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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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Key words: SARS-CoV-2; COVID-19; network meta-analysis; treatment.

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.

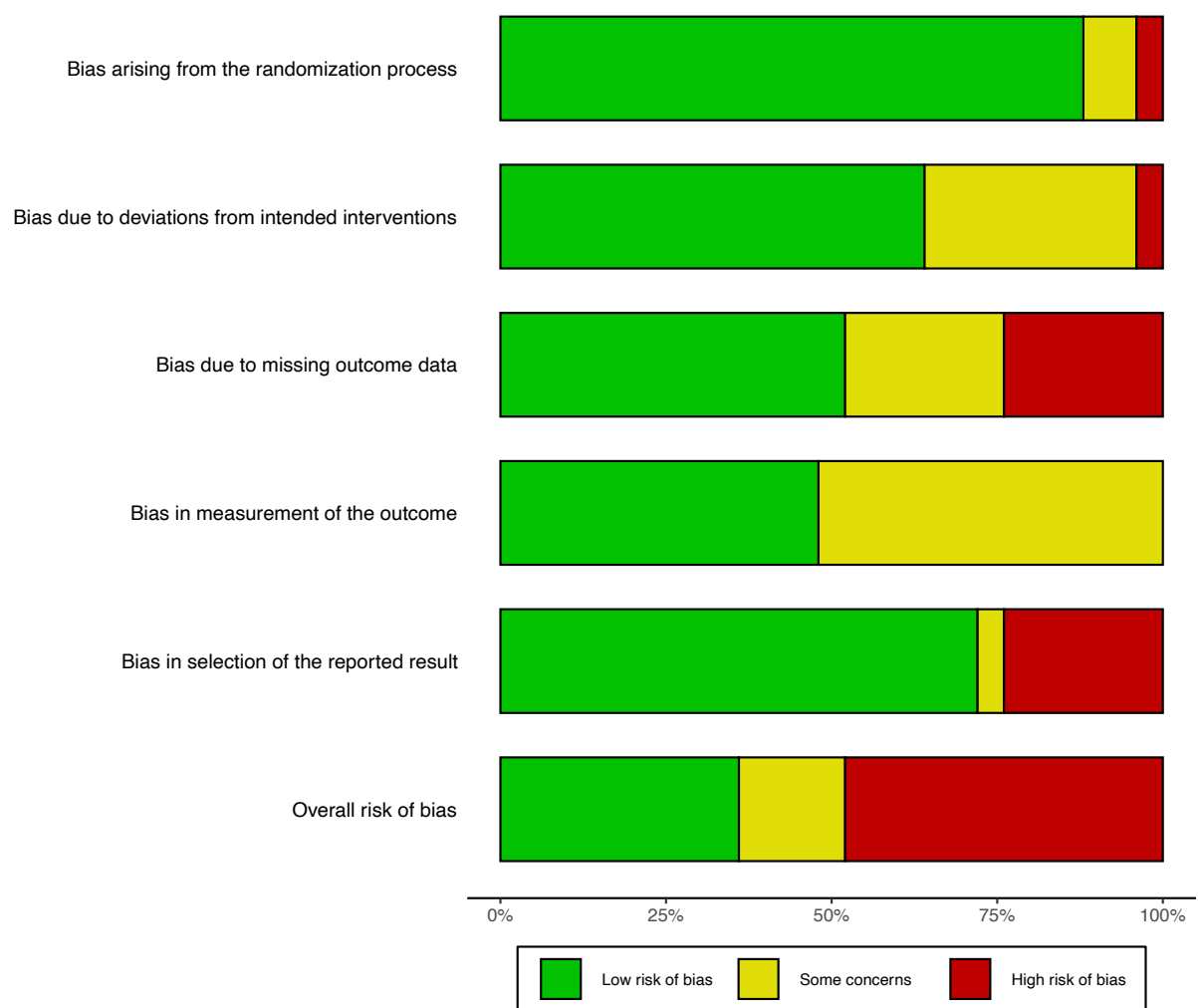


Figure 2. Summary of risk bias assessment for RCTs SARS-CoV-2 treatments comparisons.

