An updated systematic review and network meta-analysis of 25 randomized trials assessing the efficacy and safety of treatments in COVID-19 disease

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METHODS
Search strategy

CENTRAL equation
#1 randomized controlled trial [pt]
#2 controlled clinical trial [pt]
#3 randomized [tiab]
#4 placebo [tiab]
#5 clinical trials as topic [mesh: noexp]
#6 randomly [tiab]
#7 trial [ti]
#8 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7
#9 animals [mh] NOT humans [mh]
#10 #8 NOT #9
#11 "SARS-CoV-2"[Mesh]
#12 "COVID-19"[Mesh]
#13 Coronavirus*[Title]
#14 #11 OR #12 OR #13
#15 "Treatment"[Mesh]
#16 Treatment*[Title]
#17 #15 OR #16
#18 #10 AND #14 AND #17

**MEDLINE equation**
(randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized [tiab] OR placebo [tiab] OR clinical trials as topic [mesh: noexp] OR randomly [tiab] OR trial [ti]) NOT (animals [mh] NOT humans [mh]) AND ("SARS-CoV-2"[Mesh] OR "COVID-19"[Mesh] OR COVID-19*[Title]) AND ("COVID-19"[Mesh] OR "SARS-CoV-2"[Mesh] SARS-CoV-2*[Title] OR COVID-19*[Title]).
**Figure 1.** Summary of risk bias assessment for SARS-CoV-2 treatment comparisons.

- **Bias arising from the randomization process**
- **Bias due to deviations from intended interventions**
- **Bias due to missing outcome data**
- **Bias in measurement of the outcome**
- **Bias in selection of the reported result**
- **Overall risk of bias**

Legend:
- **Low risk of bias**
- **Some concerns**
- **High risk of bias**
Figure 2. Summary of risk bias assessment for RCTs SARS-CoV-2 treatments comparisons.

| Study                        | D1 | D2 | D3 | D4 | D5 | Overall |
|------------------------------|----|----|----|----|----|---------|
| Cao                          | +  | +  | +  | X  | +  | x       |
| Chen Zhaowei                 | +  | +  | +  | +  | +  | +       |
| Li Y                         | +  | +  | +  | +  | +  | +       |
| Chen Jun                     | +  | +  | +  | +  | +  | +       |
| Wang                         | +  | +  | +  | +  | +  | +       |
| Goldman                      | +  | +  | +  | X  | X  | x       |
| Borba                        | +  | +  | +  | +  | +  | +       |
| Chen Chang                   | +  | +  | +  | Y  | X  | x       |
| Tang                         | +  | +  | X  | +  | +  | x       |
| Ling Li                      | +  | +  | X  | +  | +  | x       |
| Hung                         | +  | +  | X  | +  | +  | x       |
| Deftereos                    | +  | +  | X  | +  | +  | x       |
| Huang                        | +  | +  | X  | +  | +  | x       |
| Beigel                       | +  | +  | X  | +  | +  | x       |
| Cavalcanti                   | +  | +  | X  | +  | +  | x       |
| Yang Cao                     | +  | +  | X  | +  | +  | x       |
| Spinner                      | +  | +  | X  | +  | +  | x       |
| Miller                       | +  | +  | X  | +  | +  | x       |
| RECOVERY                     | +  | +  | X  | +  | +  | x       |
| CAPE COVID                   | +  | +  | X  | +  | +  | x       |
| CoDex                        | +  | +  | X  | +  | +  | x       |
| REMAP–CAP                    | +  | +  | X  | +  | +  | x       |
| DEXA–COVID 19                | +  | +  | X  | +  | +  | x       |
| COVID STEROID                | +  | +  | X  | +  | +  | x       |
| Steroids–SARI                | +  | +  | X  | +  | +  | x       |

Domains:
D1: Bias due to randomisation.
D2: Bias due to deviations from intended intervention.
D3: Bias due to missing data.
D4: Bias due to outcome measurement.
D5: Bias due to selection of reported result.

Judgement
High
Some concerns
Low

Number in parenthesis are references
**Figure 3.** Direct and indirect comparison for 28-day all-cause mortality.

