COVID-19 as cause of viral sepsis: A Systematic Review and Meta-Analysis.

"Online Supplement"

Eleni Karakike, Evangelos J. Giamarellos-Bourboulis, Miltiades Kyprianou, Carolin Fleischmann-Struzek, Mathias W. Pletz, Mihai G. Netea, Konrad Reinhart, Evdoxia Kyriazopoulou

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Search strategy

PubMed (Date Run: 29/03/2021)		
Step	**Search strategy**	**Found**
#1	[(Covid AND sepsis) OR (Covid AND septic*) OR (Covid and "organ failure") OR (Covid and "organ dysfunction") OR (Covid AND "organ support") OR (Covid AND SOFA) OR (Covid and "intensive care") OR (Covid AND "organ replacement") OR (Covid AND "host response") OR (Covid AND "immune response") OR (Covid AND "renal failure") OR (Covid AND "renal dysfunction") OR (Covid AND „pulmonary failure") OR (Covid AND „pulmonary dysfunction") OR (Covid AND „respiratory failure") OR (Covid AND „respiratory dysfunction") OR (Covid AND „liver failure") OR (Covid AND „liver dysfunction") OR (Covid AND „cardiac failure") OR (Covid AND „cardiac dysfunction") OR (Covid AND „shock") OR (Covid AND „neurologic dysfunction") OR (Covid AND „neurological dysfunction") OR (Covid AND thrombocytopenia) OR (Covid AND acidosis)] OR [(SARS-CoV-2 AND sepsis) OR (SARS-CoV-2 AND septic*) OR (SARS-CoV-2 AND "organ failure") OR (Covid and "organ dysfunction") OR (SARS-CoV-2 AND "organ support") OR (SARS-CoV-2 AND SOFA) OR (SARS-CoV-2 AND "intensive care") OR (SARS-CoV-2 AND "organ replacement") OR (SARS-CoV-2 AND "host response") OR (SARS-CoV-2 AND "immune response") OR (SARS-CoV-2 AND "renal failure") OR (SARS-CoV-2 AND "renal dysfunction") OR (SARS-CoV-2 AND „pulmonary failure") OR (SARS-CoV-2 AND „pulmonary dysfunction") OR (SARS-CoV-2 AND „respiratory failure") OR (SARS-CoV-2 AND „respiratory dysfunction") OR (SARS-CoV-2 AND „liver failure") OR (SARS-CoV-2 AND „liver dysfunction") OR (SARS-CoV-2 AND „cardiac failure") OR (SARS-CoV-2 AND „cardiac dysfunction") OR (SARS-CoV-2 AND „shock") OR (SARS-CoV-2 AND „neurologic dysfunction") OR (SARS-CoV-2 AND „neurological dysfunction") OR (SARS-CoV-2 AND thrombocytopenia) OR (SARS-CoV-2 AND acidosis)] Filters: Full text, Clinical Study, Clinical Trial, Clinical Trial, Phase I, Clinical Trial, Phase II, Clinical Trial, Phase III, Clinical Trial, Phase IV, Comparative Study, Controlled Clinical Trial, Multicenter Study, Observational Study, Pragmatic Clinical Trial, Randomized Controlled Trial, Humans, English	1703

Cochrane Central Register of Clinical Trials (Date Run: 29/03/21)		
ID	**Search strategy**	**Found**
#1	(COVID-19):ti,ab,kw OR ("SARS Co-V"):ti,ab,kw	4287
#2	("sepsis"):ti,ab,kw OR ("organ damage"):ti,ab,kw OR ("organ failure"):ti,ab,kw OR ("sofa"):ti,ab,kw OR ("intensive care"):ti,ab,kw	35319
#3	("immune response"):ti,ab,kw OR ("host reaction"):ti,ab,kw	9291
#4	("renal failure"):ti,ab,kw OR ("renal dysfunction"):ti,ab,kw	8807
#5	("respiratory failure"):ti,ab,kw OR ("respiratory distress"):ti,ab,kw	10780
#6	("liver damage"):ti,ab,kw OR (liver replacement):ti,ab,kw	1331
#7	("cardiac failure"):ti,ab,kw OR ("cardiovascular collapse"):ti,ab,kw	968
#8	("shock"):ti,ab,kw OR ("acidosis"):ti,ab,kw	13122
#9	("neurological impairment"):ti,ab,kw OR ("encephalopathy"):ti,ab,kw	3663
#10	("thrombocytopenia"):ti,ab,kw OR ("thrombopenia"):ti,ab,kw	9810
#11	#2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10	81622
#12	#1 AND #11	1245

Google Scholar (Date Run: 29/03/21)		
Step	**Search strategy**	**Found**
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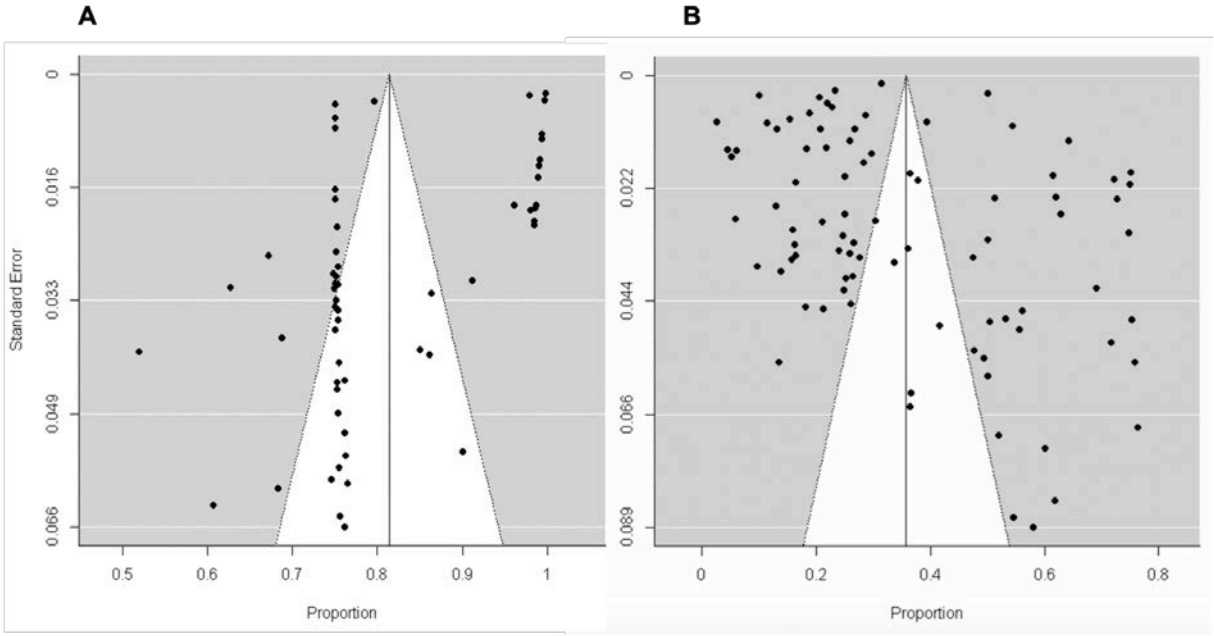
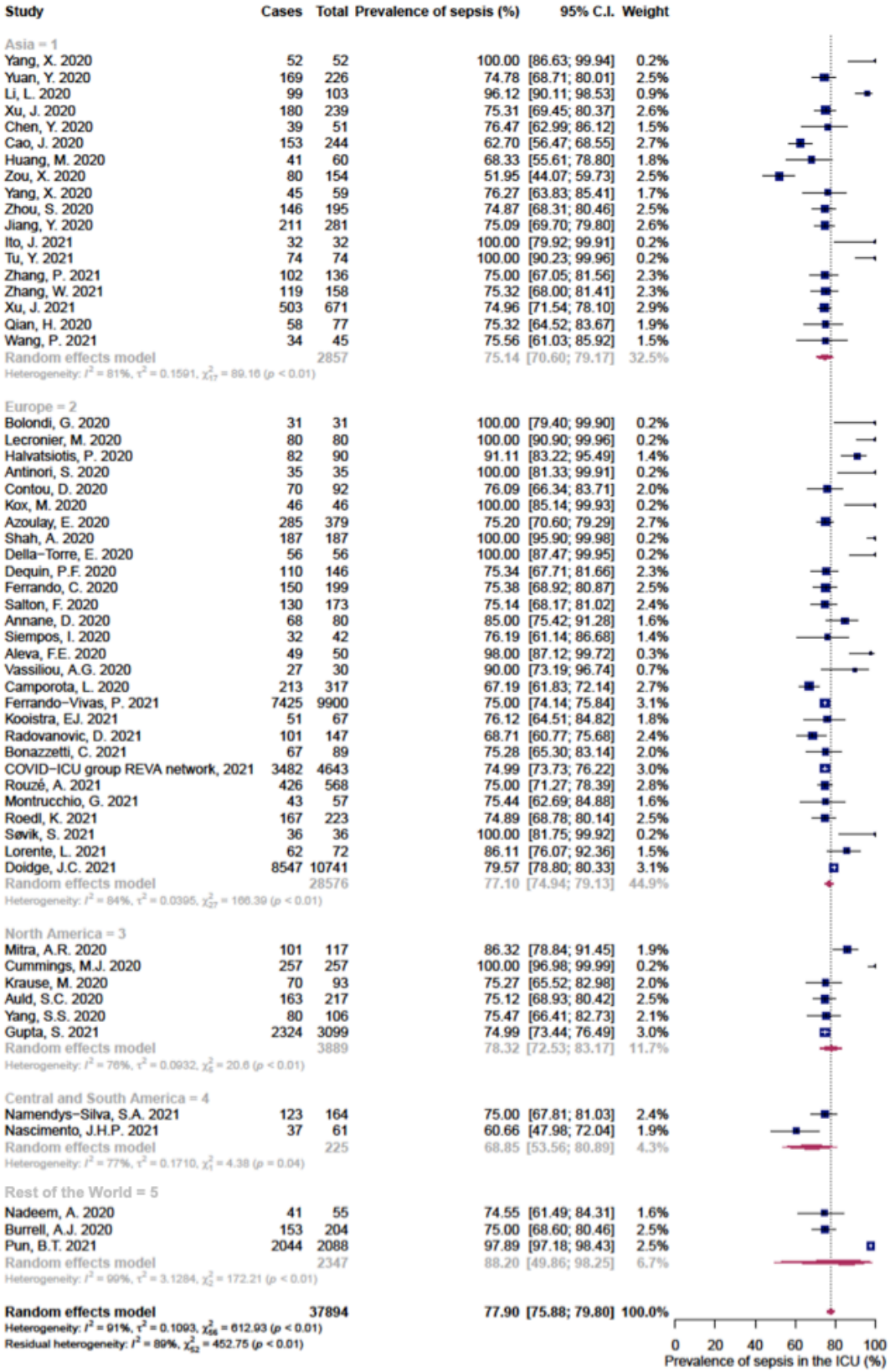
Supplementary Figures.