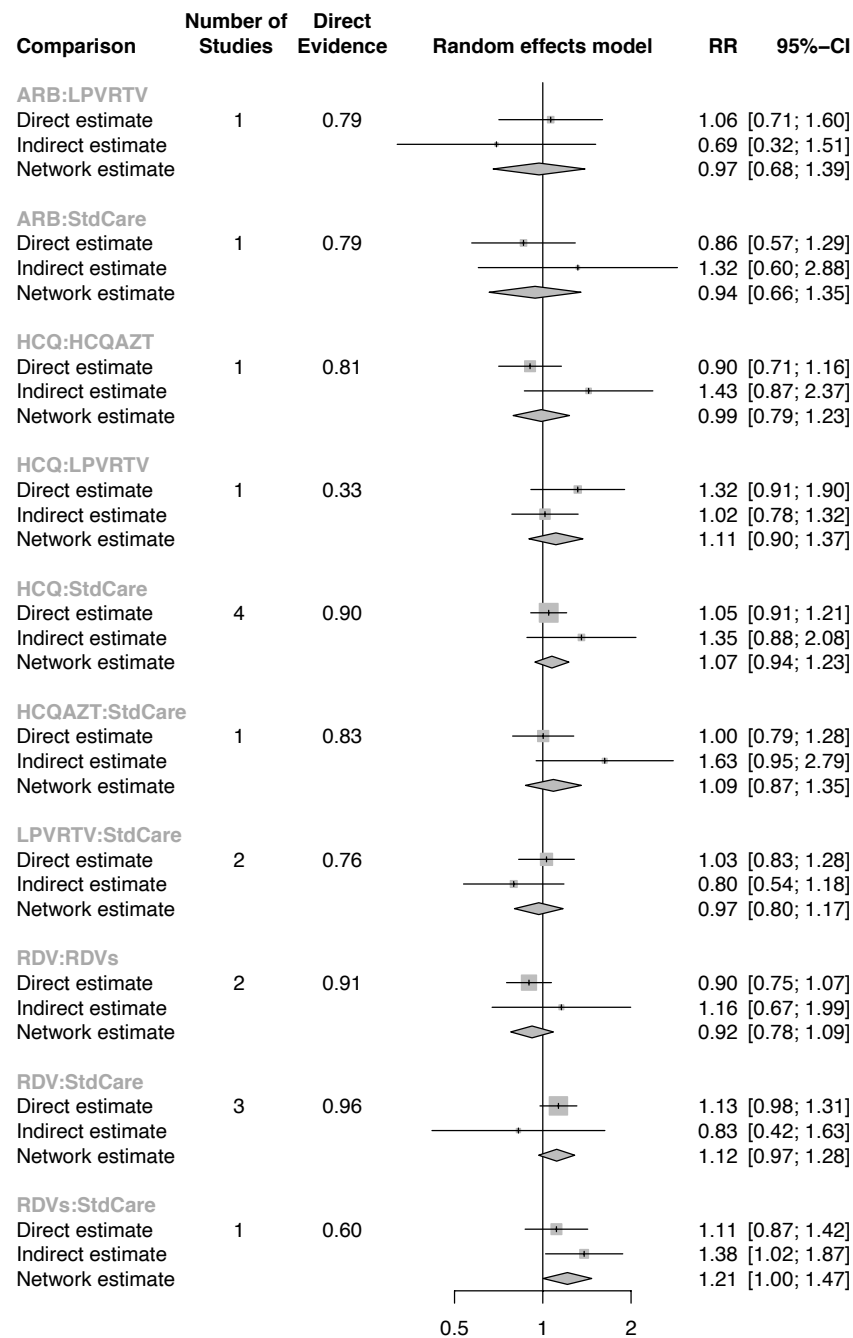
Study	Risk of bias domains					Overall
	D1	D2	D3	D4	D5	
Cao	+	+	X	-	+	X
Chen Zhaowei	+	-	+	-	+	-
Li Y	+	+	+	+	+	+
Chen Jun	-	-	-	-	-	-
Wang	+	+	+	-	X	X
Goldman	+	-	X	-	X	X
Borba	+	+	+	+	+	+
Chen Chang	+	-	-	-	X	X
Tang	+	+	X	+	+	X
Ling Li	+	+	X	+	+	X
Hung	+	-	X	-	+	X
Deftereos	+	+	-	-	X	X
Huang	+	-	-	-	+	-
Beigel	+	-	+	-	X	X
Cavalcanti	+	+	X	-	+	X
Yang Cao	+	+	+	+	+	+
Spinner	+	+	-	-	X	X
Miller	-	-	-	-	+	-
RECOVERY	+	+	+	+	+	+
CAPE COVID	+	+	+	+	+	+
CoDex	+	+	+	+	+	+
REMAP-CAP	+	+	+	+	+	+
DEXA-COVID 19	+	+	+	+	+	+
COVID STEROID	+	+	+	+	+	+
Steroids-SARI	X	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
X High
- Some concerns
+ Low

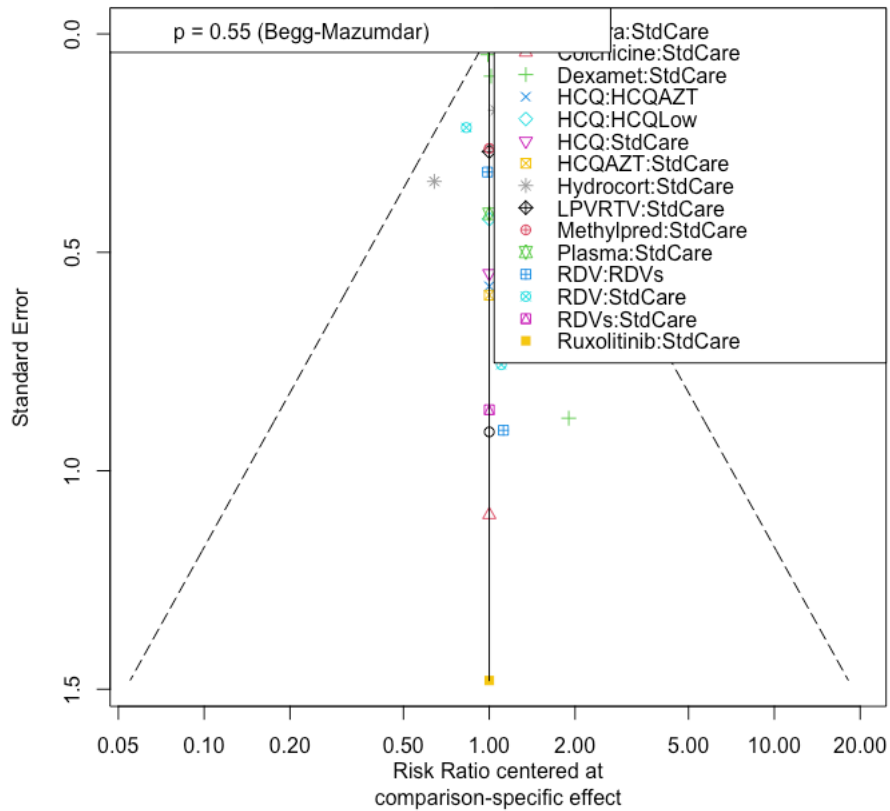
Number in parenthesis are references

Figure 3. Direct and indirect comparison for 28-day all-cause mortality.