| Comparison          | Number of Studies | Direct Evidence | Random effects model | RR   | 95% CI     |
|---------------------|-------------------|-----------------|----------------------|------|-----------|
| ARB:LPVRTV          |                   |                 |                      |      |           |
| Direct estimate     | 1                 | 0.79            |                      | 1.06 | [0.71; 1.60] |
| Indirect estimate   |                   |                 |                      | 0.69 | [0.32; 1.51] |
| Network estimate    |                   |                 |                      | 0.97 | [0.68; 1.39] |
| ARB:StdCare         |                   |                 |                      |      |           |
| Direct estimate     | 1                 | 0.79            |                      | 0.86 | [0.57; 1.29] |
| Indirect estimate   |                   |                 |                      | 1.32 | [0.60; 2.88] |
| Network estimate    |                   |                 |                      | 0.94 | [0.66; 1.55] |
| HCQ:HCQAZT          |                   |                 |                      |      |           |
| Direct estimate     | 1                 | 0.81            |                      | 0.90 | [0.71; 1.16] |
| Indirect estimate   |                   |                 |                      | 1.43 | [0.87; 2.37] |
| Network estimate    |                   |                 |                      | 0.99 | [0.79; 1.23] |
| HCQ:LPVRTV          |                   |                 |                      |      |           |
| Direct estimate     | 1                 | 0.33            |                      | 1.32 | [0.91; 1.90] |
| Indirect estimate   |                   |                 |                      | 1.02 | [0.78; 1.32] |
| Network estimate    |                   |                 |                      | 1.11 | [0.90; 1.37] |
| HCQ:StdCare         |                   |                 |                      |      |           |
| Direct estimate     | 4                 | 0.90            |                      | 1.05 | [0.91; 1.21] |
| Indirect estimate   |                   |                 |                      | 1.35 | [0.88; 2.08] |
| Network estimate    |                   |                 |                      | 1.07 | [0.94; 1.23] |
| HCQAZT:StdCare      |                   |                 |                      |      |           |
| Direct estimate     | 1                 | 0.83            |                      | 1.00 | [0.79; 1.28] |
| Indirect estimate   |                   |                 |                      | 1.63 | [0.95; 2.79] |
| Network estimate    |                   |                 |                      | 1.09 | [0.87; 1.35] |
| LPVRTV:StdCare      |                   |                 |                      |      |           |
| Direct estimate     | 2                 | 0.76            |                      | 1.03 | [0.83; 1.28] |
| Indirect estimate   |                   |                 |                      | 0.80 | [0.54; 1.18] |
| Network estimate    |                   |                 |                      | 0.97 | [0.80; 1.17] |
| RDV:RDVs            |                   |                 |                      |      |           |
| Direct estimate     | 2                 | 0.91            |                      | 0.90 | [0.75; 1.07] |
| Indirect estimate   |                   |                 |                      | 1.16 | [0.67; 1.99] |
| Network estimate    |                   |                 |                      | 0.92 | [0.78; 1.09] |
| RDV:StdCare         |                   |                 |                      |      |           |
| Direct estimate     | 3                 | 0.96            |                      | 1.13 | [0.98; 1.31] |
| Indirect estimate   |                   |                 |                      | 0.83 | [0.42; 1.63] |
| Network estimate    |                   |                 |                      | 1.12 | [0.97; 1.28] |
| RDVs:StdCare        |                   |                 |                      |      |           |
| Direct estimate     | 1                 | 0.60            |                      | 1.11 | [0.87; 1.42] |
| Indirect estimate   |                   |                 |                      | 1.38 | [1.02; 1.87] |
| Network estimate    |                   |                 |                      | 1.21 | [1.00; 1.47] |

RDVs: remdesivir for 5-day; RDV: remdesivir more than 5-day; FPV: favipiravir; LPVRTV: lopinavir/ritonavir; ARB: arbidol (umafenovir). Plasma: convalescent plasma; StdCare: standard of care; HCQ: hydroxychloroquine; HCQAZT: association hydroxychloroquine and azithromycin; HCQlow: low dose of hydroxychloroquine (400 mg); HCQ: hydroxychloroquine.
RDVs: remdesivir for 5-day; RDV: remdesivir more than 5-day; FPV: favipiravir; LPVRTV: lopinavir/ritonavir; ARB: arbidol (umafenovir). Plasma: convalescent plasma; StdCare: standard of care; HCQ: hydroxychloroquine; HCQAZT: association hydroxychloroquine and azithromycin; HCQlow: low dose of hydroxychloroquine (400 mg); HCQ: hydroxychloroquine.
**Figure 5.** Heatmap to identify points of single design heterogeneity for 28-day all-cause mortality.

RDVs: remdesivir for 5-day; RDV: remdesivir more than 5-day; FPV: favipiravir; LPVRTV: lopinavir/ritonavir; ARB: arbidol (umafenovir). Plasma: convalescent plasma; StdCare: standard of care; HCQ: hydroxychloroquine.
**Figure 6.** Heatmap to identify points of single design heterogeneity for clinical improvement.

RDVs: remdesivir for 5-day; RDV: remdesivir more than 5-day; FPV: favipiravir; LPVRTV: lopinavir/ritonavir; ARB: arbidol (umafenovir). Plasma: convalescent plasma; StdCare: standard of care; HCQ: hydroxychloroquine.
**Figure 7.** Heatmap to identify points of single design heterogeneity for any adverse event.

|   | RDV:StdCare  | RDV:RDVs:StdCare  | RDV:RDVs:StdCare  | RDV:RDVs:StdCare  | RDV:RDVs:StdCare  | RDV:RDVs:StdCare  | RDV:RDVs:StdCare  | RDV:RDVs:StdCare  | RDV:RDVs:StdCare  |
|---|---------------|--------------------|--------------------|--------------------|--------------------|--------------------|--------------------|--------------------|--------------------|
| RDV:StdCare |          |                    |                    |                    |                    |                    |                    |                    |                    |
| RDV:RDVs:StdCare |          |                    |                    |                    |                    |                    |                    |                    |                    |
| HCQ:StdCare |          |                    |                    |                    |                    |                    |                    |                    |                    |
| ARB:StdCare |          |                    |                    |                    |                    |                    |                    |                    |                    |
| LPVTV:StdCare |          |                    |                    |                    |                    |                    |                    |                    |                    |
| RDV:RDVs:StdCare |          |                    |                    |                    |                    |                    |                    |                    |                    |
| ARB:LPVTV:StdCare |          |                    |                    |                    |                    |                    |                    |                    |                    |

RDVs: remdesivir for 5-day; RDV: remdesivir more than 5-day; FPV: favipiravir; LPVTV: lopinavir/ritonavir; ARB: arbidol (umafenovir). Plasma: convalescent plasma; StdCare: standard of care; HCQ: hydroxychloroquine.
Figure 8. Heatmap to identify points of single design heterogeneity for any severe adverse event.