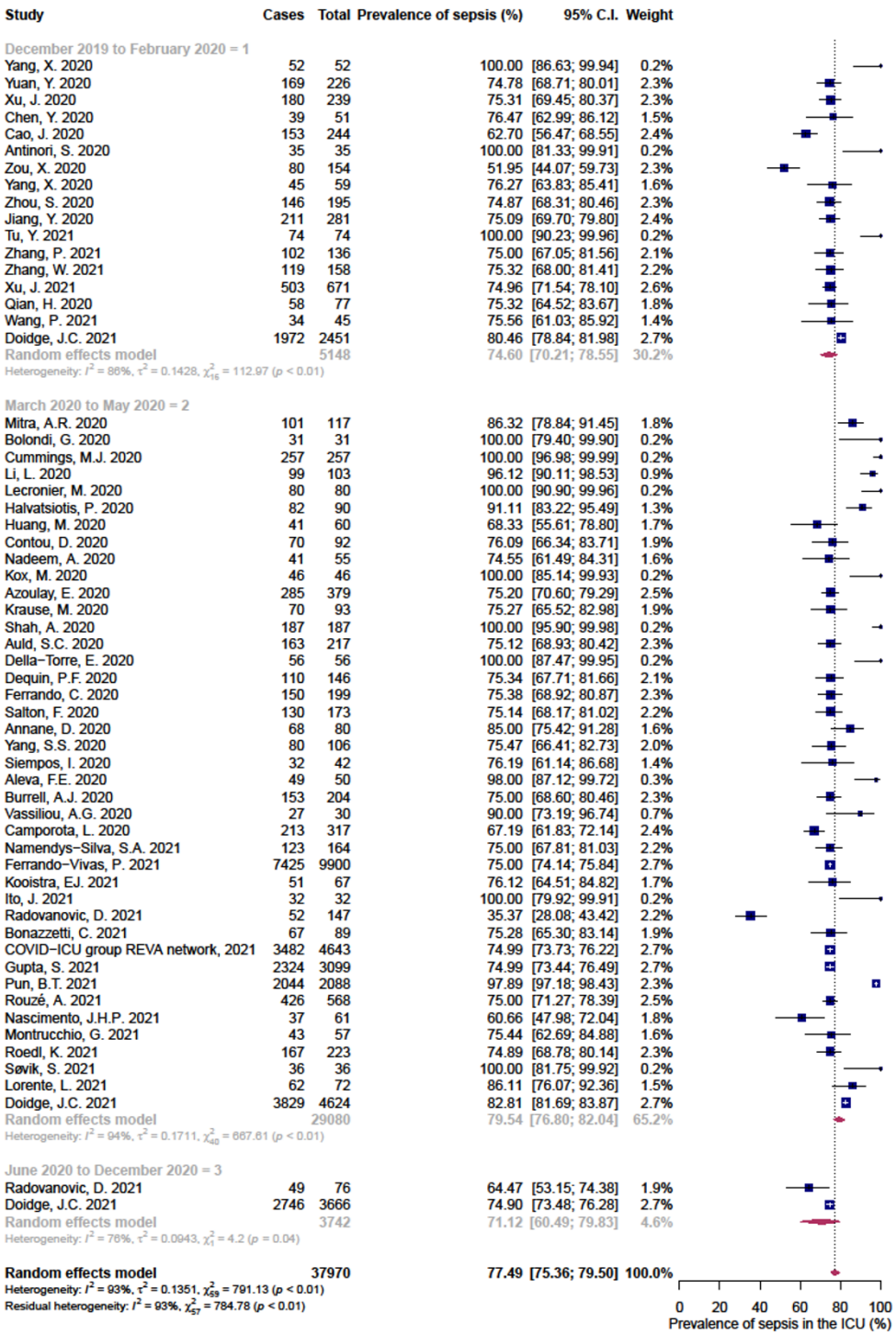
Supplementary Figure 1. Funnel plots of publication bias for studies estimating COVID-19 related sepsis prevalence A) in the Intensive Care Unit and B) in the general ward. Respective test for funnel plot asymmetry was A) t = -2.616, df = 55, p 0 .012 and B) t = 0.897, df = 84, p = 0.372.



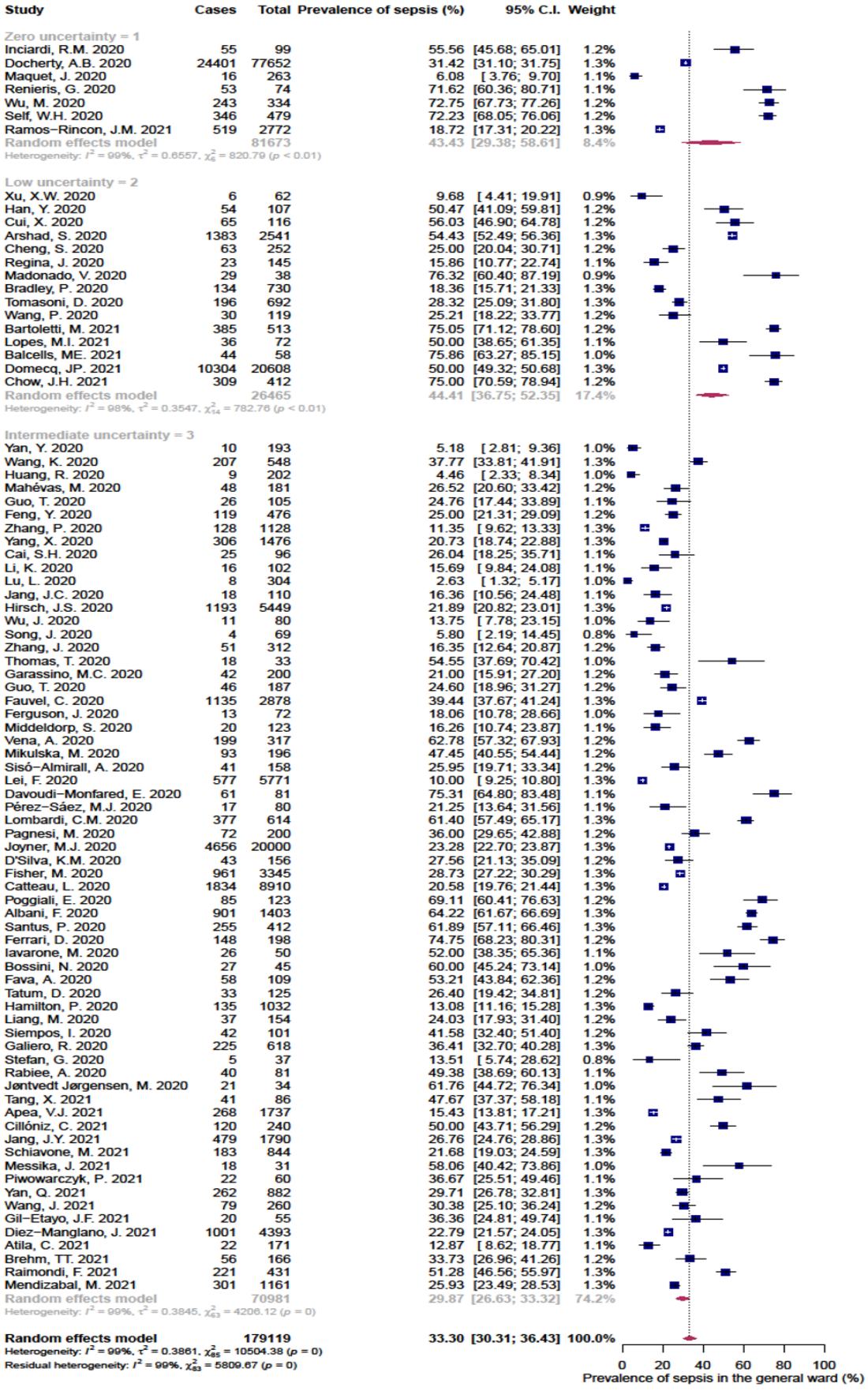
Supplementary Figure 2. Subgroup analysis for the primary endpoint among adult patients with COVID-19 in the Intensive Care Unit, according to geographical location. Rest of the world included 1 study from Australia, and 2 multi-national studies. Abbreviation: CI, confidence interval. P-value for comparisons between groups= 0.543