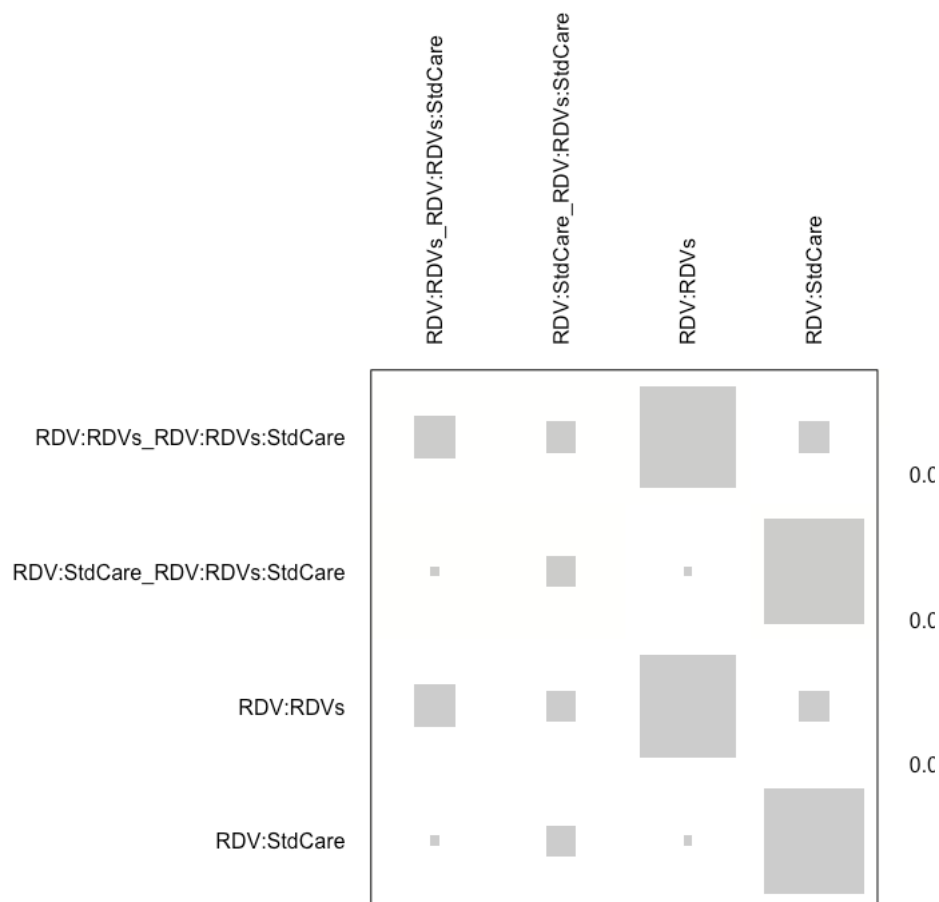
RDVs: remdesivir for 5-day; RDV: remdesivir more than 5-day; FPV: favipiravir; LPVRTV: lopinavir/ritonavir; ARB: arbidol (umafenovir). Plasma: convalescent plasma; StdCare: standard of care; HCQ: hydroxychloroquine; HCQAZT: association hydroxychloroquine and azithromycin; HCQlow: low dose of hydroxychloroquine (400 mg); HCQ: hydroxychloroquine.

Figure 4. Comparison-adjusted funnel plot for SARS-CoV-2 comparisons for 28-day all-cause mortality.