RDVs: remdesivir for 5-day; RDV: remdesivir more than 5-day; FPV: favipiravir; LPVRTV: lopinavir/ritonavir; LPVRTV RBV: lopinavir/ritonavir and ribavirin; ARB: arbidol (umafenovir). Plasma: convalescent plasma; StdCare: standard of care; HCQlow: low dose of hydroxychloroquine (400 mg); HCQ: hydroxychloroquine.
**Figure 9.** Heatmap to identify points of single design heterogeneity for Viral clearance rate (negative conversion rate).

RDVs: remdesivir for 5-day; RDV: remdesivir more than 5-day; FPV: favipiravir; LPVRTV: lopinavir/ritonavir; LPVRTVRBV: lopinavir/ritonavir and ribavirin; ARB: arbidol (umafenovir). Plasma: convalescent plasma; StdCare: standard of care; AZT: azithromycin; HCQlow: low dose of hydroxychloroquine (400 mg); HCQ: hydroxychloroquine; HCQAZT: association hydroxychloroquine and azithromycin.
Table 1. League table of pairwise comparisons in network meta-analysis for 28-day all-cause mortality.

| Treatment           | RR (95% CI) | RDVs | Plasma | HCQLow | Auxora | RDV | LPVRTV | Hydrocort | LCQAZT | StdCare |
|---------------------|-------------|------|--------|--------|--------|-----|--------|-----------|--------|---------|
| Ruxolitinib         | -           | -    | -      | -      | -      | -   | -      | -         | -      | -       |
| Colchicine          | 0.66 (0.02- 2.49) | -    | -      | -      | -      | -   | -      | -         | -      | -       |
| Dexamet: dexamethasone | 0.29 (0.01-5.76) | 4.26 | -      | -      | -      | -   | -      | -         | -      | -       |
| Methylpred: methylprednisolone | 0.33 (0.01-8.05) | 0.49 (0.04-1.11) | 1.11 (0.24-5.11) | 0.74 (0.41-1.34) | -    | -   | -      | -         | -      | -       |
| RDVs                | -           | -    | -      | -      | -      | -   | -      | -         | -      | -       |
| Plasma              | 0.28 (0.01-8.57) | 0.43 (0.03-7.10) | 0.97 (0.14-6.54) | 0.87 (0.09-8.28) | -    | -   | -      | -         | -      | -       |
| Hydrocort           | 0.22 (0.01-4.05) | 0.33 (0.04-2.95) | 0.74 (0.41-1.33) | 0.67 (0.16-2.75) | 0.77 (0.12-4.76) | -   | -      | -         | -      | -       |
| RDVs                | -           | -    | -      | -      | -      | -   | -      | -         | -      | -       |
| LPVRTV              | 0.23 (0.01-4.67) | 0.35 (0.03-2.50) | 0.78 (0.27-2.25) | 0.70 (0.14-3.46) | 0.81 (0.11-2.57) | 1.05 (0.43-2.57) | -   | -      | -         | -      | -       |
| Plasma              | 0.20 (0.01-3.74) | 0.30 (0.03-2.75) | 0.67 (0.28-1.58) | 0.60 (0.14-2.61) | 0.69 (0.11-1.72) | 0.90 (0.47-2.26) | 0.85 (0.32-2.61) | -   | -      | -         | -      | -       |
| Remdesivir          | 0.18 (0.01-3.37) | 0.28 (0.03-1.30) | 0.62 (0.30-2.28) | 0.56 (0.14-3.95) | 0.64 (0.10-1.34) | 0.84 (0.52-1.90) | 0.79 (0.33-1.90) | -   | -      | -         | -      | -       |
| Remdesivir more than 5-day | 0.17 (0.01-3.94) | 0.26 (0.02-2.45) | 0.59 (0.15-2.28) | 0.53 (0.13-2.17) | 0.61 (0.07-2.71) | 0.79 (0.23-3.14) | 0.75 (0.18-3.14) | -   | -      | -         | -      | -       |
| LPVRTV              | 0.17 (0.01-3.04) | 0.25 (0.03-2.19) | 0.57 (0.29-1.12) | 0.51 (0.13-2.02) | 0.59 (0.10-1.12) | 0.76 (0.52-1.65) | 0.72 (0.32-1.48) | -   | -      | -         | -      | -       |
| Plasma              | 0.16 (0.01-2.99) | 0.24 (0.03-2.19) | 0.53 (0.23-1.25) | 0.48 (0.11-2.08) | 0.55 (0.09-3.57) | 0.72 (0.38-1.36) | 0.68 (0.26-1.80) | 0.80 (0.38-1.80) | -   | -      | -         | -      | -       |
| Remdesivir          | 0.13 (0.01-2.77) | 0.19 (0.02-2.12) | 0.43 (0.12-1.53) | 0.38 (0.17-0.89) | 0.44 (0.05-2.11) | 0.58 (0.18-2.11) | 0.55 (0.14-2.14) | 0.64 (0.19-2.14) | -   | -      | -         | -      | -       |
| Remdesivir more than 5-day | 0.15 (0.01-2.73) | 0.23 (0.03-1.97) | 0.51 (0.26-1.81) | 0.46 (0.12-3.17) | 0.53 (0.09-3.69) | 0.69 (0.48-1.98) | 0.69 (0.29-1.48) | 0.77 (0.45-1.32) | -   | -      | -         | -      | -       |
| Plasma              | -           | -    | -      | -      | -      | -   | -      | -         | -      | -       |

