

Identification ^a

Clinical trials identified through *Clinicaltrials.gov*
(Dec 2019 - May 2022)

- Drugs ^b used for treatment of Covid-19 patients
(n= 972)

Screening

- Excluded:
- Non-RCTs (n= 340)

RCTs of COVID-19 patients
(n= 632)

- Excluded:
- Data was not available
(n= 519)

Trials with full information
(n= 113)

- Excluded:
- Non-inpatient (n= 16)
 - Combination drug therapy (n= 32)
 - Positive control (n= 11)

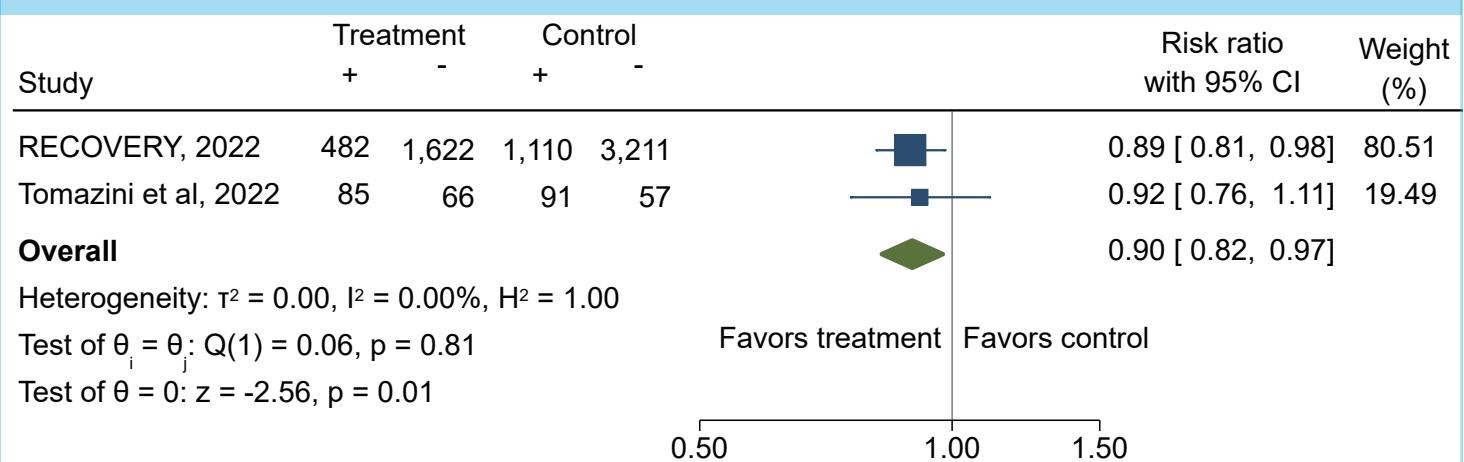
Eligibility

Trials for eligibility
(n= 54)

a Two authors (C.Y. and X.Y.) independently screened relevant trials.