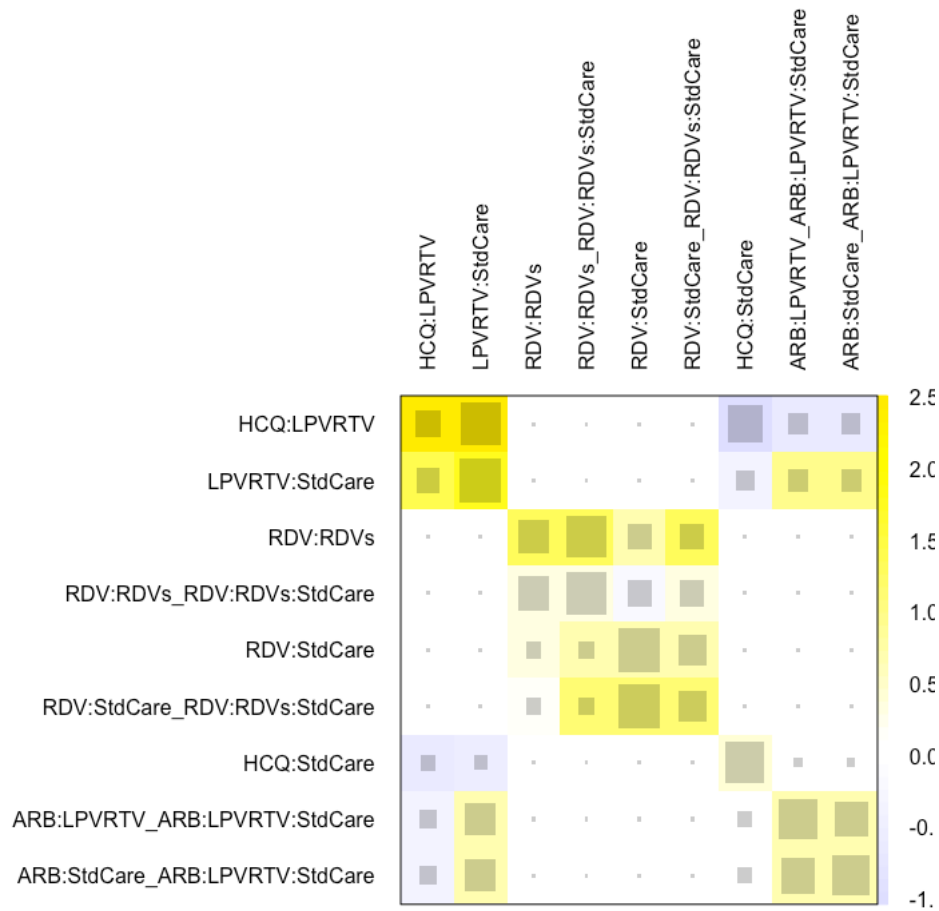
RDVs: remdesivir for 5-day; RDV: remdesivir more than 5-day; FPV: favipiravir; LPVRTV: lopinavir/ritonavir; ARB: arbidol (umafenovir). Plasma: convalescent plasma; StdCare: standard of care; HCQ: hydroxychloroquine; HCQAZT: association hydroxychloroquine and azithromycin; HCQlow: low dose of hydroxychloroquine (400 mg); HCQ: hydroxychloroquine.

Figure 5. Heatmap to identify points of single design heterogeneity for 28-day all-cause mortality.



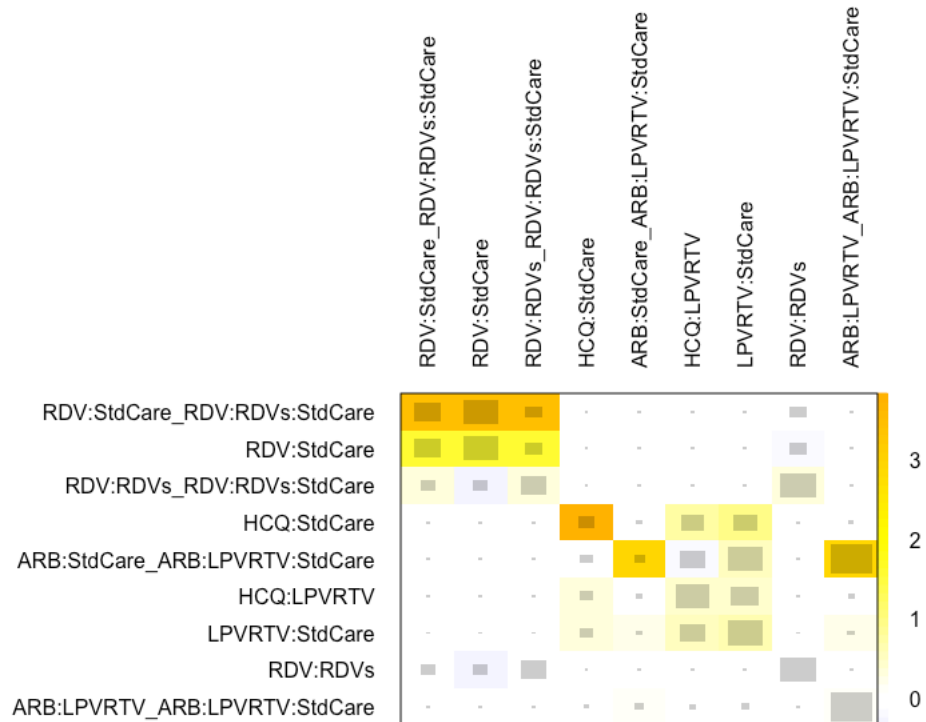
RDVs: remdesivir for 5-day; RDV: remdesivir more than 5-day; FPV: favipiravir; LPVRTV: lopinavir/ritonavir; ARB: arbidol (umafenovir). Plasma: convalescent plasma; StdCare: standard of care; HCQ: hydroxychloroquine.

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.