Treatment are ordered in the rank of their chance of being the best option. Treatment estimates are provided as risk ratios (RR) with 95% CIs. RR values >1 favor the column-defining treatment for the network estimates; Bold text correspond to statistically significant value; Upper triangle were direct comparison, and lower triangle were indirect comparison; RDVs: remdesivir for 5-day; RDV: remdesivir more than 5-day; LPVRTV: lopinavir/ritonavir; Hydrocort: hydrocortisone; Dexamat: dexamethasone; Methylpred: methylprednisolone.
Table 2. League table of pairwise comparisons in network meta-analysis for clinical improvement.

| Treatment | RDVs | Plasma | Colechicine | RDV | HCQAZT | HCQ | FPV | LPVRTV | ARB | Auxora | StdCare | Dexamethasone |
|-----------|------|--------|-------------|-----|--------|-----|-----|--------|-----|--------|---------|---------------|
| Ruxolitinib | .    | .      | .            | .   | .      | .   | .   | .      | .   | .      | .       | 1.40 (0.74-) |
| 1.15 (0.59-) | .    | .      | 1.11 (0.93-) | .   | 1.11 (0.87-) | .   | .   | .      | .   | .      | .       | 2.66) |
| 2.25 | RDVs | .      | .            | 1.33 | .      | .   | .   | .      | .   | .      | .       | 1.42) |
| 1.16 (0.53-) | 1.01 (0.62-) | . | .            | .   | 1.20 (0.76-) | .   | .   | .      | .   | .      | .       | 1.90) |
| 2.55 | 1.65 | Plasma | .            | .   | .      | .   | .   | .      | .   | .      | .       | 1.43) |
| 1.23 (0.62-) | 1.06 (0.79-) | 1.05 (0.63-) | . | . | .      | 1.14 (0.91-) | .   | .   | .      | .   | .      | .       | 1.90) |
| 2.42 | 1.43 | 1.75 | .            | .   | .      | .   | .   | .      | .   | .      | .       | 1.43) |
| 1.26 (0.65-) | 1.09 (0.92-) | 1.08 (0.67-) | 1.02 (0.78-) | . | .      | .   | .   | .      | .   | .      | .       | 1.13 (0.98-) |
| 2.42 | .    | 1.74 | 1.34 | . | .      | 1.31) | .   | .   | .      | .   | .      | .       | 1.43) |
| 1.29 (0.65-) | 1.12 (0.84-) | 1.11 (0.67-) | 1.05 (0.77-) | 1.03 (0.79-) | 1.11 (0.86-) | .   | .   | .      | .   | .      | .       | 1.00 (0.79-) |
| 2.54 | 1.49 | 1.83 | 1.44 | 1.33 | .      | .   | .   | .      | .   | .      | .       | 1.28) |
| 1.30 (0.68-) | 1.13 (0.89-) | 1.12 (0.70-) | 1.06 (0.82-) | 1.04 (0.85-) | 1.01 (0.81-) | .   | .   | .      | .   | .      | .       | 1.21) |
| 2.51 | 1.43 | 1.80 | 1.39 | 1.26 | .      | .   | .   | .      | .   | .      | .       | 1.90) |
| 1.30 (0.59-) | 1.13 (0.68-) | 1.12 (0.58-) | 1.06 (0.63-) | 1.03 (0.63-) | 1.01 (0.60-) | 1.00 (0.61-) | . | . | FPV | . | . | 1.15 (0.85-) |
| 2.87 | 1.87 | 2.15 | 1.79 | 1.69 | 1.69 | 1.62) | . | . | . | FPV | . | . | 1.55) |
| 1.44 (0.59-) | 1.25 (0.66-) | 1.24 (0.58-) | 1.18 (0.61-) | 1.15 (0.61-) | 1.12 (0.58-) | 1.11 (0.59-) | 1.11 (0.51-) | . | . | . | . | 0.97 (0.53-)
| 3.50 | 2.37 | 2.66 | 2.26 | 2.15 | 2.15 | 2.07 | 2.40) | Auxora | 1.79) | . | . | . | . |
| 1.40 (0.74-) | 1.21 (1.00-) | 1.20 (0.76-) | 1.14 (0.91-) | 1.12 (0.97-) | 1.09 (0.87-) | 1.07 (0.94-) | 1.08 (0.67-) | 0.97 (0.53-) | 0.97 (0.78-) | . | . | 1.16 (0.77-) | 1.07 (0.87-)
| 2.66 | 1.47 | 1.90 | 1.43 | 1.28 | 1.35 | 1.23) | 1.72 | 1.79) | . | . | . | . | StdCare | 1.21) |
| 1.44 (0.74-) | 1.25 (0.96-) | 1.24 (0.76-) | 1.18 (0.87-) | 1.15 (0.91-) | 1.12 (0.84-) | 1.11 (0.90-) | 1.11 (0.70-) | 1.00 (0.53-) | 1.03 (0.85-) | 1.03 (0.53-) | 0.94 (0.63-)
| 2.82 | 1.64 | 2.03 | 1.59 | 1.46 | 1.49 | 1.37) | 1.78 | 1.90) | . | . | . | . | LPVRTV | 1.41) |
| 1.49 (0.71-) | 1.29 (0.86-) | 1.28 (0.72-) | 1.21 (0.79-) | 1.19 (0.80-) | 1.15 (0.76-) | 1.14 (0.78-) | 1.15 (0.85-) | 1.03 (0.51-) | 1.06 (0.74-) | 1.03 (0.72-) | . |
| 3.10 | 1.94 | 2.28 | 1.86 | 1.75 | 1.76 | 1.67 | 1.55 | 2.10 | 1.52 | 1.48 | ARB | . |
| 1.49 (0.76-) | 1.29 (0.98-) | 1.28 (0.78-) | 1.22 (0.89-) | 1.19 (0.92-) | 1.16 (0.86-) | 1.14 (0.89-) | 1.15 (0.69-) | 1.03 (0.54-) | 1.07 (0.87-) | 1.03 (0.78-) | 1.00 (0.66-)
| 2.93 | 1.71 | 2.11 | 1.66 | 1.53 | 1.57 | 1.47 | 1.92 | 1.98 | 1.31 | 1.37 | 1.52) | Dexamethasone |