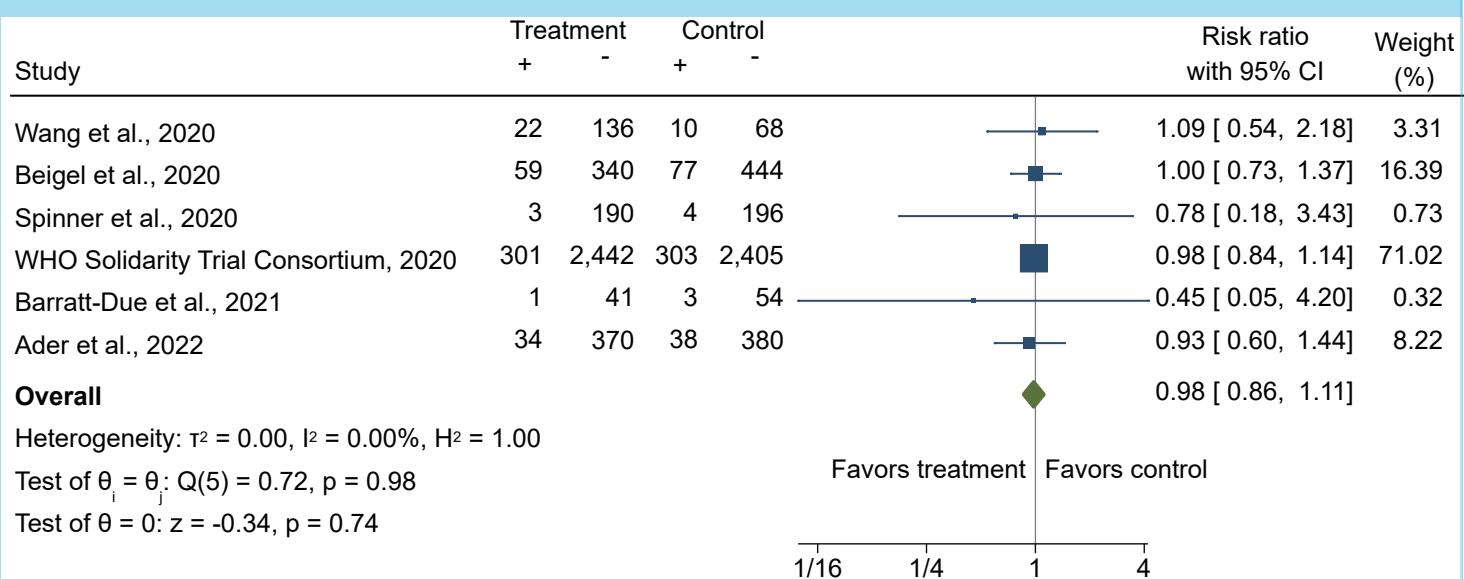
b Drugs used for treatment include Angiotensin receptor blockers (ARB), as well as drugs recommended/emergency use authorized by the Chinese Clinical Guidance for COVID-19 Pneumonia Diagnosis and Treatment (China 9th Edition), the U.S. Food and Drug Administration (FDA), the European Medicines Agency (EMA) and those strongly recommended by the Guideline Therapeutics and COVID-19 of World Health Organization (WHO).