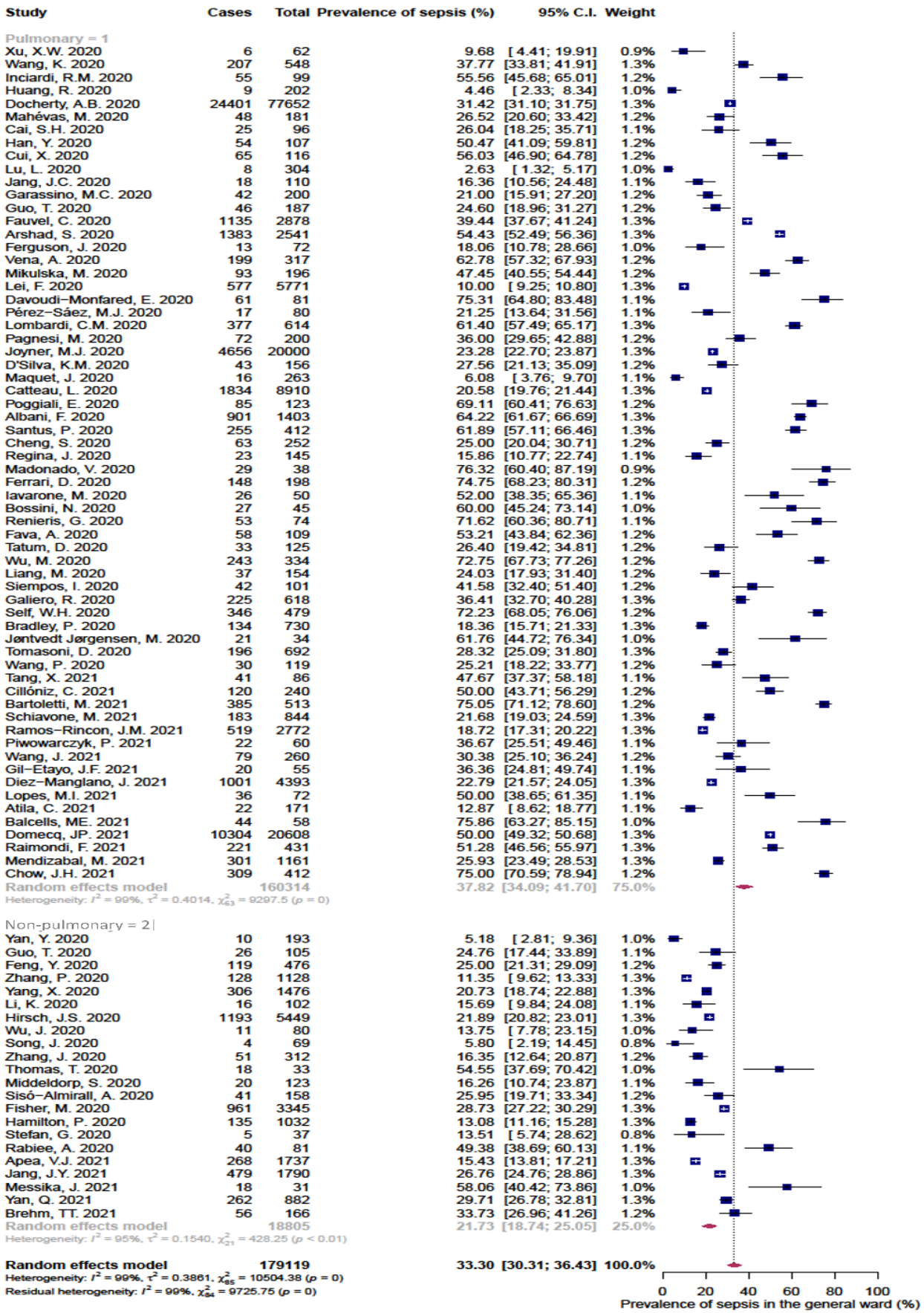
Supplementary Figure 3. Subgroup analysis for the primary endpoint among adult patients with COVID-19 in the Intensive Care Unit, according to chronological period of enrollment. Abbreviation: CI, confidence interval. P-value for comparisons between groups= 0.047



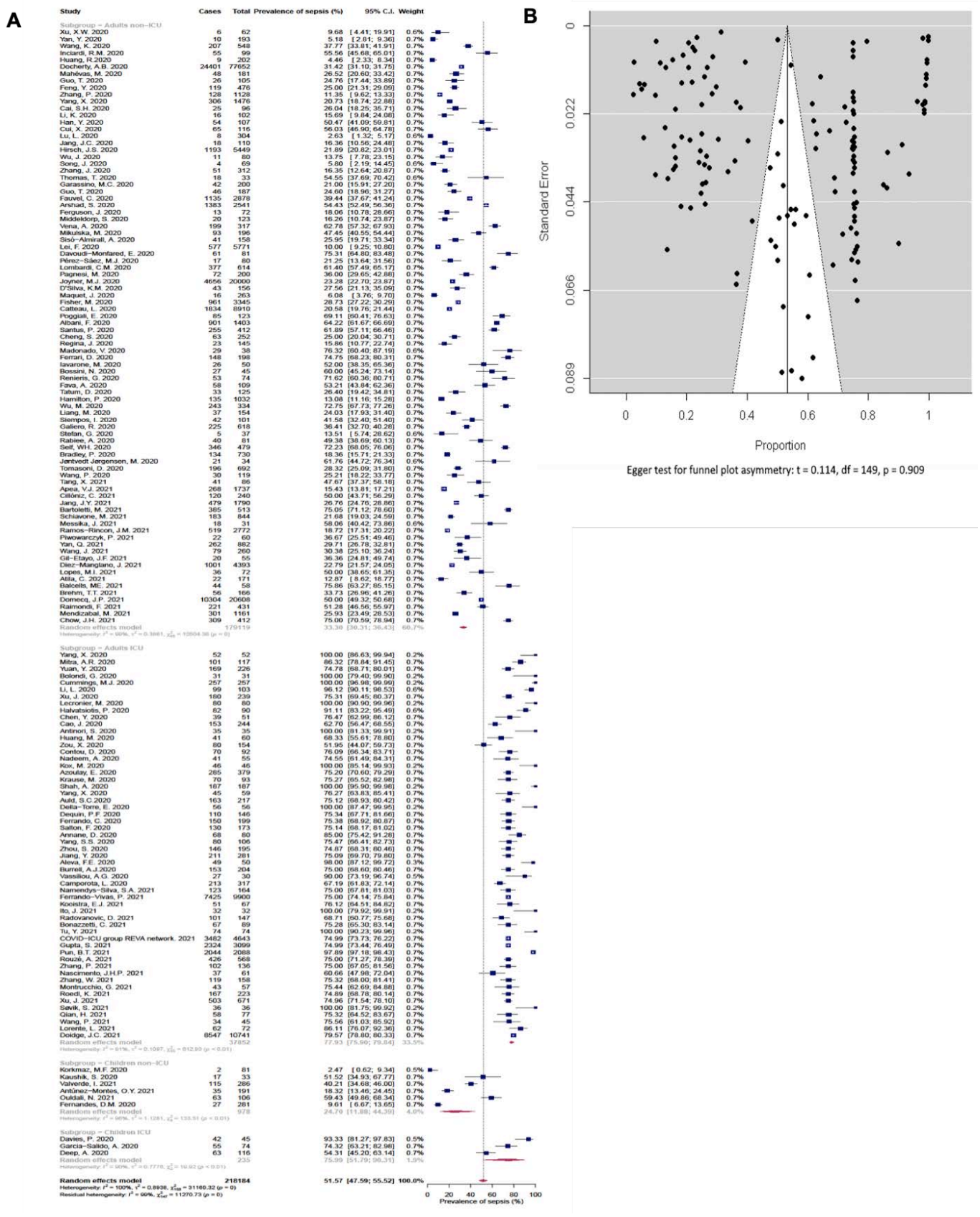
Supplementary Figure 4. Forest plot of COVID-19-related sepsis prevalence in adult patients initially hospitalized in the general ward. Abbreviation: CI, confidence interval.



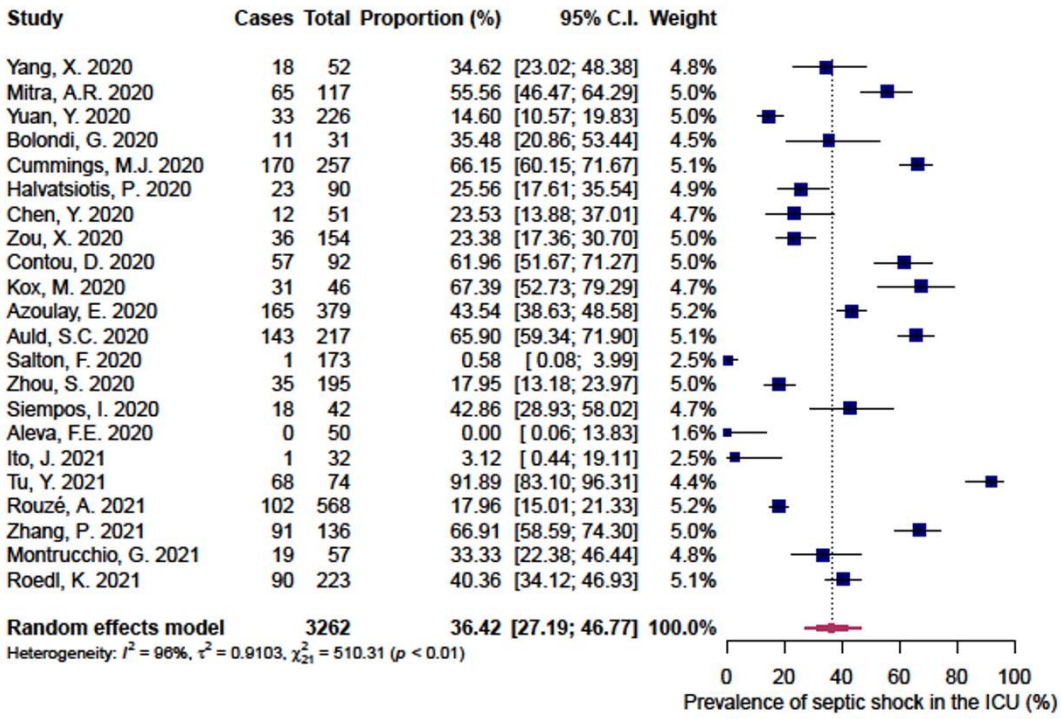
Supplementary Figure 5. Subgroup analysis for the primary endpoint among adult patients with COVID-19, initially hospitalized in the general ward. Forest plot of sepsis prevalence among patients with non-pulmonary versus pulmonary acute organ dysfunction. Abbreviation: CI, confidence interval.



