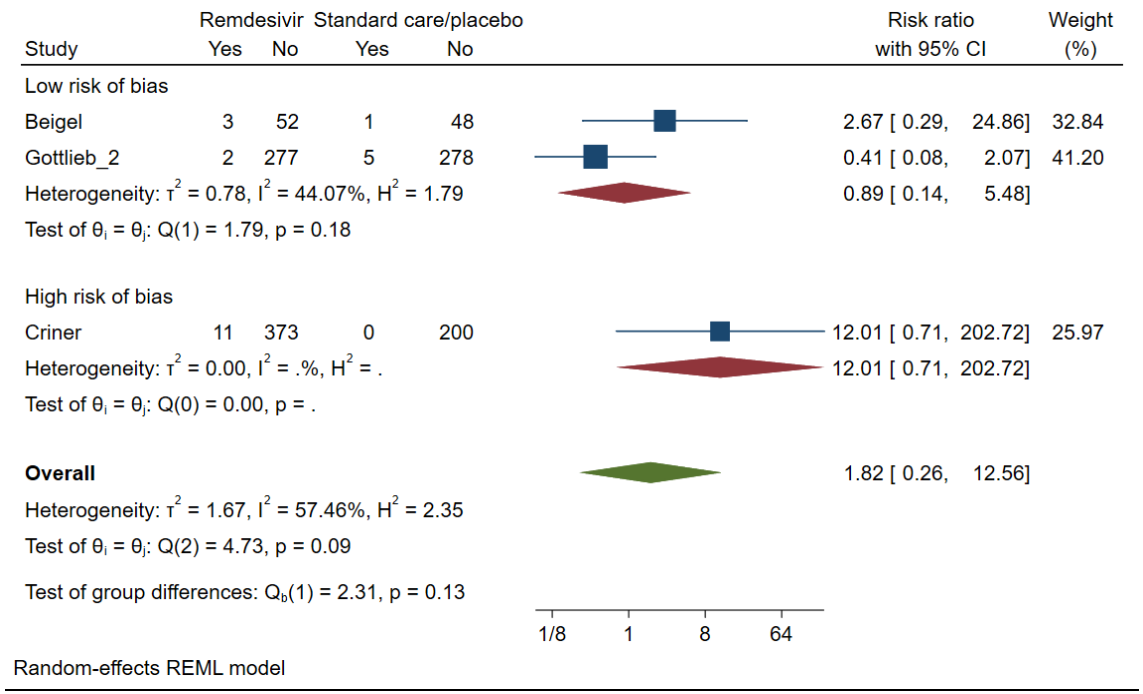


Adverse events leading to drug discontinuation subgroups

Molnupiravir - risk of bias

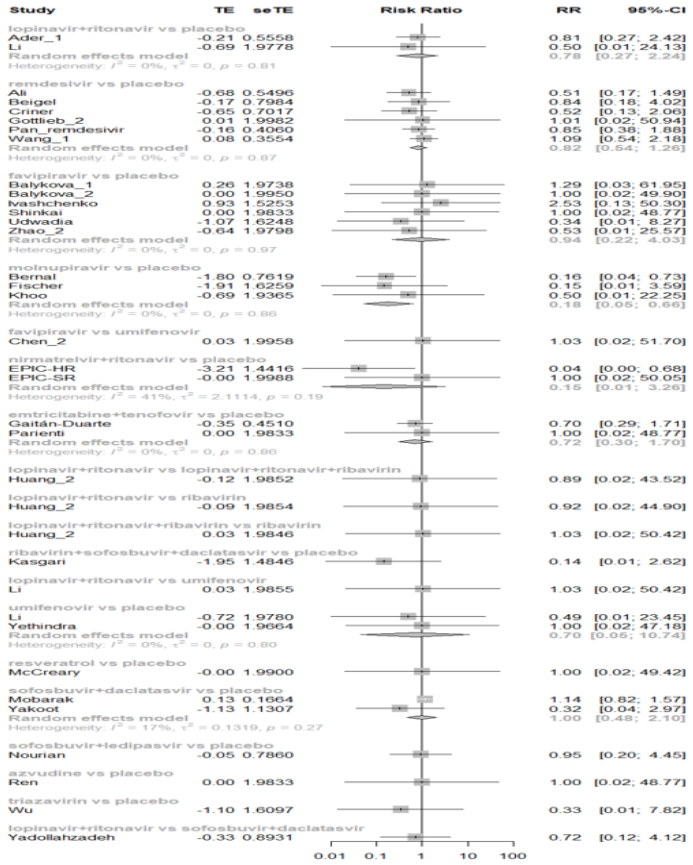


Remdesivir - risk of bias

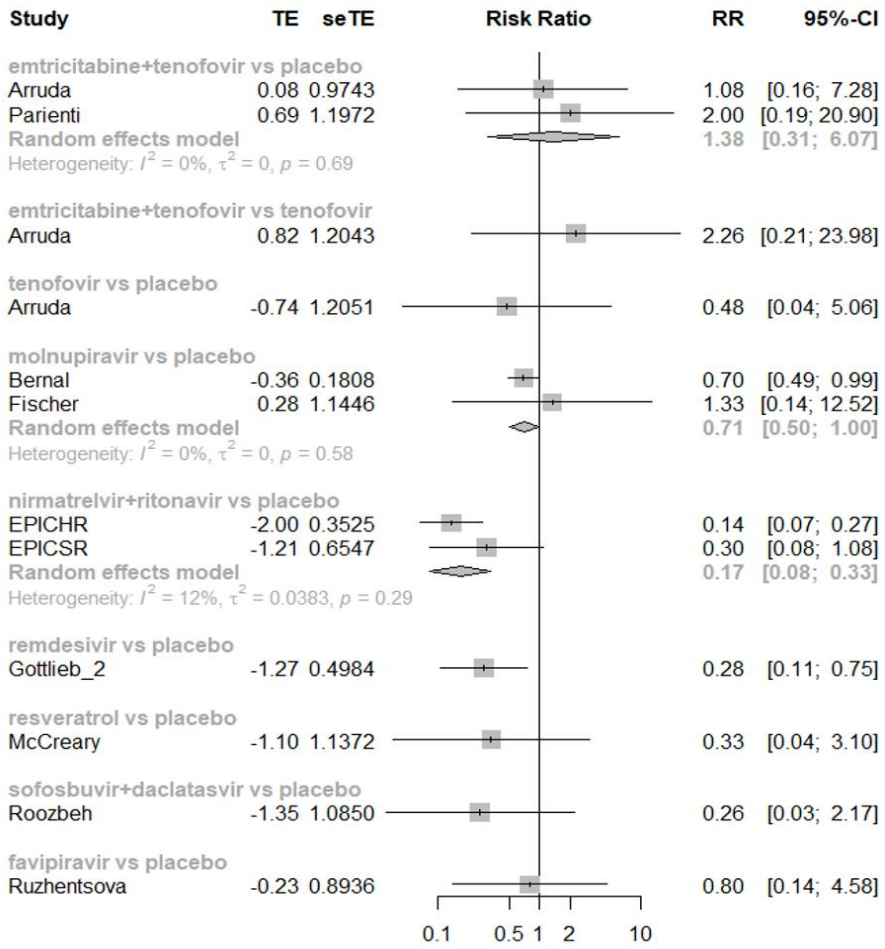