Treatments are ordered in the rank of their chance of being the best option. Treatment estimates are provided as risk ratios (RR) with 95% CIs. Indirect comparisons between treatment should be read left to right, and their RR is in the cell in common between the column-defining treatment and the row-defining treatment. RR >1 favor the column-defining treatment for the network estimates; Bold value correspond to statistically significant value; Upper triangle were direct comparison, and lower triangle were indirect comparison; RDVs: remdesivir for 5-day; RDV: remdesivir more than 5-day; FPV: favipiravir; LPVRTV: lopinavir/ritonavir; ARB: arbidol (umafenovir). Plasma: convalescent plasma; StdCare: standard of care; HCQlow: low dose of hydroxychloroquine (400 mg); HCQ: hydroxychloroquine.
Table 3. League table of pairwise comparisons in network meta-analysis for viral clearance rate (negative conversion rate).

| Treatments | Plasma | ARB | ARB | StdCare | StdCare | HCQ | HCQ | LPVRTV | LPVRTV | RDV | RDV |
|------------|--------|-----|-----|---------|---------|-----|-----|--------|--------|-----|-----|
| Plasma     | 2.68 (1.71-4.20) | 2.49 (1.53-4.05) | 2.68 (1.71-4.20) | 2.70 (1.69-4.30) | 2.74 (1.72-4.39) | 2.87 (1.76-4.68) | . | 1.20 (0.90-1.59) | . | 1.07 (0.90-1.27) | . |
| ARB        | .      | 1.08 (0.89-1.31) | 1.08 (0.89-1.32) | 1.10 (0.94-1.30) | 1.15 (0.88-1.52) | 1.08 (0.89-1.31) | 1.06 (0.91-1.24) | . | 1.06 (0.89-1.30) | 1.07 (0.90-1.27) |
| StdCare    | 1.06 (0.91-1.24) | . | 1.01 (0.88-1.14) | 1.02 (0.89-1.18) | 1.07 (0.88-1.30) | 1.01 (0.88-1.14) | . | . | 1.07 (0.90-1.27) | 1.07 (0.90-1.27) |
| StdCare    | 0.94 (0.79-1.13) | 0.94 (0.79-1.13) | . | 1.01 (0.88-1.14) | 1.06 (0.89-1.30) | . | 0.94 (0.79-1.13) | 0.94 (0.79-1.13) | 1.07 (0.90-1.27) |
| HCQ        | 1.07 (0.90-1.27) | 1.07 (0.90-1.27) | 1.07 (0.90-1.27) | . | 1.09 (0.92-1.28) | 1.07 (0.90-1.27) | 1.07 (0.90-1.27) | . | 1.07 (0.90-1.27) | 1.07 (0.90-1.27) |
| LPVRTV     | 1.02 (0.89-1.16) | 1.02 (0.89-1.16) | . | . | . | 1.02 (0.89-1.16) | . |
| RDV        | .       | . | . | . | . | . | . | . | . | . | . |

Treatments are ordered in the rank of their chance of being the best option. Treatment estimates are provided as risk ratios (RR) with 95% CIs. Indirect comparisons between treatment should be read left to right, and their RR is in the cell in common between the column-defining treatment and the row-defining treatment. RRs >1 favor the column-defining treatment for the network estimates. Bold value correspond to statistically significant value; Upper triangle were direct comparison, and lower triangle were indirect comparison; RDV: remdesivir more than 5-day; LPVRTV: lopinavir/ritonavir; ARB: arbidol (umafenovir). Plasma: convalescent plasma; StdCare: standard of care; HCQ: hydroxychloroquine.
Table 4. League table of pairwise comparisons in network meta-analysis for any adverse event.