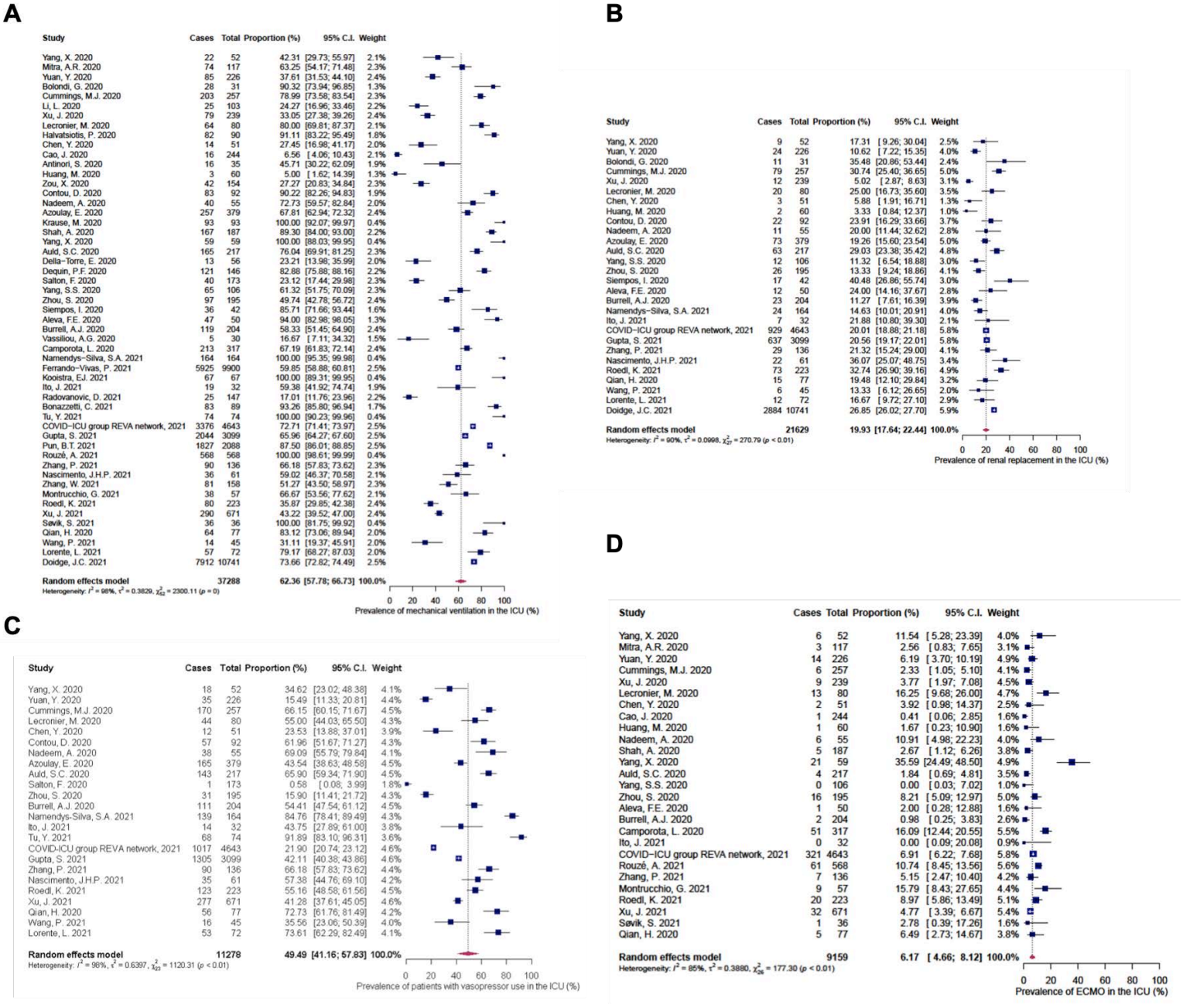
Supplementary Figure 6. A) Forest plot of the overall COVID-19-related sepsis prevalence in included studies with B) respective Funnel plot of publication bias. Abbreviation: CI, confidence interval.



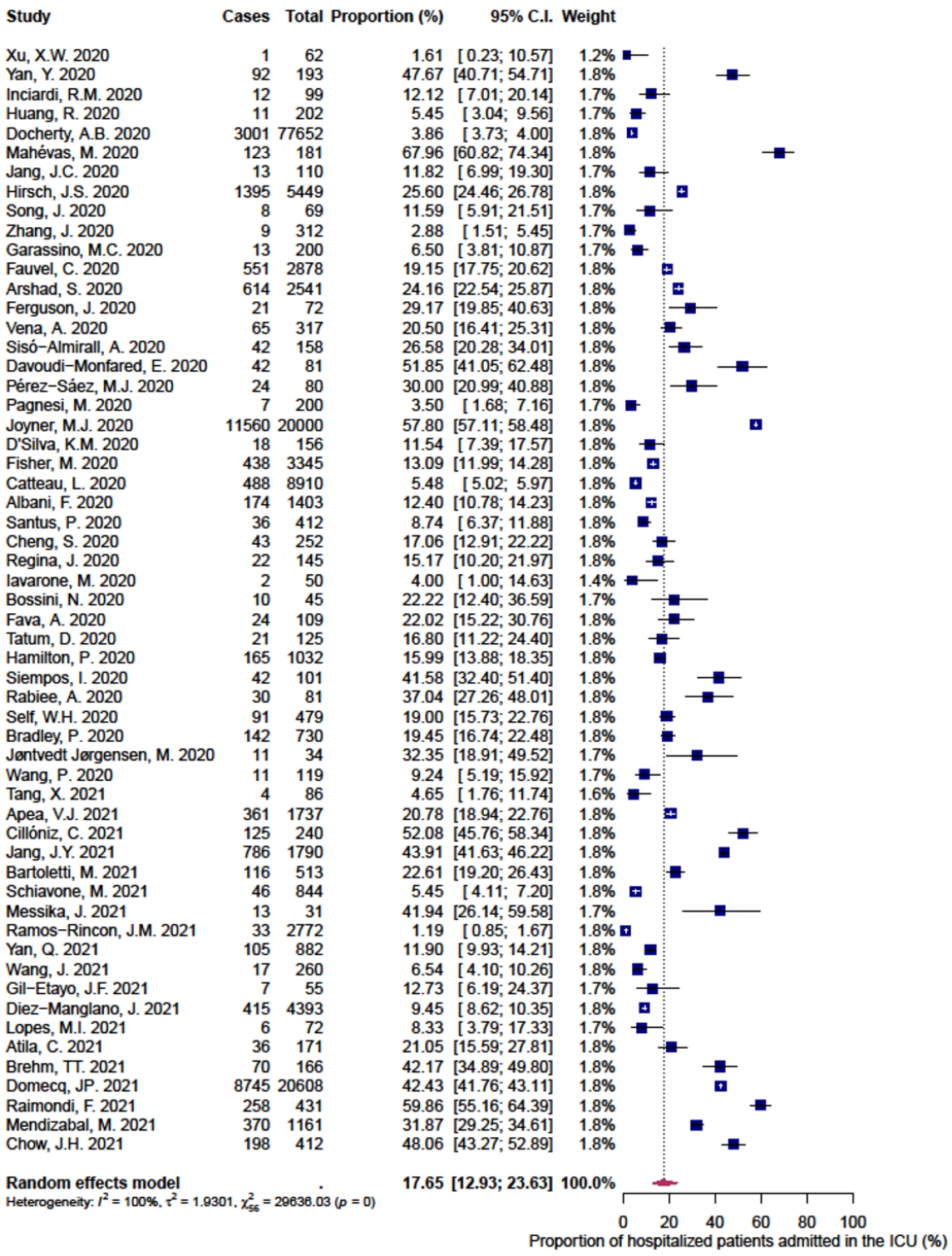
Supplementary Figure 7. Forest plot of septic shock prevalence among adult patients with COVID-19, hospitalized in the Intensive Care Unit (ICU). Septic shock was defined by Sepsis-3 in included publications. Egger's test for Funnel plot asymmetry was: t= 4.940, df= 20, p<0.0001. Abbreviation: CI, confidence interval.



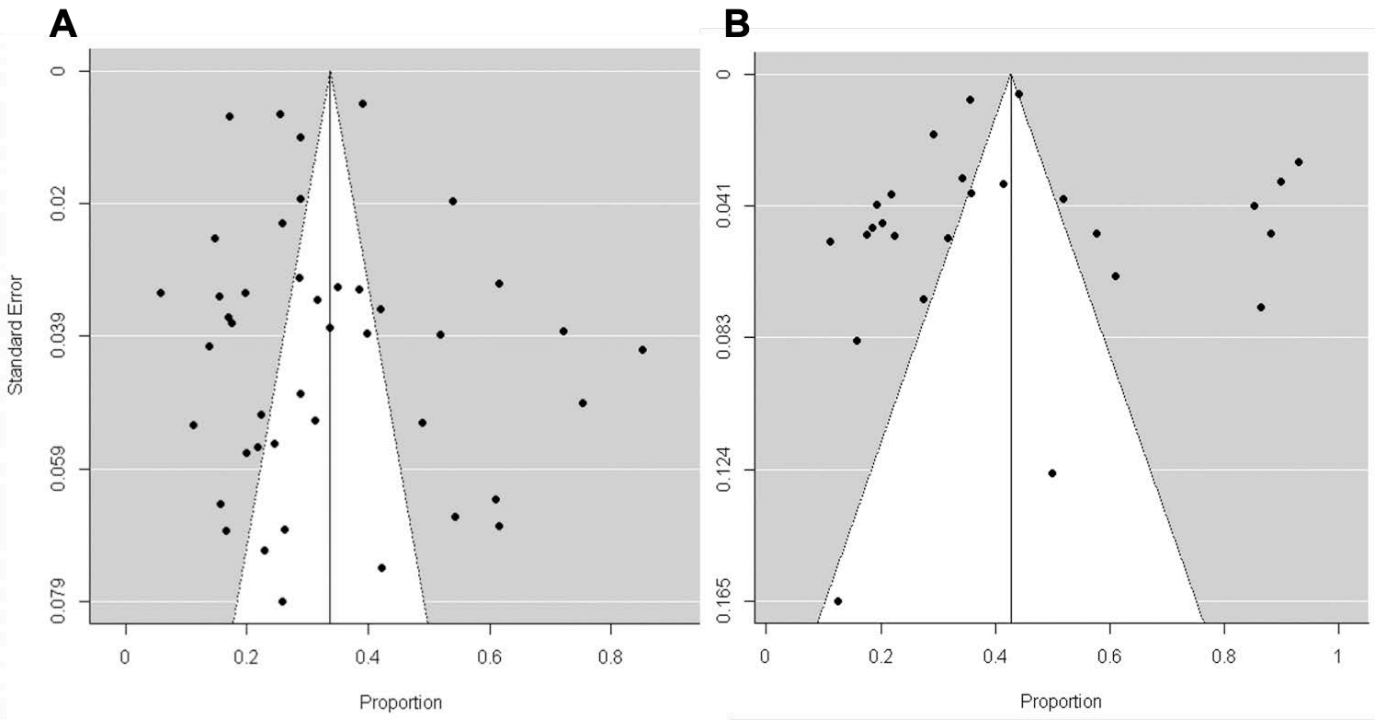
Supplementary Figure 8. Forest plot of organ support or replacement prevalence among adult patients with COVID-19, hospitalized in the Intensive Care Unit (ICU): A) mechanical ventilation; B) renal replacement; C) vasopressor use and D) extracorporeal membrane oxygenation (ECMO). Egger's tests for Funnel plot asymmetry were t= -4.876, df= 51, p<0.0001; t= -1.665, df= 26, p= 0.108; t= 3.859, df= 22, p=0.0009; and t= 1.720, df= 25, p=0.098, respectively. Abbreviation: CI, confidence interval.