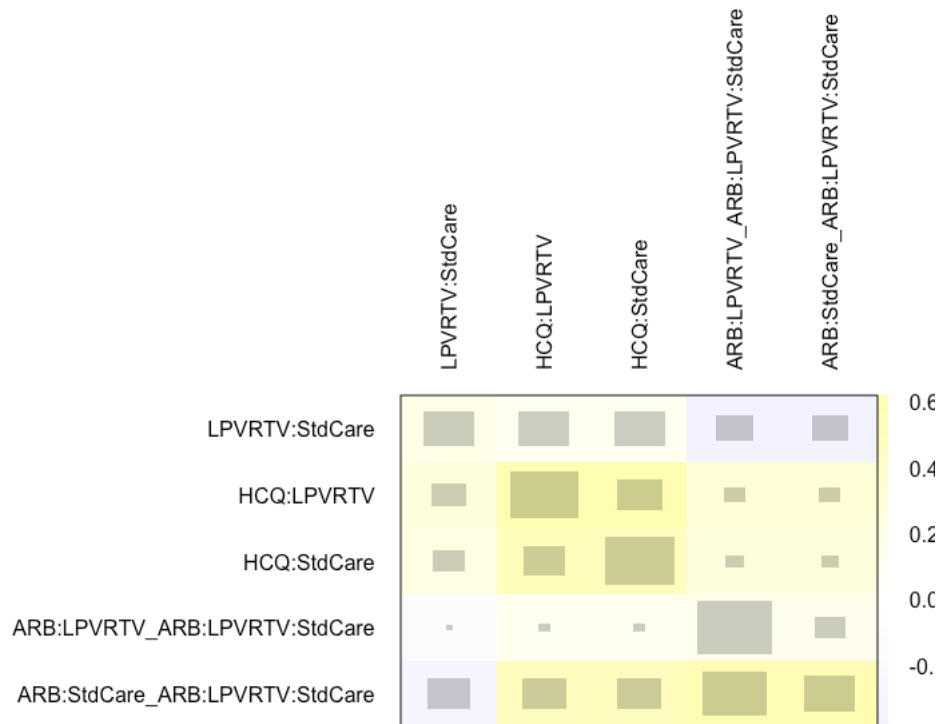
RDVs: remdesivir for 5-day; RDV: remdesivir more than 5-day; FPV: favipiravir; LPVRTV: lopinavir/ritonavir; ARB: arbidol (umafenovir). Plasma: convalescent plasma; StdCare: standard of care; HCQ: hydroxychloroquine.

Figure 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; LPVRTVRBV: 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; 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.

Table 1. League table of pairwise comparisons in network meta-analysis for 28-day all-cause mortality.

Ruxolitinib	0.15 (0.01-2.73)
0.66 (0.02-24.59)																			0.23 (0.03-1.97)
Colchicine	0.50 (0.09-2.72)
0.29 (0.01-5.76)	0.44 (0.05-4.26)					0.74 (0.41-1.34)													0.38 (0.17-0.89)
RDVs	
0.33 (0.01-8.05)	0.49 (0.04-6.37)	1.11 (0.24-5.11)																	
HCQLow	
0.28 (0.01-8.57)	0.43 (0.03-7.10)	0.97 (0.14-6.54)	0.87 (0.09-8.28)																0.53 (0.09-3.17)
Auxora	
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)															0.69 (0.48-0.99)
RDV	
0.23 (0.01-4.67)	0.35 (0.03-3.50)	0.78 (0.27-2.25)	0.70 (0.14-3.46)	0.81 (0.11-5.78)	1.05 (0.43-2.57)														0.65 (0.29-1.48)
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 (0.11-4.47)	0.90 (0.47-1.72)	0.85 (0.32-2.26)													0.77 (0.45-1.32)
LPVRTV	
0.18 (0.01-3.37)	0.28 (0.03-2.45)	0.62 (0.30-1.30)	0.56 (0.14-2.28)	0.64 (0.10-3.95)	0.84 (0.52-1.34)	0.79 (0.33-1.90)	0.93 (0.50-1.74)												0.82 (0.60-.12)
Hydrocort	
0.17 (0.01-3.94)	0.26 (0.02-3.05)	0.59 (0.15-2.28)	0.53 (0.13-2.17)	0.61 (0.07-5.17)	0.79 (0.23-2.71)	0.75 (0.18-3.14)	0.88 (0.24-3.22)	0.94 (0.28-3.19)											0.73 (0.23-2.27)
HCQAZT	
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 (0.10-3.53)	0.76 (0.52-1.12)	0.72 (0.32-1.65)	0.85 (0.49-1.48)	0.91 (0.65-1.27)	0.97 (0.30-3.16)										0.90 (0.80-1.02)
Dexamet	
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 (0.38-1.70)	0.86 (0.47-1.58)	0.91 (0.25-3.31)	0.94 (0.55-1.62)									0.96 (0.57-1.62)
Methylpred	
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 (0.05-3.57)	0.58 (0.18-1.80)	0.55 (0.14-2.11)	0.64 (0.19-2.14)	0.69 (0.22-2.11)	0.73 (0.23-2.27)	0.75 (0.25-2.23)	0.80 (0.24-2.66)								1.20 (0.41-.53)
HCQ	
0.15 (0.01-2.73)	0.23 (0.03-1.97)	0.51 (0.26-1.00)	0.46 (0.12-1.81)	0.53 (0.09-3.17)	0.69 (0.48-0.99)	0.65 (0.29-1.48)	0.77 (0.45-1.32)	0.82 (0.60-1.12)	0.87 (0.27-2.83)	0.90 (0.80-1.02)	0.96 (0.57-1.62)	1.20 (0.41-3.53)							StdCare

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. Indirect comparisons between treatment should be red 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; Dexamet: dexamethasone; Methylpred: methylprednisolone.

Table 2. League table of pairwise comparisons in network meta-analysis for clinical improvement.