|        | Dexamet | ARB | HCQLow | FPV | RDVs | Hydrocort | StdCare | Auxora |
|--------|---------|-----|--------|-----|------|-----------|---------|--------|
| 0.46   | 0.76    | 1.25| 2.30   | 0.76| 1.00 | 0.76      | 0.53    | 0.44   |
| (0.18-1.14) | (0.46-0.31) | (0.25-0.17) | (0.16-0.30) | (0.18-0.36) | (0.53-0.29) | (0.46-0.18) | (0.18-0.35) | (0.18-0.35) |
| 0.89   | 0.76    | 1.25| 2.30   | 0.76| 1.00 | 0.76      | 0.53    | 0.44   |
| (0.18-1.14) | (0.46-0.31) | (0.25-0.17) | (0.16-0.30) | (0.18-0.36) | (0.53-0.29) | (0.46-0.18) | (0.18-0.35) | (0.18-0.35) |
| 0.89   | 0.76    | 1.25| 2.30   | 0.76| 1.00 | 0.76      | 0.53    | 0.44   |
| (0.18-1.14) | (0.46-0.31) | (0.25-0.17) | (0.16-0.30) | (0.18-0.36) | (0.53-0.29) | (0.46-0.18) | (0.18-0.35) | (0.18-0.35) |
| 0.50   | 0.76    | 1.25| 2.30   | 0.76| 1.00 | 0.76      | 0.53    | 0.44   |
| (0.18-1.14) | (0.46-0.31) | (0.25-0.17) | (0.16-0.30) | (0.18-0.36) | (0.53-0.29) | (0.46-0.18) | (0.18-0.35) | (0.18-0.35) |
| 0.46   | 0.76    | 1.25| 2.30   | 0.76| 1.00 | 0.76      | 0.53    | 0.44   |
| (0.18-1.14) | (0.46-0.31) | (0.25-0.17) | (0.16-0.30) | (0.18-0.36) | (0.53-0.29) | (0.46-0.18) | (0.18-0.35) | (0.18-0.35) |
| 0.46   | 0.76    | 1.25| 2.30   | 0.76| 1.00 | 0.76      | 0.53    | 0.44   |
| (0.18-1.14) | (0.46-0.31) | (0.25-0.17) | (0.16-0.30) | (0.18-0.36) | (0.53-0.29) | (0.46-0.18) | (0.18-0.35) | (0.18-0.35) |
| 0.46   | 0.76    | 1.25| 2.30   | 0.76| 1.00 | 0.76      | 0.53    | 0.44   |
| (0.18-1.14) | (0.46-0.31) | (0.25-0.17) | (0.16-0.30) | (0.18-0.36) | (0.53-0.29) | (0.46-0.18) | (0.18-0.35) | (0.18-0.35) |
| 0.46   | 0.76    | 1.25| 2.30   | 0.76| 1.00 | 0.76      | 0.53    | 0.44   |
| (0.18-1.14) | (0.46-0.31) | (0.25-0.17) | (0.16-0.30) | (0.18-0.36) | (0.53-0.29) | (0.46-0.18) | (0.18-0.35) | (0.18-0.35) |
| 0.46   | 0.76    | 1.25| 2.30   | 0.76| 1.00 | 0.76      | 0.53    | 0.44   |
| (0.18-1.14) | (0.46-0.31) | (0.25-0.17) | (0.16-0.30) | (0.18-0.36) | (0.53-0.29) | (0.46-0.18) | (0.18-0.35) | (0.18-0.35) |
| 0.46   | 0.76    | 1.25| 2.30   | 0.76| 1.00 | 0.76      | 0.53    | 0.44   |
| (0.18-1.14) | (0.46-0.31) | (0.25-0.17) | (0.16-0.30) | (0.18-0.36) | (0.53-0.29) | (0.46-0.18) | (0.18-0.35) | (0.18-0.35) |
| 0.46   | 0.76    | 1.25| 2.30   | 0.76| 1.00 | 0.76      | 0.53    | 0.44   |
| (0.18-1.14) | (0.46-0.31) | (0.25-0.17) | (0.16-0.30) | (0.18-0.36) | (0.53-0.29) | (0.46-0.18) | (0.18-0.35) | (0.18-0.35) |
| 0.46   | 0.76    | 1.25| 2.30   | 0.76| 1.00 | 0.76      | 0.53    | 0.44   |
| (0.18-1.14) | (0.46-0.31) | (0.25-0.17) | (0.16-0.30) | (0.18-0.36) | (0.53-0.29) | (0.46-0.18) | (0.18-0.35) | (0.18-0.35) |
| 0.46   | 0.76    | 1.25| 2.30   | 0.76| 1.00 | 0.76      | 0.53    | 0.44   |
| (0.18-1.14) | (0.46-0.31) | (0.25-0.17) | (0.16-0.30) | (0.18-0.36) | (0.53-0.29) | (0.46-0.18) | (0.18-0.35) | (0.18-0.35) |
| 0.46   | 0.76    | 1.25| 2.30   | 0.76| 1.00 | 0.76      | 0.53    | 0.44   |
| (0.18-1.14) | (0.46-0.31) | (0.25-0.17) | (0.16-0.30) | (0.18-0.36) | (0.53-0.29) | (0.46-0.18) | (0.18-0.35) | (0.18-0.35) |
|       | 0.34 | 0.38 | 0.50 | 0.50 | 0.71 | 0.70 | 0.73 | 0.72 | 0.76 | 0.82 | 0.89 |
|-------|------|------|------|------|------|------|------|------|------|------|------|
| (0.13-|      |      |      |      |      |      |      |      |      |      |      |
| 0.88) | 1.00 | 0.83 | 1.50 | 1.06 | 1.23 | 0.99 | 1.31 | 1.07 | 1.42 | 1.40 | 1.14 |
| 0.31  | 0.35 | 0.46 | 0.46 | 0.66 | 0.65 | 0.68 | 0.67 | 0.70 | 0.75 | 0.92 |
| (0.12-|      |      |      |      |      |      |      |      |      |      |      |
| 0.83) | 0.96 | 0.86 | 1.43 | 1.03 | 1.18 | 0.97 | 1.25 | 1.05 | 1.40 | 1.35 | 1.17 |
| 0.09  | 0.10 | 0.14 | 0.14 | 0.20 | 0.20 | 0.20 | 0.20 | 0.21 | 0.23 | 0.28 | 0.30 |
| (0.00-|      |      |      |      |      |      |      |      |      |      |      |
| 2.20) | 2.51 | 3.00 | 3.45 | 4.13 | 4.18 | 4.20 | 4.31 | 4.35 | 4.82 | 4.86 | 4.75 |
| (0.06-|      |      |      |      |      |      |      |      |      |      |      |
| 0.50  | 0.60 | 0.57 | 0.88 | 0.67 | 0.75 | 0.65 | 0.79 | 0.91 | 0.85 | 0.79 | 0.95 |