Supplementary Figure 9. Forest plot of admission in the Intensive Care Unit (ICU), among adult patients with COVID-19, initially hospitalized in the general ward. Egger's test for Funnel plot asymmetry was t= 2.850, df= 55, p= 0.006. Abbreviation: CI, confidence interval.

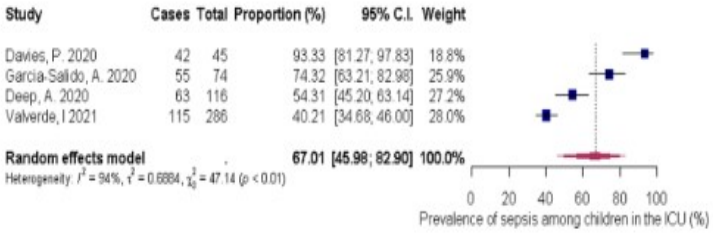


Supplementary Figure 10. Funnel plots of publication bias for studies estimating mortality A) in the Intensive Care Unit and B) among patients under Invasive mechanical ventilation. Egger's tests for asymmetry were t= 0.683, df= 41, p= 0.498; and t= 0.338, df= 24, p= 0.739, respectively.



Supplementary Figure 11. Forest plot of COVID-19-related sepsis prevalence among hospitalized children A) in the Intensive Care Unit (ICU) and B) in the general ward. Abbreviation: CI, confidence interval. C) Funnel plot of publication bias for studies in the ICU and D) in general ward.

A



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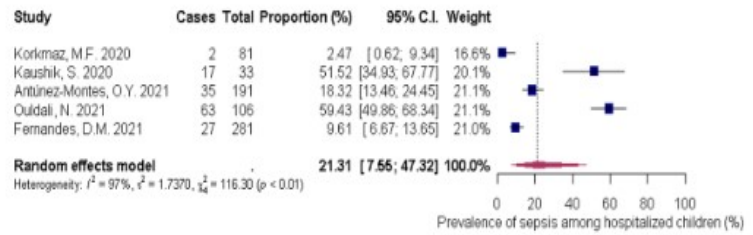

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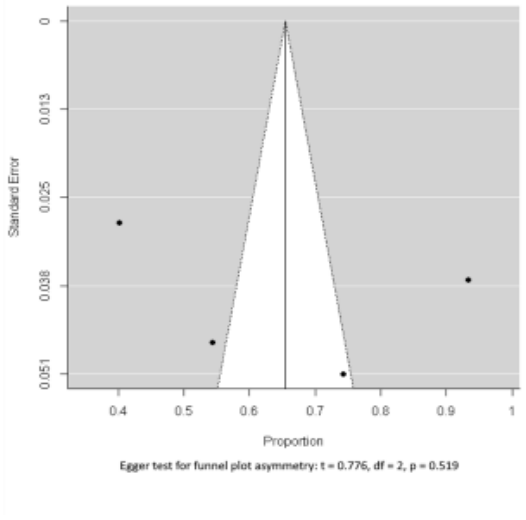

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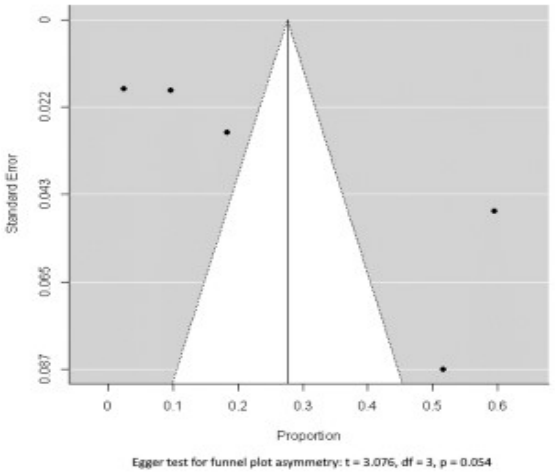
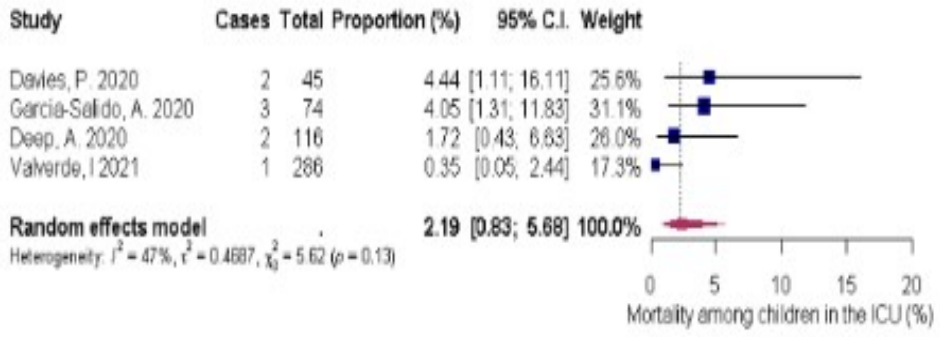
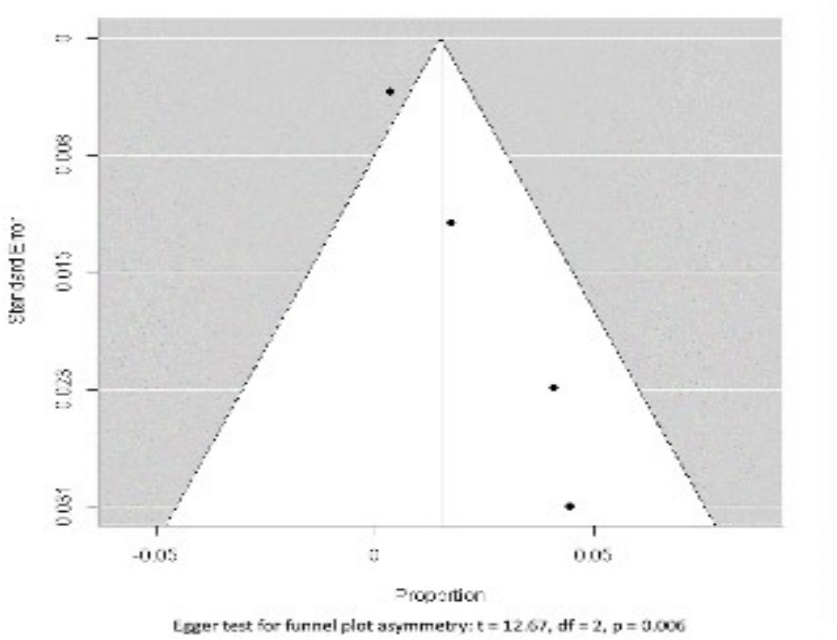


Supplementary Figure 12. A) Forest plot of mortality among children with COVID-19 hospitalized in the Intensive Care Unit (ICU) with B) respective Funnel plot of publication bias. Abbreviation: CI, confidence interval.

A



B



Supplementary Tables

Supplementary Table 1. Characteristics of the included studies.

Ref.	Author	Study design	Study period	Country	N of patients	Incidence of sepsis (%)	Inclusion of consecutive patients	Level of uncertainty
19	Xu, X.W. 2020	Retrospective observational	December 2019-January 2020	China	62	9.7	Yes-all comers	**
20	Yan, Y. 2020	Retrospective observational	January 2020-February 20	China	193	5.2	Yes-all comers	***
21	Wang, K. 2020	Retrospective observational	March 2020-April 2020	China	548	37.8	Yes-all comers	***
22	Yang, X. 2020	Retrospective observational	December 2019-January 2020	China	52	100.0	Critically ill	**
23	Inciardi, R.M. 2020	Prospective	March 20	Italy	99	55.6	Yes-all comers	*
24	Mitra, A.R. 2020	Retrospective observational	February 2020-April 2020	Canada	117	86.3	Yes-all comers	*
25	Huang, R. 2020	Retrospective observational	January 2020-February 2020	China	202	4.5	Yes-all comers	***
26	Docherty, A.B. 2020	Retrospective observational	February 2020-April 2020	UK	20133	21.5	Yes-all comers	*
27	Yuan, Y. 2020	Retrospective observational	February 2020	China	226	74.8	ICU	**
28	Mahévas, M. 2020	Retrospective observational	March 2020	France	181	26.5	Yes-all comers	***
29	Guo, T. 2020	Observational	January 2020-February 2020	China	105	24.8	Elderly	***
30	Feng, Y. 2020	Observational	January 2020-February 2020	China	476	25.0	Yes-all comers	***
31	Zhang, P. 2020	Retrospective observational	December 2019-February 2020	China	1128	11.3	Hypertension	***
32	Yang, X. 2020	Retrospective observational	December 2019-February 2020	China	1476	20.7	Yes-all comers	***
33	Cai, S.H. 2020	RCT	January 2020-February 2020	China	96	26.0	Yes-all comers	***
34	Li, K. 2020	Retrospective observational	January 2020-March 2020	China	102	15.7	Yes-all comers	***
35	Korkmaz, M.F. 2020	Retrospective observational	March 2020-May 2020	Turkey	81	2.5	Yes-all comers	**
36	Han, Y. 2020	Retrospective observational	January 2020-February 2020	China	107	50.5	Yes-all comers	**
37	Cui, X. 2020	Retrospective observational	January 2020-March 2020	China	116	56.0	Yes-all comers	**
38	Bolondi, G. 2020	Observational	March 2020-April 2020	Italy	31	100.0	Yes-all comers	*
39	Cummings, M.J. 2020	Retrospective observational	March 2020-April 2020	USA	257	100.0	ICU	**
40	Lu, L. 2020	Pragmatic trial	January 2020-February 2020	China	304	2.6	Yes-all comers	***