Supplement 12. Pairwise forest plots for each outcome.

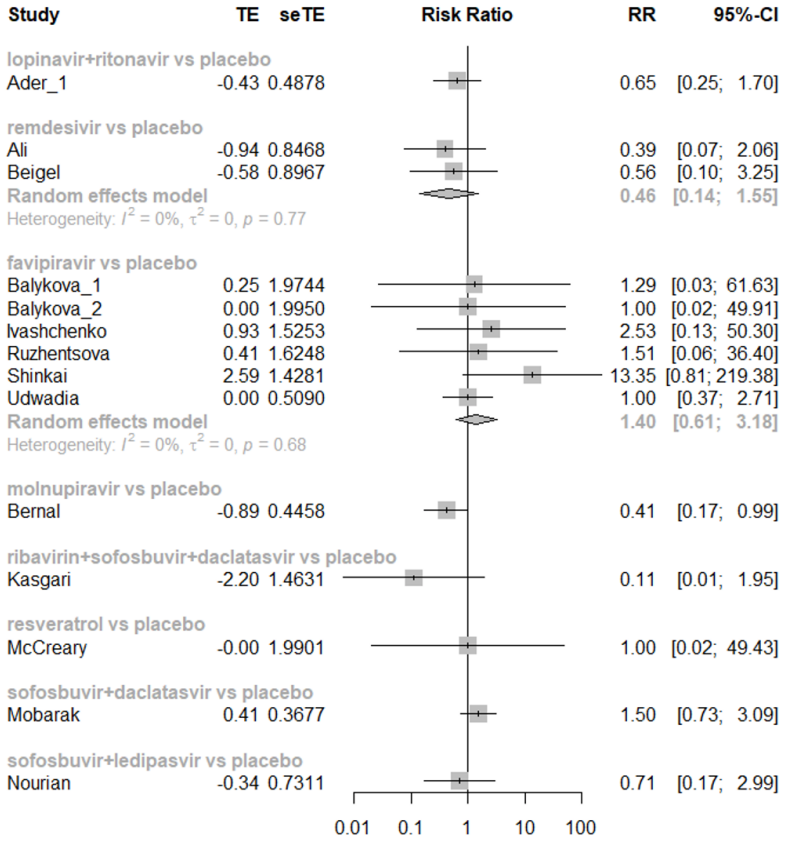
Mortality pairwise comparisons



Hospitalization pairwise comparisons



Mechanical ventilation pairwise comparisons



Adverse events leading to drug discontinuation pairwise comparisons