Ruxolitinib	1.40 (0.74-2.66)	.	.	.	
1.15 (0.59-2.25)	RDV5	1.11 (0.87-1.42)	.	.	.	
1.16 (0.53-2.55)	1.01 (0.62-1.65)	Plasma	1.20 (0.76-1.90)	.	.	.	
1.23 (0.62-2.42)	1.06 (0.79-1.43)	1.05 (0.63-1.75)	Colchicine	1.14 (0.91-1.43)	.	.	.	
1.26 (0.65-2.42)	1.09 (0.92-1.29)	1.08 (0.67-1.74)	1.02 (0.78-1.34)	RDV	1.13 (0.98-1.31)	.	.	.	
1.29 (0.65-2.54)	1.12 (0.84-1.49)	1.11 (0.67-1.83)	1.05 (0.77-1.44)	1.03 (0.79-1.33)	HCQAZT	1.00 (0.79-1.28)	.	.	.	
1.30 (0.68-2.51)	1.13 (0.89-1.43)	1.12 (0.70-1.80)	1.06 (0.82-1.39)	1.04 (0.85-1.26)	1.01 (0.81-1.26)	HCQ	1.05 (0.91-1.21)	1.32 (0.91-1.90)	.	.	
1.30 (0.59-2.87)	1.13 (0.68-1.87)	1.12 (0.58-2.15)	1.06 (0.63-1.79)	1.03 (0.63-1.69)	1.01 (0.60-1.69)	1.00 (0.61-1.62)	FPV	1.15 (0.85-1.55)	
1.44 (0.59-3.50)	1.25 (0.66-2.37)	1.24 (0.58-2.66)	1.18 (0.61-2.26)	1.15 (0.61-2.15)	1.12 (0.58-2.15)	1.11 (0.59-2.07)	1.11 (0.51-2.40)	Auxora	0.97 (0.53-1.79)	.	.	.
1.40 (0.74-2.66)	1.21 (1.00-1.47)	1.20 (0.76-1.90)	1.14 (0.91-1.43)	1.12 (0.97-1.28)	1.09 (0.87-1.35)	1.07 (0.94-1.23)	1.08 (0.67-1.72)	0.97 (0.53-1.79)	StdCare	0.97 (0.78-1.21)	1.16 (0.77-1.75)	1.07 (0.87-1.31)	
1.44 (0.74-2.82)	1.25 (0.96-1.64)	1.24 (0.76-2.03)	1.18 (0.87-1.59)	1.15 (0.91-1.46)	1.12 (0.84-1.49)	1.11 (0.90-1.37)	1.11 (0.70-1.78)	1.00 (0.53-1.90)	1.03 (0.85-1.25)	LPVRTV	1.03 (0.85-1.25)	0.94 (0.63-1.41)	.	
1.49 (0.71-3.10)	1.29 (0.86-1.94)	1.28 (0.72-2.28)	1.21 (0.79-1.86)	1.19 (0.80-1.75)	1.15 (0.76-1.76)	1.14 (0.78-1.67)	1.15 (0.85-1.55)	1.03 (0.51-2.10)	1.06 (0.74-1.52)	1.03 (0.72-1.48)	ARB	1.06 (0.74-1.48)	1.00 (0.66-1.52)	.	
1.49 (0.76-2.93)	1.29 (0.98-1.71)	1.28 (0.78-2.11)	1.22 (0.89-1.66)	1.19 (0.92-1.53)	1.16 (0.86-1.57)	1.14 (0.89-1.47)	1.15 (0.69-1.92)	1.03 (0.54-1.98)	1.07 (0.87-1.31)	1.03 (0.78-1.37)	1.00 (0.66-1.52)	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 red 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; RDV5: 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).