Dexamethasone



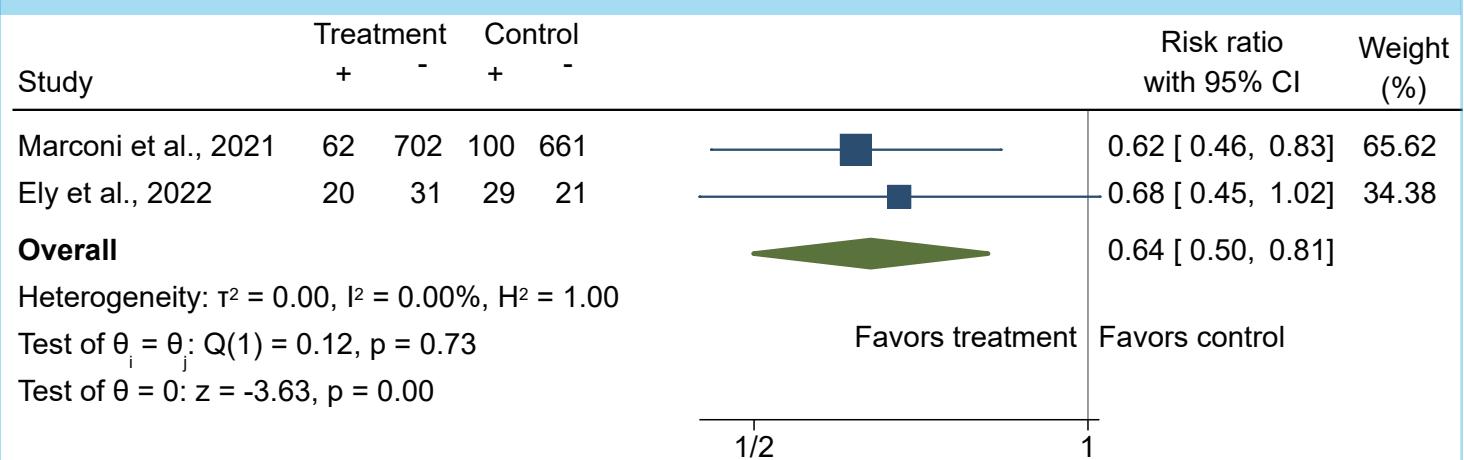
Random-effects DerSimonian–Laird model

Remdesivir



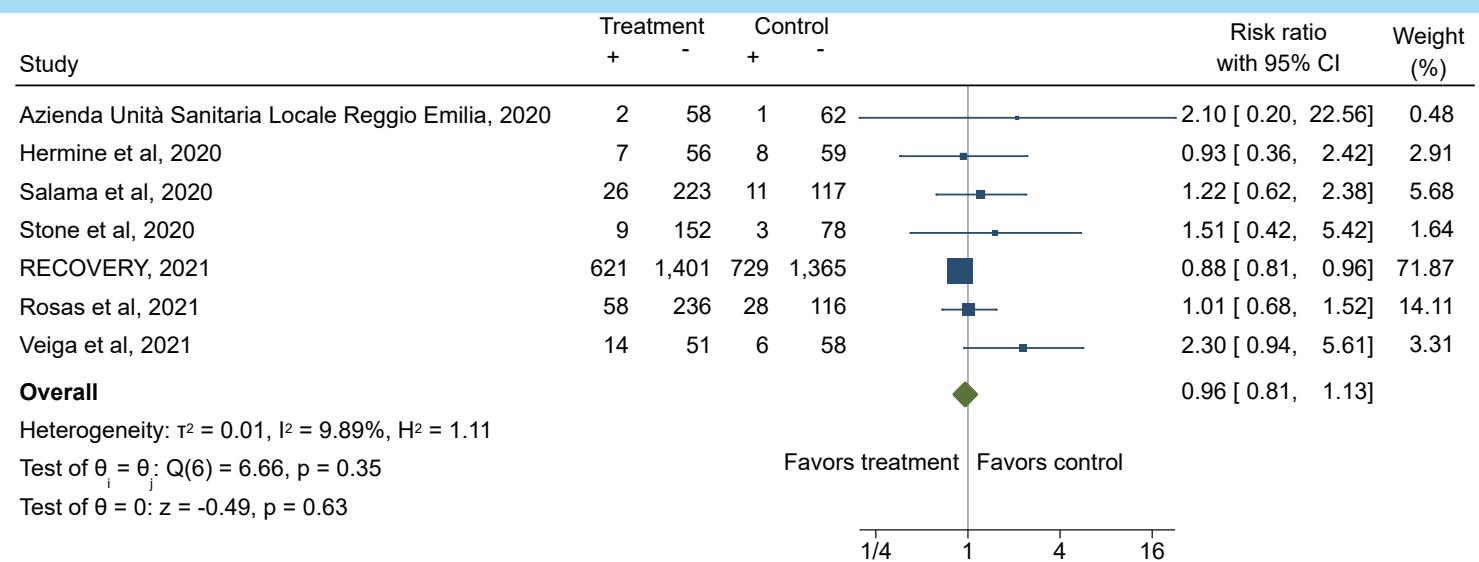