Treatments are ordered in the rank of their chance of being the best option. Treatment estimates are provided as risk ratios (RR) with 95% CIs. Indirect comparisons between treatment should be read left to right, and their RR is in the cell in common between the column-defining treatment and the row-defining treatment. RRs >1 favor the column-defining treatment for the network estimates; Bold value correspond to statistically significant value; Upper triangle were direct comparison, and lower triangle were indirect comparison.; RDVs: remdesivir for 5-day; RDV: remdesivir more than 5-day; FPV: favipiravir; LPVRTV: lopinavir/ritonavir; LPVRTV RBV: lopinavir/ritonavir and ribavirin; ARB: arbidol (umafenovir). Plasma: convalescent plasma; StdCare: standard of care; AZT: azithromycin; HCQlow: low dose of hydroxychloroquine (400 mg); HCQ: hydroxychloroquine; HCQAZT: association hydroxychloroquine and azithromycin; Hydrocort: hydrocortisone; Dexamet: dexamethasone; Methylpred: methylprednisolone.
Table 5. League table of pairwise comparisons in network meta-analysis for any severe adverse event.

| Treatment | LPVRTV | Ruxolitinib | RDVs | Dexamet | Methylpred | HCQAZT | StdCare | HCQ | Hydrocort |
|-----------|--------|-------------|------|---------|------------|--------|---------|-----|----------|
| LPVRTV | 0.16 (0.01-3.84) | . | . | . | . | . | . | 0.12 (0.01-2.03) | . |
| Ruxolitinib | 0.20 (0.01-60.89) | 0.64 (0.47-1.09) | 0.50 (0.23-1.09) | . | 0.50 (0.25-1.09) | . | 0.60 (0.37-1.09) | . | . |
| RDVs | 4.35 | . | . | . | 0.12 (0.01-2.03) | 0.19 (0.01-2.03) | 0.20 (0.01-2.03) | 0.24 (0.01-4.35) | . |
| Dexamet | 4.42 | . | . | . | . | . | . | 0.64 (0.47-0.98) | . |
| Methylpred | 3.53 | . | . | . | . | . | . | 0.50 (0.25-0.98) | . |
| HCQAZT | 0.15 (0.01-6.30) | 0.65 (0.32-1.91) | 0.79 (0.46-2.03) | 0.75 (0.62-2.03) | 0.96 (0.88-2.03) | . | . | . | . |
| StdCare | 0.10 (0.00-0.34) | 0.52 (0.26-1.03) | 0.63 (0.38-1.03) | 0.79 (0.64-1.03) | 0.96 (0.88-1.03) | 0.91 | . | 1.05 (0.21-1.02) | 1.04 |
| HCQ | 0.09 (0.00-0.34) | 0.50 (0.26-1.03) | 0.63 (0.38-1.03) | 0.79 (0.64-1.03) | 0.96 (0.88-1.03) | 0.91 | . | 1.05 (0.21-1.02) | 1.04 |
| Hydrocort | 0.08 (0.00-0.34) | 0.40 (0.07-0.71) | 0.48 (0.10-1.02) | 0.61 (0.13-1.00) | 0.77 (0.16-1.03) | 0.97 | . | 1.05 (0.21-1.02) | 1.04 |
| RDV | 2.94 | 0.85 | 1.32 | 1.34 | RDV | . | . | 0.91 | . |
| Methylpred | 2.69 | . | . | . | RDV | . | . | . | . |
| HCQAZT | 0.12 (0.01-0.34) | 0.25 (0.02-0.60) | 0.60 (0.37-1.91) | 0.96 (0.63-1.91) | 1.24 (0.26-1.91) | 3.63 | . | 5.13 | 4.99 |
| StdCare | 0.09 (0.00-0.34) | 0.40 (0.07-0.71) | 0.48 (0.10-1.02) | 0.61 (0.13-1.00) | 0.77 (0.16-1.03) | 0.97 | . | 1.05 (0.21-1.02) | 1.04 |
| HCQ | 0.08 (0.00-0.34) | 0.33 (0.08-0.85) | 0.34 (0.07-0.85) | 0.41 (0.09-0.85) | 0.52 (0.13-1.00) | 0.92 | . | 1.04 | 5.83 |
| Hydrocort | 0.07 (0.00-0.34) | 0.33 (0.08-0.85) | 0.34 (0.07-0.85) | 0.41 (0.09-0.85) | 0.52 (0.13-1.00) | 0.92 | . | 1.04 | 5.83 |
| RDVs | 0.05 (0.00-0.34) | 0.25 (0.04-0.30) | 0.25 (0.04-0.30) | 0.30 (0.06-0.30) | 0.48 (0.10-0.48) | 0.62 (0.07-0.62) | 0.73 (0.09-0.73) | 0.76 (0.63-0.92) | 2.47 |
| StdCare | 0.05 (0.00-0.34) | 0.25 (0.04-0.30) | 0.25 (0.04-0.30) | 0.30 (0.06-0.30) | 0.48 (0.10-0.48) | 0.62 (0.07-0.62) | 0.73 (0.09-0.73) | 0.76 (0.63-0.92) | 2.47 |