Plasma	.	2.68 (1.71-4.20)	.	.	.
2.49 (1.53-4.05)	ARB	1.20 (0.90-1.59)	.	1.07 (0.90-1.27)	.
2.68 (1.71-4.20)	1.08 (0.89-1.31)	StdCare	1.06 (0.91-1.24)	0.94 (0.79-1.13)	1.07 (0.88-1.30)
2.70 (1.69-4.30)	1.08 (0.89-1.32)	1.01 (0.88-1.14)	HCQ	1.09 (0.92-1.28)	.
2.74 (1.72-4.39)	1.10 (0.94-1.30)	1.02 (0.89-1.18)	1.02 (0.89-1.16)	LPVRTV	.
2.87 (1.76-4.68)	1.15 (0.88-1.52)	1.07 (0.88-1.30)	1.06 (0.84-1.35)	1.05 (0.82-1.33)	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 red 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	0.46 (0.18- 1.14)
0.89 (0.23- 3.39)	ARB	.	0.76 (0.46- 1.25)	.	.	5.42 (0.31- 93.86)	0.43 (0.17- 1.08)
0.68 (0.23- 2.01)	0.76 (0.25- 2.30)	HCQLow	0.50 (0.30- 0.83)
0.68 (0.16- 2.81)	0.76 (0.46- 1.25)	1.00 (0.30- 3.37)	FPV
0.47 (0.18- 1.21)	0.53 (0.19- 1.44)	0.69 (0.36- 1.33)	0.70 (0.23- 2.15)	RDVs	.	1.06 (0.75- 1.49)	.	0.91 (0.73- 1.14)
0.48 (0.17- 1.33)	0.53 (0.18- 1.58)	0.70 (0.33- 1.51)	0.71 (0.21- 2.33)	1.01 (0.59- 1.74)	Hydrocort	0.96 (0.60- 1.54)
0.46 (0.18- 1.14)	0.51 (0.19- 1.36)	0.68 (0.37- 1.22)	0.68 (0.23- 2.03)	0.97 (0.75- 1.26)	0.96 (0.60- 1.54)	1.02 (0.61- 1.71)	0.97 (0.80- 1.18)	.	.	0.89 (0.57- 1.39)	1.00 (0.67- 1.49)	0.68 (0.48- 0.96)	0.71 (0.48- 1.05)	0.20 (0.01- 4.20)	0.38 (0.23- 0.65)
0.47 (0.16- 1.33)	0.52 (0.17- 1.57)	0.69 (0.31- 1.51)	0.69 (0.20- 2.32)	0.99 (0.56- 1.76)	0.98 (0.48- 1.97)	1.02 (0.61- 1.71)	.	.	Auxora
0.44 (0.18- 1.13)	0.50 (0.18- 1.35)	0.66 (0.35- 1.23)	0.66 (0.22- 2.00)	0.95 (0.76- 1.17)	0.93 (0.56- 1.56)	0.97 (0.80- 1.17)	0.96 (0.55- 1.66)
0.42 (0.14- 1.23)	0.47 (0.17- 1.33)	0.62 (0.29- 1.35)	0.62 (0.20- 1.97)	0.89 (0.48- 1.67)	0.88 (0.42- 1.86)	0.92 (0.52- 1.63)	0.90 (0.42- 1.95)	0.95 (0.52- 1.73)	RDV
0.41 (0.15- 1.13)	0.46 (0.16- 1.34)	0.60 (0.29- 1.27)	0.60 (0.18- 1.98)	0.87 (0.52- 1.45)	0.86 (0.45- 1.64)	0.89 (0.57- 1.39)	0.88 (0.44- 1.74)	0.92 (0.57- 1.49)	LPVRTVRBV	0.97 (0.47- 2.00)
0.41 (0.16- 1.08)	0.46 (0.18- 1.16)	0.61 (0.33- 1.12)	0.61 (0.21- 1.74)	0.87 (0.58- 1.32)	0.86 (0.49- 1.53)	0.90 (0.65- 1.24)	0.88 (0.48- 1.62)	0.92 (0.64- 1.34)	.	.	0.98 (0.61- 1.57)	1.01 (0.58- 1.74)
													0.93 (0.60- 1.42)	LPVRTV

0.34 (0.13- 0.88)	0.38 (0.14- 1.00)	0.50 (0.30- 0.83)	0.50 (0.17- 1.50)	0.71 (0.48- 1.06)	0.70 (0.40- 1.23)	0.73 (0.55- 0.99)	0.72 (0.40- 1.31)	0.76 (0.53- 1.07)	0.80 (0.45- 1.42)	0.82 (0.48- 1.40)	0.82 (0.59- 1.14)	0.89 (0.61- 1.29)	HCQ	.	.
0.31 (0.12- 0.83)	0.35 (0.13- 0.96)	0.46 (0.24- 0.86)	0.46 (0.15- 1.43)	0.66 (0.42- 1.03)	0.65 (0.36- 1.18)	0.68 (0.47- 0.97)	0.67 (0.35- 1.25)	0.70 (0.46- 1.05)	0.74 (0.39- 1.40)	0.76 (0.43- 1.35)	0.75 (0.49- 1.17)	0.92 (0.65- 1.32)	HCQAZT	.	.
0.09 (0.00- 2.20)	0.10 (0.00- 2.51)	0.14 (0.01- 3.00)	0.14 (0.01- 3.45)	0.20 (0.01- 4.13)	0.20 (0.01- 4.18)	0.20 (0.01- 4.20)	0.20 (0.01- 4.31)	0.21 (0.01- 4.35)	0.22 (0.01- 4.82)	0.23 (0.01- 4.86)	0.23 (0.01- 4.75)	0.28 (0.01- 5.80)	0.30 (0.01- 6.33)	Plasma	.
0.18 (0.06- 0.50)	0.20 (0.06- 0.60)	0.26 (0.12- 0.57)	0.26 (0.08- 0.88)	0.37 (0.21- 0.67)	0.37 (0.18- 0.75)	0.38 (0.23- 0.65)	0.38 (0.18- 0.79)	0.39 (0.23- 0.69)	0.42 (0.19- 0.91)	0.43 (0.22- 0.85)	0.43 (0.23- 0.79)	0.52 (0.29- 0.95)	0.57 (0.30- 1.07)	1.88 (0.09- 40.53)	Colchicine

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 red 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; 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; Hydrocort: hydrocortisone; Dexamet: dexamethasone; Methylpred: methylprednisolone.

Table 5. League table of pairwise comparisons in network meta-analysis for any severe adverse event.