41	Jang, J.C. 2020	Retrospective observational	February 2020-March 2020	South Corea	110	16.4	Yes-all comers	***
42	Li, L. 2020	Retrospective observational	February 2020-April 2020	China	103	96.1	Critically ill	***
43	Hirsch, J.S. 2020	Retrospective observational	March 2020-April 2020	USA	5449	21.9	Yes-all comers	***
44	Xu, J. 2020	Retrospective observational	January 2020-February 2020	China	239	75.3	Critically ill	**
45	Wu, J. 2020	Retrospective observational	January 2020-February 2020	China	80	13.8	Yes-all comers	***
46	Song, J. 2020	Retrospective observational	January 2020-February 2020	China	69	5.8	Yes-all comers	***
47	Zhang, J. 2020	Retrospective observational	January 2020-March 2020	China	312	16.3	Yes-all comers	***
48	Thomas, T. 2020	Retrospective observational	Not reported	USA	33	54.5	Yes-all comers	***
49	Garassino, M.C. 2020	Observational	March 2020-April2020	Italy, Spain, France, Switzerland, Netherlands, USA, UK and China	200	21.0	Oncological	***
50	Lecronier, M. 2020	Retrospective observational	March 2020-April2020	France	80	100.0	ICU	**
51	Halvatsiotis, P. 2020	Retrospective observational	March 2020-April2020	Greece	90	91.1	ICU	***
52	Chen, Y. 2020	Observational	January 2020-March 2020	China	51	76.5	Critically ill	**
53	Cao, J. 2020	RCT	February 2020	China	244	62.7	Yes-all comers	***
54	Guo, T. 2020	Prospective observational	January 2020-February 2020	China	187	24.6	Yes-all comers	***
55	Fauvel, C. 2020	Observational	February 2020-April 2020	France	1240	36.0	CTPA referral	***
56	Arshad, S. 2020	Observational	March 2020-May 2020	USA	2541	54.4	Yes-all comers	**
57	Antinori, S. 2020	Prospective observational	February 2020-March 2020	Italy	35	100.0	Ventilation	***
58	Ferguson, J. 2020	Retrospective observational	March 2020-April 2020	USA	72	18.1	Yes-all comers	***
59	Huang, M. 2020	Prospective observational	January 2020-April 2020	China	60	68.3	Severe illness	***
60	Zou, X. 2020	Retrospective observational	January 2020-February 2020	China	154	51.9	Yes-all comers	**
61	Middeldorp, S. 2020	Retrospective observational	April 2020	Netherlands	123	16.3	Yes-all comers	***
62	Vena, A. 2020	RCT	February 2020-March 2020	Italy	317	62.8	Yes-all comers	***
63	Mikulska, M. 2020	Retrospective observational	Not reported	Italy	196	47.4	Severe cases	***
64	Sisó-Almirall, A. 2020	Prospective observational	February 2020-April 2020	Spain	158	25.9	Yes-all comers	***
65	Contou, D. 2020	Retrospective observational	March 2020-April 2020	France	92	76.1	ICU	**
66	Lei, F. 2020	Observational	December 2019-March 2020	China	5771	10.0	Yes-all comers	***
67	Davoudi-Monfared, E. 2020	Prospective observational	February 2020-April 2020	Iran	81	75.3	Severe illness	***
68	Nadeem, A. 2020	Retrospective observational	March 2020-May 2020	UAE	55	74.5	ICU	**
69	Pérez-Sáez, M.J. 2020	Retrospective observational	March 2020-May 2020	Spain	80	21.3	Renal transplant	***

70	Lombardi, C.M. 2020	Retrospective observational	March 2020-April 2020	Italy	614	61.4	Yes-all comers	***	
71	Kox, M. 2020	Retrospective observational	March 2020-April 2020	Netherlands	46	100.0	ICU		*
72	Pagnesi, M. 2020	Retrospective observational	Not reported	Italy	200	36.0	Yes-all comers	***	
73	Azoulay, E. 2020	Retrospective observational	February 2020-April 2020	France	379	75.2	ICU		**
74	Joyner, M.J. 2020	Retrospective observational	April 2020-June 2020	USA	20000	23.3	Severe or critical		***
75	Krause, M. 2020	Retrospective observational	March 2020-April 2020	USA	93	75.3	ICU		**
76	Shah, A. 2020	Retrospective observational	March 2020-May 2020	UK	187	100.0	ICU		***
77	Yang, X. 2020	Prospective observational	January 2020-March 2020	China	59	76.3	ICU		**
78	Auld, S.C. 2020	Retrospective observational	March 2020-April 2020	USA	217	75.1	ICU		**
79	D'Silva, K.M. 2020	Retrospective observational	January 2020-April 2020	USA	156	27.6	Rheumatologic		***
80	Kaushik, S. 2020	Observational	April 2020-May 2020	USA	33	51.5	MIS-C		***
81	Maquet, J. 2020	Prospective observational	March 2020-April 2020	France	263	6.1	Yes-all comers		*
82	Fisher, M. 2020	Observational	March 2020-April 2020	USA	3345	28.7	AKI		***
83	Dabies, P. 2020	Retrospective observational	April 2020-May 2020	UK	45	93.3	PICU		**
84	Catteau, L. 2020	RCT	March 2020-May 2020	Belgium	8910	20.6	Yes-all comers		***
85	Poggiali, E. 2020	Prospective observational	February 2020-March 2020	Italy	123	69.1	Yes-all comers		***
86	Della-Torre, E. 2020	Prospective observational	Not reported	Italy	56	100.0	Severe illness		***
87	Dequin, P.F. 2020	Retrospective observational	March 2020-June2020	France	146	75.3	ICU		**
88	Ferrando, C. 2020	Retrospective observational	March 2020-June2020	Spain	199	75.4	ICU		**
89	Salton, F. 2020	Prospective observational	February 2020-April 2020	Italy	173	75.1	ICU		**
90	Albani, F. 2020	Prospective observational	February 2020-May2020	Italy	1403	64.2	Yes-all comers		***
91	Santus, P. 2020	Prospective observational	March 2020-May 2020	Italy	412	61.9	Yes-all comers		***
92	Cheng, S. 2020	Observational	January 2020-March 2020	China	252	25.0	Yes-all comers		**
93	Annane, D. 2020	Retrospective observational	March 2020-May 2020	France	80	85.0	Severe illness		**
94	Regina, J. 2020	Prospective observational	March 2020	Switzerland	145	15.9	Yes-all comers		**
95	Yang, S.S. 2020	Retrospective observational	March 2020-May 2020	Canada	106	75.5	ICU		**
96	Madonado, V. 2020	Prospective observational	July 2020-August 2020	Mexico	38	76.3	Yes-all comers		**
97	Ferrari, D. 2020	Retrospective observational	February 2020-April 2020	Italy	198	74.7	Yes-all comers		***
98	Garcia-Salido, A. 2020	Retrospective observational	March 2020-June 2020	Spain	74	74.3	PICU		**
99	Iavarone, M. 2020	Retrospective observational	March 2020	Italy	50	52.0	Cirrhosis		***

100	Bossini, N. 2020	Prospective observational	March 2020-April 2020	Italy	45	60.0	Renal transplant	***
101	Renieris, G. 2020	Observational	March 2020	Greece	74	71.6	Yes-all comers	*
102	Fava, A. 2020	Real-time internet-based survey	March 2020-April 2020	Spain	109	53.2	Renal transplant	***
103	Tatum, D. 2020	Retrospective observational	Not reported	USA	125	26.4	Yes-all comers	***
104	Zhou, S. 2020	Retrospective observational	January 2020-April 2020	China	195	74.9	ICU	**
105	Hamilton, P. 2020	Retrospective observational	1March 2020-April 2020	UK	1032	13.1	Yes-all comers	***
106	Wu, M. 2020	Prospective observational	December 2019-March 2020	China	334	72.8	Severe cases	*
107	Jiang, Y. 2020	Retrospective observational	January 2020-March 2020	China	281	75.1	ICU	**
108	Liang, M. 2020	Prospective observational	January 2020-March 2020	China	154	24.0	Yes-all comers	***
109	Siempos, I. 2020	Retrospective observational	March 11 and April 15, 2020	Greece	101	41.6	Yes-all comers	***
110	Aleva, F.E. 2020	Observational	March 2020-April 2020	Netherlands	50	98.0	Critically ill	**
111	Burrell, A.J. 2020	Retrospective observational	February 2020-June 2020	Australia	204	75.0	ICU	**
112	Galiero, R. 2020	Retrospective observational	March 2020-July 2020	Italy	618	36.4	Yes-all comers	***
113	Stefan, G. 2020	Retrospective observational	March 2020-May 2020	Romania	37	13.5	Hemodialysis	***
114	Rabiee, A. 2020	Observational	before May 2020	US	81	49.4	Liver transplant	***
115	Vassiliou, A.G. 2020	Retrospective observational	22 March to 3 August 2020	Greece	30	90.0	ICU	**
116	Deep, A. 2020	Prospective observational	March 2020-May 2020	UK	116	54.3	MIS-C	***
117	Camporota, L. 2020	Prospective observational	March 2020-May 2020	UK	317	67.2	ICU	***
118	Self, W.H. 2020	Retrospective observational	April 2020-June 2020	USA	479	72.2	Yes-all comers	*
119	Bradley, P. 2020	Prospective observational	April 2020	UK	730	18.4	Yes-all comers	**
120	Jøntvedt Jørgensen, M. 2020	RCT	March 2020-April 2020	Norway	34	61.8	Yes-all comers	***
121	Tomasoni, D. 2020	Observational	March 2020-April 2020	Italy	692	28.3	Yes-all comers	**
122	Wang, P. 2020	Retrospective observational	January 2020-April 2020	China	119	25.2	Yes-all comers	**
123	Namendys-Silva, S.A. 2021	Retrospective observational	April 2020	Mexico	164	75.0	ICU	**
124	Tang, X. 2021	Prospective observational	February 2020-March 2020	China	86	47.7	Yes-all comers	***
125	Apea, V.J. 2021	Retrospective observational	January 2020- May 2020	UK	1737	15.4	Yes-all comers	***
126	Ferrando-Vivas, P. 2021	Prospective observational	March 2020-June 2020	UK	9900	75.0	ICU	***
127	Cillóniz, C. 2021	RCT	February 2020-April 2020	Spain	240	50.0	Yes-all comers	***