Treatments are ordered in the rank of their chance of being the best option. Treatment estimates are provided as risk ratios (RR) with 95% CIs. Indirect comparisons between treatment should be read left to right, and their RR is in the cell in common between the column-defining treatment and the row-defining treatment. RRs >1 favor the column-defining treatment for the network estimates; Bold value correspond to statistically significant value; Upper triangle were direct comparison, and lower triangle were indirect comparison; RDVs: remdesivir for 5-day; RDV: remdesivir more than 5-day; LPVRTV: lopinavir/ritonavir; LPVRTV RBV: lopinavir/ritonavir and ribavirin; ARB: arbidol (umafenovir). Plasma: convalescent plasma; StdCare: standard of care; HCQ: hydroxychloroquine; Hydrocort: hydrocortisone; Dexamet: dexamethasone; Methylpred: methylprednisolone; HCQAZT: association hydroxychloroquine and azithromycin.
### Table 6. League table of pairwise comparisons in network meta-analysis for 28-day all-cause mortality from sensitivity analysis.

| Treatment | Rank | RR | 95% CI |
|-----------|------|----|--------|
| Ruxolitinib | 1.01 | 0.13 | (0.01-2.67) |
| 0.61 | 0.21 | (0.02-1.97) |
| Colchicine | 0.13 | 0.61 | (0.01-25.98) |
| 0.64 | 0.50 | (0.09-2.75) |
| HCQLow | 0.13 | 0.28 | (0.09-0.80) |
| 0.60 | 0.47 | (0.05-4.03) |
| RDVs | 0.27 | 0.72 | (0.38-1.36) |
| 0.26 | 0.50 | (0.05-2.75) |
| Auxora | 0.28 | 0.28 | (0.01-11.37) |
| 0.56 | 0.28 | (0.01-6.08) |
| RDV | 0.27 | 0.72 | (0.38-1.36) |
| 0.50 | 0.27 | (0.01-6.08) |
| Plasma | 0.47 | 0.28 | (0.01-11.37) |
| 0.44 | 0.46 | (0.02-10.12) |
| LPVRTV | 0.47 | 0.28 | (0.01-11.37) |
| 0.52 | 0.46 | (0.02-10.12) |
| HCQAZT | 0.47 | 0.47 | (0.05-4.03) |
| 0.25 | 0.56 | (0.06-4.75) |
| Corticosteroid | 0.47 | 0.47 | (0.05-4.03) |
| 0.25 | 0.56 | (0.06-4.75) |
| HCQ | 0.13 | 0.48 | (0.23-0.23) |
| 0.28 | 0.66 | (0.45-1.15) |
| HCQlow | 0.13 | 0.48 | (0.23-0.23) |
| 0.28 | 0.66 | (0.45-1.15) |

Treatments are ordered in the rank of their chance of being the best option. Treatment estimates are provided as risk ratios (RR) with 95% CIs. Indirect comparisons between treatment should be read left to right, and their RR is in the cell in common between the column-defining treatment and the row-defining treatment. RRs > 1 favor the column-defining treatment for the network estimates; Bold value correspond to statistically significant value; Upper triangle were direct comparison, and lower triangle were indirect comparison; RDVs: remdesivir for 5-day; RDV: remdesivir more than 5-day; LPVRTV: lopinavir/ritonavir; Hydrocort: hydrocortisone; Dexanet: dexamethasone; Methylpred: methylprednisolone; HCQAZT: association hydroxychloroquine and azithromycin; HCQ: hydroxychloroquine; HCQlow: low dose of hydroxychloroquine (400 mg).