LPVRTVRBV	.	.	.	0.16 (0.01-3.84)
0.82 (0.01-60.89)	Ruxolitinib	0.12 (0.01-2.03)	.	.
0.20 (0.01-5.11)	0.24 (0.01-4.35)	RDVs	.	.	0.64 (0.47-0.87)	.	.	.	0.50 (0.23-1.09)	.	.
0.19 (0.01-5.17)	0.23 (0.01-4.42)	0.96 (0.45-2.05)	Dexamet	0.50 (0.25-0.98)	.	.
0.16 (0.01-3.84)	0.19 (0.01-3.53)	0.80 (0.43-1.45)	0.83 (0.36-1.91)	LPVRTV	0.60 (0.37-0.98)	.	.
0.13 (0.01-3.17)	0.15 (0.01-2.69)	0.63 (0.46-0.85)	0.65 (0.32-1.32)	0.79 (0.46-1.34)	RDV	.	.	.	0.75 (0.62-0.91)	.	.
0.10 (0.00-2.50)	0.12 (0.01-2.12)	0.50 (0.35-0.71)	0.52 (0.26-1.02)	0.63 (0.38-1.03)	0.79 (0.64-0.97)	Methylpred	.	.	0.96 (0.88-1.04)	.	.
0.08 (0.00-2.74)	0.09 (0.00-2.42)	0.38 (0.08-1.87)	0.40 (0.07-2.16)	0.48 (0.10-2.45)	0.61 (0.13-2.90)	0.77 (0.16-3.63)	HCQAZT	.	1.05 (0.21-5.13)	1.02 (0.21-4.99)	.
0.10 (0.00-2.39)	0.12 (0.01-2.03)	0.48 (0.34-0.67)	0.50 (0.25-0.98)	0.60 (0.37-0.98)	0.76 (0.63-0.92)	0.96 (0.88-1.04)	1.24 (0.26-5.83)	StdCare	0.69 (0.17-2.82)	0.50 (0.10-2.47)	.
0.07 (0.00-2.22)	0.08 (0.00-1.95)	0.33 (0.08-1.40)	0.34 (0.07-1.63)	0.41 (0.09-1.84)	0.52 (0.13-2.17)	0.66 (0.16-2.71)	0.86 (0.18-4.02)	0.69 (0.17-2.82)	HCQ	.	.
0.05 (0.00-1.75)	0.06 (0.00-1.54)	0.24 (0.05-1.22)	0.25 (0.04-1.41)	0.30 (0.06-1.60)	0.38 (0.08-1.90)	0.48 (0.10-2.38)	0.62 (0.07-5.74)	0.50 (0.10-2.47)	0.73 (0.09-6.09)	Hydrocort	.

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 red 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; LPVRTVRBV: 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.

Ruxolitinib	0.13 (0.01-2.67)
0.61 (0.01-25.98)	Colchicine	0.21 (0.02-1.97)
0.39 (0.01-11.61)	0.64 (0.04-9.61)	HCQLow	0.28 (0.09-0.80)	.
0.27 (0.01-6.08)	0.45 (0.04-4.63)	0.70 (0.13-3.81)	RDVs	0.72 (0.38-1.36)	0.50 (0.09-2.75)
0.28 (0.01-11.37)	0.46 (0.02-10.12)	0.71 (0.05-10.07)	1.02 (0.11-9.90)	Auxora	0.47 (0.05-4.03)
0.22 (0.01-5.29)	0.36 (0.03-4.13)	0.56 (0.09-3.51)	0.81 (0.24-2.74)	0.79 (0.07-8.48)	Plasma	0.59 (0.22-1.60)
0.20 (0.01-4.16)	0.32 (0.03-3.10)	0.51 (0.10-2.47)	0.73 (0.39-1.36)	0.71 (0.08-6.34)	0.90 (0.31-2.61)	RDV	0.66 (0.45-0.96)
0.18 (0.01-4.03)	0.30 (0.03-3.06)	0.47 (0.09-2.50)	0.67 (0.25-1.79)	0.65 (0.07-6.27)	0.83 (0.25-2.75)	0.92 (0.42-2.00)	LPVRTV	0.71 (0.36-1.40)
0.15 (0.01-3.86)	0.25 (0.02-3.08)	0.38 (0.08-1.86)	0.55 (0.14-2.22)	0.54 (0.05-6.34)	0.68 (0.14-3.23)	0.76 (0.21-2.67)	0.82 (0.21-3.25)	HCQAZT	0.72 (0.23-2.31)
0.15 (0.01-3.14)	0.25 (0.03-2.33)	0.39 (0.08-1.83)	0.56 (0.27-1.16)	0.55 (0.06-4.75)	0.69 (0.26-1.89)	0.77 (0.52-1.15)	0.84 (0.42-1.66)	1.02 (0.31-3.41)	Corticosteroid	0.85 (0.76-0.95)
0.11 (0.00-2.69)	0.18 (0.01-2.12)	0.28 (0.09-0.80)	0.40 (0.11-1.48)	0.39 (0.03-4.37)	0.49 (0.11-2.17)	0.55 (0.17-1.76)	0.59 (0.16-2.16)	0.72 (0.23-2.31)	0.71 (0.23-2.15)	HCQ	1.20 (0.40-3.64)
0.13 (0.01-2.67)	0.21 (0.02-1.97)	0.33 (0.07-1.55)	0.48 (0.23-0.98)	0.47 (0.05-4.03)	0.59 (0.22-1.60)	0.66 (0.45-0.96)	0.71 (0.36-1.40)	0.87 (0.26-2.89)	0.85 (0.76-0.95)	1.20 (0.40-3.64)	StdCare

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; Dexamet: dexamethasone; Methylpred: methylprednisolone; HCQAZT: association hydroxychloroquine and azithromycin; HCQ: hydroxychloroquine; HCQlow: low dose of hydroxychloroquine (400 mg).