Random-effects DerSimonian–Laird model

Baricitinib



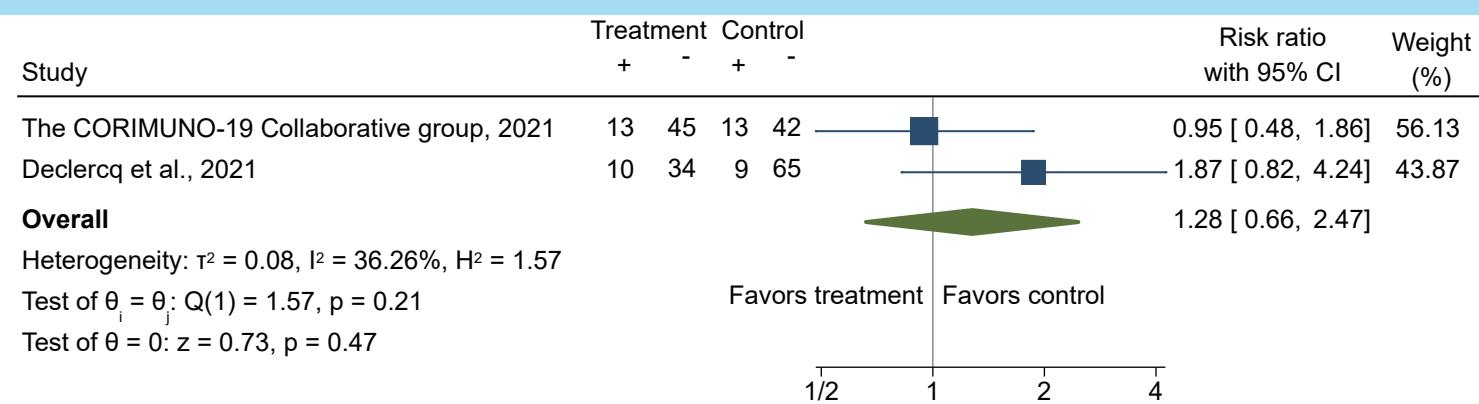
Random-effects DerSimonian–Laird model

Tocilizumab



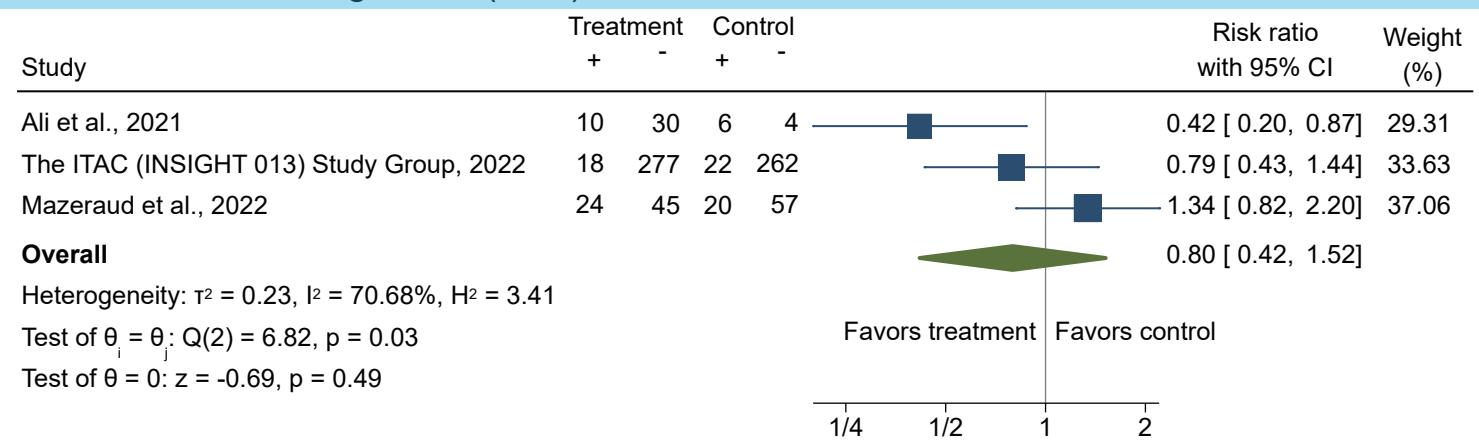