128	Kooistra, EJ. 2021	Retrospective observational	March 2020-April 2020	Netherlands	67	76.1	ICU	**
129	Ito, J. 2021	Cross-sectional observational	March 2020-June2020	Japan	32	100.0	ICU	*
130	Radovanovic, D. 2021	Retrospective observational	March 2020-November 2020	Italy	147	68.7	ICU	***
131	Jang, J.Y. 2021	Retrospective observational	April 2020-June2020	USA	1790	26.8	Yes-all comers	***
132	Bonazzetti, C. 2021	Retrospective observational	February 2020-April 2020	Italy	89	75.3	ICU	**
133	Tu, Y. 2021	Prospective observational	January 2020-February 2020	China	74	100.0	ICU	*
134	COVID-ICU group REVA network, 2021	Observational	February 2020-May 2020	France, Belgium, Switzerland	4643	75.0	ICU	***
135	Gupta, S. 2021	Prospective observational	March 2020-April 2020	USA	3099	75.0	ICU	***
136	Valverde, I 2021	Retrospective observational	February 2020-June 2020	17 European Countries	286	40.2	MIS-C	***
137	Bartoletti, M. 2021	Observational	February 2020-June 2020	Italy	513	75.0	Yes-all comers	**
138	Schiavone, M. 2021	Retrospective observational	February 2020-April 2020	Italy	844	21.7	Yes-all comers	***
139	Messika, J. 2021	Retrospective observational	March 2020-May 2020	France	31	58.1	Lung transplant	***
140	Pun, B.T. 2021	Retrospective observational	January 2020-April 2020	Europe, America, Africa	2088	97.9	ICU	***
141	Rouzé, A. 2021	Retrospective observational	April 2020-May 2020	France, Spain, Greece, Portugal, Ireland	568	75.0	ICU	**
142	Antúnez-Montes, O.Y. 2021	Prospective Retrospective observational	July 2020-August 2020	Mexico, Colombia, Peru, Costa Rica, Brazil	191	18.3	Yes-all comers	***
143	Zhang, P. 2021	Retrospective observational	January 2020-February 2020	China	136	75.0	ICU	**
144	Ramos-Rincon, J.M. 2021	Retrospective observational	March 2020-May 2020	Spain	2772	18.7	>80 years old	*
145	Nascimento, J.H.P. 2021	Retrospective observational	March 2020-April 2020	Brazil	61	60.7	ICU	***
146	Ouldali, N. 2021	Retrospective observational	April 2020-January 2021	France	106	59.4	MISC	***
147	Zhang, W. 2021	Retrospective observational	January 2020-February 2020	China	158	75.3	ICU	**
148	Piwowarczyk, P. 2021	Observational	March 2020-May 2020	Poland	60	36.7	Yes-all comers	***
149	Yan, Q. 2021	Observational	January 2020-February 2020	China	882	29.7	>65 years old	***
150	Wang, J. 2021	Retrospective observational	January 2020-February 2020	China	260	30.4	Yes-all comers	***
151	Gil-Etayo, J.F. 2021	Retrospective observational	Not reported	Spain	55	36.4	Yes-all comers	***
152	Diez-Manglano, J. 2021	RCT	March 2020-May 22 2020	Spain	4393	22.8	Yes-all comers	***
153	Montrucchio, G. 2021	Retrospective observational	March 2020-April 2020	Italy	57	75.4	ICU	**

154	Lopes, M.I. 2021	Retrospective observational	April 2020-August 2020	Brazil	72	50.0	Yes-all comers	**
155	Roedl, K. 2021	Retrospective observational	February 2020-June 2020	Germany	223	74.9	ICU	**
156	Xu, J. 2021	Observational, cross-sectional	January 2020-February 2020	China	671	75.0	ICU	**
157	Søvik, S. 2021	Retrospective observational	March 2020-May 2020	Norway	36	100.0	ICU	***
158	Qian, H. 2020	Observational	February 2020-March 2020	China	77	75.3	Critically ill	**
159	Atila, C. 2021	Retrospective observational	March 2020-July 2020	Switzerland	171	12.9	Yes-all comers	***
160	Balcells, ME. 2021	Retrospective observational	May 2020-July 2020	Chile	58	75.9	Yes-all comers	**
161	Brehm, TT. 2021	Retrospective observational	February 2020-June 2020	Germany	166	33.7	Yes-all comers	***
162	Domecq, JP. 2021	Observational	February 2020-November 2020	USA	20608	50.0	Yes-all comers	**
163	Raimondi, F. 2021	Observational	February 2020-March 2020	Italy	431	51.3	Yes-all comers	***
164	Wang, P. 2021	Retrospective observational	January 2020-March 2020	China	45	75.6	ICU	***
165	Lorente, L. 2021	Retrospective observational	Not reported	Spain	72	86.1	ICU	***
166	Fernandes, D.M. 2021	Observational	March 2020-May 2020	USA	281	9.6	Yes-all comers	***
167	Mendizabal, M. 2021	Retrospective observational	April 2020-July 2020	Argentina, Brazil, Chile, Colombia, Dominican Rupublic, Ecuador, Guatemala, Mexico, Paraguay, Peru and Uruguay	1161	25.9	Yes-all comers	***
168	Doidge, J.C. 2021	Retrospective observational	February 2020-July 2020	UK	10741	79.6	ICU	***
169	Chow, J.H. 2021	Observational	March 2020-July 2020	USA	412	75.0	Yes-all comers	**

Abbreviations: AKI Acute Kidney Injury; CTPA Computed Tomography-Pulmonary Angiogram; ICU Intensive Care Unit; MIS Multisystem Inflammatory Syndrome; PICU Pediatric Intensive Care Unit; RCT Randomized Clinical Trial.

Level of Uncertainty: * zero – contacted authors provided the exact proportion of patients with sepsis-3 based on Sequential Organ Failure Assessment (SOFA) score; ** low – SOFA score was provided in articles as median with respective interquartile range; ***intermediate/high – proportion of patients with sepsis was extracted by the highest proportion of patients with a specific organ dysfunction raising SOFA score ≥ 2 points.

Supplementary Table 2. Risk assessment of included studies according to Newcastle-Ottawa Quality Assessment Scale.

	Selection				Comparability	Outcome			
Ref.	**Representativeness of the exposed cohort**	**Selection of the non-exposed cohort**	**Ascertainment of exposure**	**Demonstration that outcome of interest was not present at study start**	**Comparability of cohorts on the basis of the design or analysis**	**Assessment of outcome**	**Was follow-up long enough for outcomes to occur**	**Adequacy of follow up of cohorts**	**Total**
19	*	NA	*	*	NA	*	*	*	6
20	*	NA	*	*	NA	*	*	*	6
21	*	NA	*	*	NA	*	*	*	6
22		NA	*	*	NA	*	*	*	5
23	*	NA	*	*	NA	*	*	*	6
24	*	NA	*	*	NA	*	*	*	6
25	*	NA	*	*	NA	*	*	*	6
26	*	NA	*	*	NA	*	*	*	6
27	*	NA	*	*	NA	*	*	*	6
28	*	NA	*	*	NA	*	*	*	6
29		NA	*	*	NA	*	*	*	5
30	*	NA	*	*	NA	*	*	*	6
31		NA	*	*	NA	*	*	*	5
32	*	NA	*	*	NA	*	*	*	6
33	*	NA	*	*	NA	*	*	*	6
34	*	NA	*	*	NA	*	*	*	6
35	*	NA	*	*	NA	*	*	*	6
36	*	NA	*	*	NA	*	*	*	6
37	*	NA	*	*	NA	*	*	*	6
38	*	NA	*	*	NA	*	*	*	6
39	*	NA	*	*	NA	*	*	*	6
40	*	NA	*	*	NA	*	*	*	6
41	*	NA	*	*	NA	*	*	*	6
42		NA	*	*	NA	*	*	*	5
43	*	NA	*	*	NA	*	*	*	6
44		NA	*	*	NA	*	*	*	5
45	*	NA	*	*	NA	*	*	*	6
46	*	NA	*	*	NA	*	*	*	6
47	*	NA	*	*	NA	*	*	*	6
48	*	NA	*	*	NA	*	*	*	6
49		NA	*	*	NA	*	*	*	5
50	*	NA	*		NA	*	*	*	5
51	*	NA	*	*	NA	*	*	*	6