Random-effects DerSimonian–Laird model

Anakinra



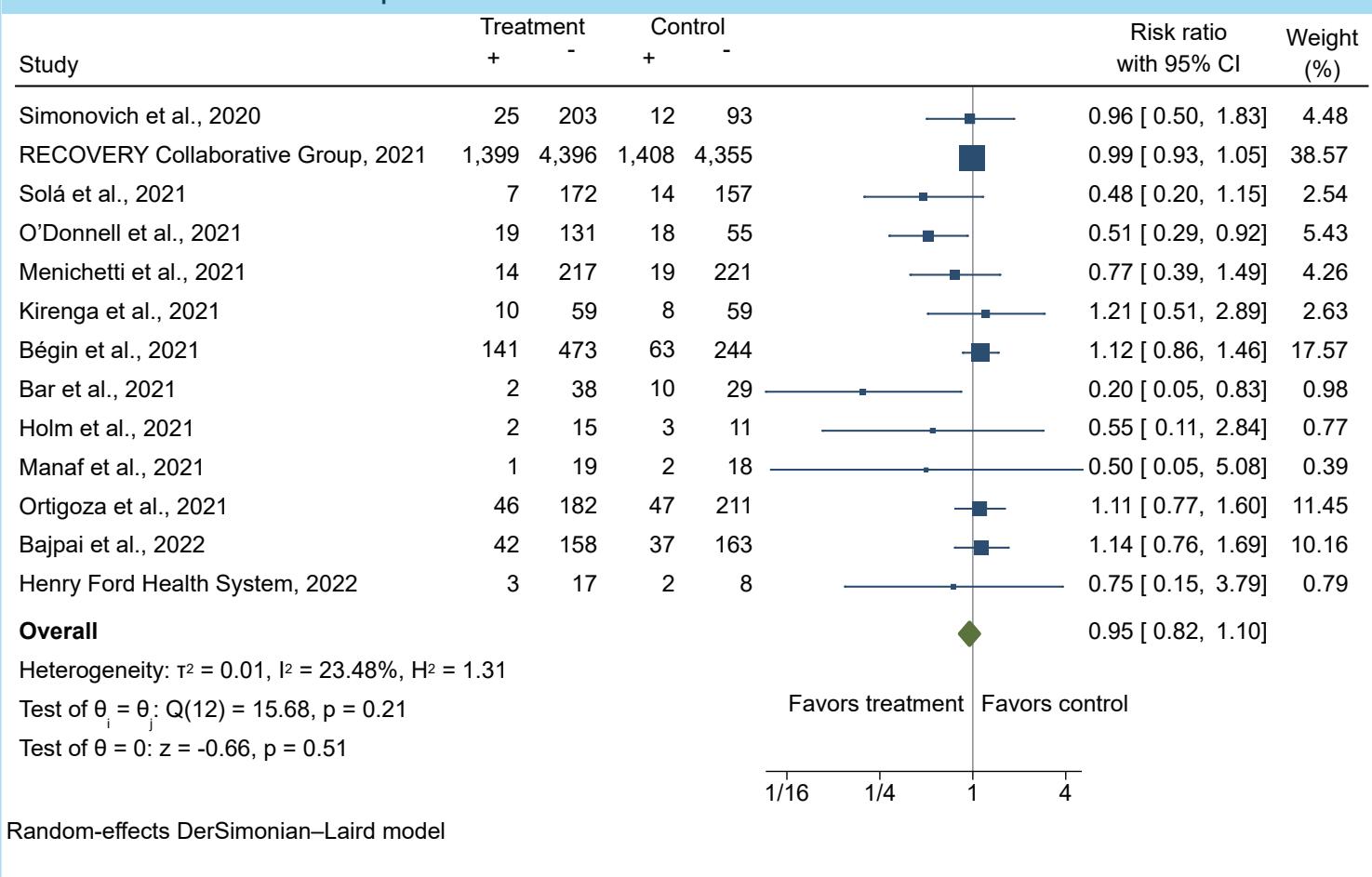
Random-effects DerSimonian–Laird model

Intravenous Immunoglobulin (IVIG)

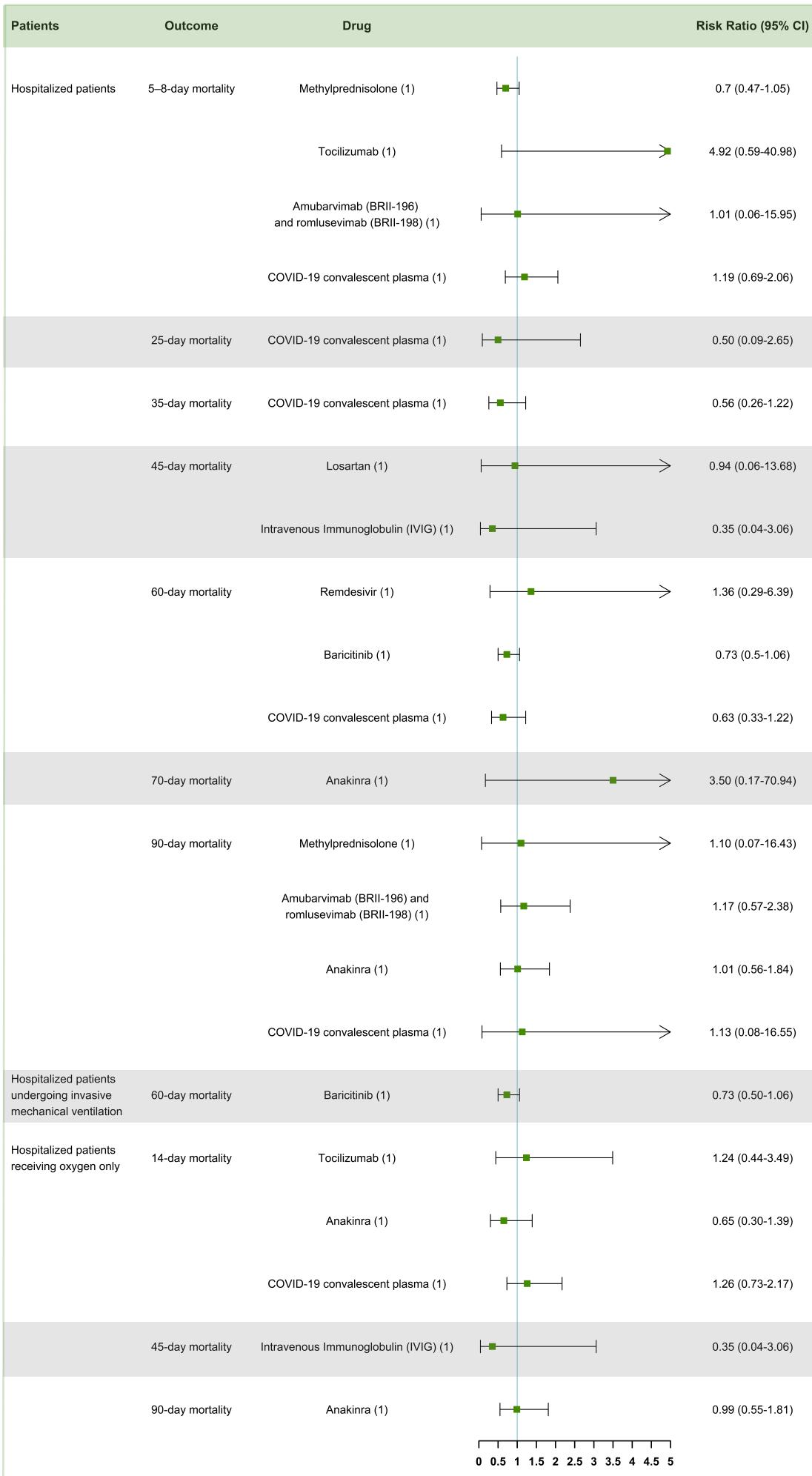


Random-effects DerSimonian–Laird model

COVID-19 convalescent plasma



Supplementary Fig. S2 Outcome (28/30-day mortality) and efficacy of different drugs in hospitalized patients with Covid-19 using meta-analysis.



Supplementary Fig. S3 Evidence of absence effect in hospitalized patients with Covid-19.

Supplementary Table S1. Search strategies.

Drug name	Other names	Condition or disease in clinicaltrials.gov	Terms in clinicaltrials.gov	Search results
ARB	Losartan, Telmisartan, Valsartan, Telsartan, Candesartan, Irbesartan, Eprosartan, Olmesartan, Azilsartan	COVID-19	Losartan OR Telmisartan OR Valsartan OR Telsartan OR Candesartan OR Irbesartan OR Eprosartan OR Olmesartan OR Azilsartan	31 Studies found for: Losartan OR Telmisartan OR Valsartan OR Telsartan OR Candesartan OR Irbesartan OR Eprosartan OR Olmesartan OR Azilsartan COVID-19
Dexamethasone	NA ^a	COVID-19	Dexamethasone	105 Studies found for: Dexamethasone COVID-19
Methylprednisolone	NA	COVID-19	Methylprednisolone	73 Studies found for: Methylprednisolone COVID-19
Therapeutic dose of low molecular weight heparin or unfractionated heparin	NA	COVID-19	Therapeutic dose of low molecular weight heparin or unfractionated heparin OR heparin	112 Studies found for: Therapeutic dose of low molecular weight heparin or unfractionated heparin OR heparin COVID-19
Remdesivir	GS-5734, Veklury	COVID-19	Remdesivir OR GS-5734 OR Veklury	136 Studies found for: Remdesivir OR GS-5734 OR Veklury COVID-19
Baricitinib	Olumiant, LY3009104	COVID-19	Baricitinib OR Olumiant OR LY3009104	27 Studies found for: Baricitinib COVID-19
Sotrovimab	VIR-7831, GSK4182136, Xevudy	COVID-19	Sotrovimab OR VIR-7831 OR GSK4182136 OR Xevudy	24 Studies found for: Sotrovimab OR VIR-7831 OR GSK4182136 OR Xevudy COVID-19
Casirivimab/Imdevimab	REGEN-COV, Ronapreve, REGN10933/REGN10987	COVID-19	Casirivimab OR Imdevimab OR REGN-COV OR Ronapreve OR REGN10933 OR REGN10987	26 Studies found for: Casirivimab OR Imdevimab OR REGN-COV OR Ronapreve OR REGN10933 OR REGN1098 COVID-19
Amubarvimab/romlusevimab	BRII-196 /BRII-198	COVID-19	Amubarvimab OR romlusevimab OR BRII—196 OR BRII—198	7 Studies found for: Amubarvimab OR romlusevimab OR BRII-196 OR BRII-198 COVID-19
Tocilizumab	NA	COVID-19	Tocilizumab OR RoActemra	101 Studies found for: Tocilizumab OR RoActemra COVID-19
Anakinra	Kineret	COVID-19	Anakinra OR Kineret	40 Studies found for: Anakinra OR Kineret COVID-19
Intravenous Immunoglobulin	IVIG	COVID-19	Intravenous Immunoglobulin OR IVIG	89 Studies found for: Intravenous Immunoglobulin OR IVIG COVID-19
COVID-19 convalescent plasma	NA	COVID-19	COVID-19 convalescent plasma	196 Studies found for: COVID-19 convalescent plasma COVID-19
Human COVID-19 immunoglobulin (Ph4) for intravenous injection	NA	COVID-19	Human COVID-19 immunoglobulin (Ph4) for intravenous injection	2 Studies found for: Human COVID-19 immunoglobulin (Ph4) for intravenous injection COVID-19

^a NA means the drug has no other name

Supplementary Table S2. The basic characteristics of eligible studies.

NO	Study	ClinicalTrials.gov Identifier	Experimental group	Guideline ^a	Control group	Multicenter	Sample size	Availability of patient data			All-cause mortality	Published or Not
								ICU	Mechanical ventilation	Receiving oxygen only		
1	Puskarich et al., 2022	NCT04312009	Losartan	NA ^b	Placebo	Yes	205	Available	Unavailable	Unavailable	28d	Yes
2	Geriak et al., 2021	NCT04340557	Losartan	NA	Standard care	Yes	31	Unavailable	Unavailable	Unavailable	45d	Yes
3	Duarte et al., 2021	NCT04355936	Telmisartan	NA	Standard care	Yes	158	Unavailable	Unavailable	Unavailable	15d, 30d	Yes
4	Tomazini et al., 2022	NCT04327401	Dexamethasone	China, WHO	Standard care	Yes	299	Available	Available	Unavailable	28d	Yes
The RECOVERY Collaborative Group, 2020												
5	Odeyemi et al., 2022	NCT03852537	Dexamethasone	China, WHO	Standard care	Yes	6425	Unavailable	Available	Available	28d	Yes
6	Tang et al., 2021	NCT04273321	Methylprednisolone	China, WHO	Standard care	No	41	Unavailable	Unavailable	Unavailable	90d	Yes
7	Christiane Maria Prado Jeronimo, 2020	NCT04343729	Methylprednisolone	China, WHO	Placebo	Yes	86	Unavailable	Unavailable	Unavailable	14d	Yes
8	The REMAP-CAP, ACTIV-4a, and ATTACC Investigators, 2021	NCT04372589	Therapeutic dose of low molecular weight heparin or unfractionated heparin	China	Standard care	Yes	416	Unavailable	Available	Available	7d, 14d, 28d	Yes
9	The ATTACC, ACTIV-4a, and REMAP-CAP Investigators, 2021	NCT04372589	Therapeutic dose of low molecular weight heparin or unfractionated heparin	China	Standard care	Yes	1207	Available	Unavailable	Unavailable	21d	Yes
10	Barratt-Due et al., 2021	NCT04321616	Remdesivir	FDA, EMA	Standard care	Yes	366	Unavailable	Unavailable	Unavailable	28, 60d	Yes
11	Wang et al., 2020	NCT04257656	Remdesivir	FDA, EMA	Placebo	Yes	236	Unavailable	Unavailable	Unavailable	28d	Yes
12	Beigel et al., 2020	NCT04280705	Remdesivir	FDA, EMA	Placebo	Yes	1062	Unavailable	Unavailable	Unavailable	29d	Yes
13	Spinner et al., 2020 WHO Solidarity Trial Consortium, 2020	NCT04292730	Remdesivir	FDA, EMA	Standard care	Yes	584	Unavailable	Unavailable	Unavailable	28d	Yes
14	Ader et al., 2022	NCT04315948	Remdesivir	FDA, EMA	Standard care	Yes	11330	Unavailable	Available	Available	28d	Yes
15	Ely et al., 2022	NCT04421027	Baricitinib	FDA, WHO	Standard care	Yes	832	Unavailable	Unavailable	Unavailable	29d	Yes
16	Marconi et al., 2021	NCT04421027	Baricitinib	FDA, WHO	Placebo	Yes	101	Unavailable	Available	Unavailable	28d, 60d	Yes
17	ACTIV-3/Therapeutics for Inpatients with COVID-19 (TICO) Study Group, 2022	NCT04501978	Sotrovimab	FDA, EMA	Placebo	Yes	1525	Unavailable	Unavailable	Available	28d	Yes
18	The RECOVERY Collaborative Group, 2022	NCT04381936	REGEN-COV (Casirivimab /Imdevimab)	FDA, EMA, WHO	Standard care	Yes	9785	Unavailable	Available	Available	28d	Yes
19	ACTIV-3/Therapeutics for Inpatients with COVID-19 (TICO) Study Group, 2022	NCT04501978	Amubarvimab/romlusevima b (BRII-196 /BRII-198)	China	Placebo	Yes	536	Unavailable	Unavailable	Unavailable	5d, 28d, 90d	Yes

47	Bégin et al., 2021 Writing Committee for the REMAP-CAP Investigators, 2021	NCT04348656	COVID-19 convalescent plasma	China, FDA	Standard care	Yes	940	Unavailable	Unavailable	Unavailable	30d	Yes
48		NCT02735707	COVID-19 convalescent plasma	China, FDA	Placebo	Yes	2011	Unavailable	Unavailable	Unavailable	21d	Yes
49	Holm et al., 2021	NCT04600440	COVID-19 convalescent plasma	China, FDA	Standard care	Yes	33	Unavailable	Unavailable	Unavailable	28d	Yes
50	Ortigoza et al., 2021	NCT04364737	COVID-19 convalescent plasma	China, FDA	Placebo	Yes	941	Unavailable	Unavailable	Available	14d, 28d	Yes
51	Bar et al., 2021	NCT04397757	COVID-19 convalescent plasma	China, FDA	Standard care	Yes	79	Unavailable	Unavailable	Unavailable	14d, 28	Yes
52	Körper et al., 2021	NCT04433910	COVID-19 convalescent plasma	China, FDA	Standard care	Yes	105	Unavailable	Unavailable	Unavailable	21, 35, 60d	Yes
53	AlQahtani et al., 2021	NCT04356534	COVID-19 convalescent plasma	China, FDA	Standard care	No	40	Unavailable	Unavailable	Unavailable	28d	Yes
54	Simonovich et al., 2021	NCT04383535	COVID-19 convalescent plasma	China, FDA	Placebo	Yes	333	Unavailable	Unavailable	Unavailable	30d	Yes

^a China: the Chinese Clinical Guidance for COVID-19 Pneumonia Diagnosis and Treatment (China 9th Edition); FDA: the U.S. Food and Drug Administration; EMA: the European Medicines Agency; WHO: the Guideline for Therapeutics and COVID-19 of World Health Organization (WHO).

^b NA means the drug was not included in any guideline.