52		NA	*	*	NA	*	*	*	5
53	*	NA	*	*	NA	*	*	*	6
54	*	NA	*	*	NA	*	*	*	6
55		NA	*	*	NA	*	*	*	5
56	*	NA	*	*	NA	*	*	*	6
57		NA	*		NA	*	*	*	4
58	*	NA	*	*	NA	*	*	*	6
59		NA	*	*	NA	*	*	*	5
60	*	NA	*	*	NA	*	*	*	6
61	*	NA	*	*	NA	*	*	*	6
62	*	NA	*	*	NA	*	*	*	6
63		NA	*	*	NA	*	*	*	5
64	*	NA	*	*	NA	*	*	*	6
65	*	NA	*	*	NA	*	*	*	6
66	*	NA	*	*	NA	*	*	*	6
67		NA	*	*	NA	*	*	*	5
68	*	NA	*	*	NA	*	*	*	6
69		NA	*	*	NA	*	*	*	5
70	*	NA	*	*	NA	*	*	*	6
71	*	NA	*		NA	*	*	*	5
72	*	NA	*	*	NA	*	*	*	6
73	*	NA	*	*	NA	*	*	*	6
74		NA	*	*	NA	*	*	*	5
75	*	NA	*		NA	*	*	*	5
76	*	NA	*	*	NA	*	*	*	6
77	*	NA	*		NA	*	*	*	5
78	*	NA	*	*	NA	*	*	*	6
79		NA	*	*	NA	*	*	*	5
80		NA	*		NA	*	*	*	4
81	*	NA	*	*	NA	*	*	*	6
82		NA	*		NA	*	*	*	4
83		NA	*	*	NA	*	*	*	5
84	*	NA	*	*	NA	*	*	*	6
85	*	NA	*	*	NA	*	*	*	6
86		NA	*	*	NA	*	*	*	5
87	*	NA	*	*	NA	*	*	*	6
88	*	NA	*	*	NA	*	*	*	6
89	*	NA	*	*	NA	*	*	*	6
90	*	NA	*	*	NA	*	*	*	6

91	*	NA	*	*	NA	*	*	*	6
92	*	NA	*	*	NA	*	*	*	6
93		NA	*	*	NA	*	*	*	5
94	*	NA	*	*	NA	*	*	*	6
95	*	NA	*	*	NA	*	*	*	6
96	*	NA	*	*	NA	*	*	*	6
97	*	NA	*	*	NA	*	*	*	6
98		NA	*	*	NA	*	*	*	5
99		NA	*	*	NA	*	*	*	5
100		NA	*	*	NA	*	*	*	5
101	*	NA	*	*	NA	*	*	*	6
102		NA	*	*	NA	*	*	*	5
103	*	NA	*	*	NA	*	*	*	6
104	*	NA	*	*	NA	*	*	*	6
105	*	NA	*	*	NA	*	*	*	6
106		NA	*	*	NA	*	*	*	5
107	*	NA	*	*	NA	*	*	*	6
108	*	NA	*	*	NA	*	*	*	6
109	*	NA	*	*	NA	*	*	*	6
110		NA	*	*	NA	*	*	*	5
111	*	NA	*	*	NA	*	*	*	6
112	*	NA	*	*	NA	*	*	*	6
113		NA	*	*	NA	*	*	*	5
114		NA	*	*	NA	*	*	*	5
115	*	NA	*	*	NA	*	*	*	6
116		NA	*		NA	*	*	*	4
117	*	NA	*	*	NA	*	*	*	6
118	*	NA	*		NA	*	*	*	5
119	*	NA	*	*	NA	*	*	*	6
120		NA	*	*	NA	*	*	*	5
121	*	NA	*	*	NA	*	*	*	1
122	*	NA	*	*	NA	*	*	*	6
123	*	NA	*	*	NA	*	*	*	6
124	*	NA	*	*	NA	*	*	*	6
125	*	NA	*	*	NA	*	*	*	6
126	*	NA	*	*	NA	*	*	*	6
127	*	NA	*	*	NA	*	*	*	6
128	*	NA	*	*	NA	*	*	*	6
129	*	NA	*	*	NA	*	*	*	6

130	*	NA	*	*	NA	*	*	*	6
131	*	NA	*	*	NA	*	*	*	6
132	*	NA	*	*	NA	*	*	*	6
133	*	NA	*	*	NA	*	*	*	6
134	*	NA	*	*	NA	*	*	*	6
135	*	NA	*	*	NA	*	*	*	6
136		NA	*	*	NA	*	*	*	6
137	*	NA	*	*	NA	*	*	*	5
138	*	NA	*	*	NA	*	*	*	6
139		NA	*	*	NA	*	*	*	6
140	*	NA	*	*	NA	*	*	*	5
141	*	NA	*	*	NA	*	*	*	6
142	*	NA	*	*	NA	*	*	*	6
143	*	NA	*	*	NA	*	*	*	6
144		NA	*	*	NA	*	*	*	6
145	*	NA	*	*	NA	*	*	*	5
146		NA	*		NA	*	*	*	6
147	*	NA	*	*	NA	*	*	*	4
148	*	NA	*	*	NA	*	*	*	6
149		NA	*	*	NA	*	*	*	6
150	*	NA	*	*	NA	*	*	*	5
151	*	NA	*	*	NA	*	*	*	6
152	*	NA	*	*	NA	*	*	*	6
153	*	NA	*	*	NA	*	*	*	6
154	*	NA	*	*	NA	*	*	*	6
155	*	NA	*	*	NA	*	*	*	6
156	*	NA	*	*	NA	*	*	*	6
157	*	NA	*		NA	*	*	*	6
158		NA	*	*	NA	*	*	*	5
159	*	NA	*	*	NA	*	*	*	5
160	*	NA	*	*	NA	*	*	*	6
161	*	NA	*	*	NA	*	*	*	6
162	*	NA	*	*	NA	*	*	*	6
163	*	NA	*	*	NA	*	*	*	6
164	*	NA	*	*	NA	*	*	*	6
165	*	NA	*	*	NA	*	*	*	6
166	*	NA	*	*	NA	*	*	*	6
167	*	NA	*	*	NA	*	*	*	6
168	*	NA	*	*	NA	*	*	*	6

169	*	NA	*	*	NA	*	*	*	6

Selection
Representativeness of the exposed cohort (* for a and b) a) truly representative of the average in the community; b) somewhat representative of the average in the community; c) selected group of users eg nurses, volunteers; d) no description of the derivation of the cohort
Selection of the non-exposed cohort (* for a) a) drawn from the same community as the exposed cohort; b) drawn from a different source; c) no description of the derivation of the non-exposed cohort
Ascertainment of exposure (* for a and b) a) secure record (eg surgical records); b) structured interview; c) written self-report; d) no description
Demonstration that outcome of interest was not present at start of study (* for a) a) yes; b) no

Comparability
Comparability of cohorts on the basis of the design or analysis a) study controls for the most important factor **; b) study controls for any additional factor*
Outcome
Assessment of outcome (* for a and b) a) independent blind assessment; b) record linkage; c) self report; d) no description
Was follow-up long enough for outcomes to occur (* for a) a) yes; b) no
Adequacy of follow up of cohorts (* for a and b) a) complete follow up - all subjects accounted for; b) subjects lost to follow up unlikely to introduce bias - small number lost; c) follow up rate large and no description of those lost; d) no statement
Abbreviations: NA, non-applicable

Supplementary Table 3. Risk assessment of included studies according to MINORS.

Ref.	Clearly stated aim	Inclusion of consecutive patients	Prospective data collection	Endpoints appropriate to study aim	Unbiased assessment of study endpoint	Follow-up period appropriate to study aim	<5% lost to follow-up	Prospective calculation of study size	Total (out of 16)
19	2	2	1	2	2	2	2	NA	13
20	2	2	1	1	1	2	2	NA	11
21	2	2	1	1	1	2	2	NA	11
22	2	0	1	2	2	2	2	NA	11
23	2	2	2	2	2	2	2	NA	14
24	2	2	1	2	2	2	2	NA	13
25	2	2	1	1	1	2	2	NA	11
26	2	2	1	2	2	2	2	NA	13
27	2	2	1	2	2	2	2	NA	13
28	2	2	1	1	1	2	2	NA	11
29	2	1	0	1	1	2	2	NA	9
30	2	2	0	1	1	2	2	NA	10
31	2	1	1	1	1	2	2	NA	10
32	2	2	1	1	1	2	2	NA	11
33	2	2	2	1	1	2	2	NA	12
34	2	2	1	1	1	2	2	NA	11
35	2	2	1	2	2	2	2	NA	13
36	2	2	1	2	2	2	2	NA	13
37	2	2	1	2	2	2	2	NA	13
38	2	2	0	2	2	2	2	NA	12
39	2	2	1	2	2	2	2	NA	13
40	2	2	2	1	1	2	2	NA	12
41	2	2	1	1	1	2	2	NA	11
42	2	0	1	1	1	2	2	NA	9
43	2	2	1	1	1	2	2	NA	11
44	2	0	1	2	2	2	2	NA	11
45	2	2	1	1	1	2	0	NA	9
46	2	2	1	1	1	2	0	NA	9
47	2	2	1	1	1	2	0	NA	9
48	2	2	1	1	1	2	2	NA	11
49	2	1	0	1	1	2	2	NA	9
50	2	2	1	2	2	2	2	NA	13
51	2	2	1	1	1	2	2	NA	11
52	2	0	0	2	2	2	2	NA	10

53	2	2	2	1	1	2	2	NA	12
54	2	2	1	1	1	2	2	NA	11
55	2	1	0	1	1	2	2	NA	9
56	2	2	0	2	2	2	2	NA	12
57	2	0	2	1	1	2	2	NA	10
58	2	2	1	1	1	2	2	NA	11
59	2	2	2	1	1	2	2	NA	12
60	2	2	1	2	2	2	2	NA	13
61	2	2	1	1	1	2	2	NA	11
62	2	2	2	1	1	2	2	NA	12
63	2	0	1	1	1	2	2	NA	9
64	2	2	2	1	1	2	2	NA	12
65	2	2	1	2	2	2	2	NA	13
66	2	2	0	1	1	2	0	NA	8
67	2	0	2	1	1	2	2	NA	10
68	2	2	1	2	2	2	2	NA	13
69	2	1	1	1	1	2	2	NA	10
70	2	2	1	1	1	2	2	NA	11
71	2	2	1	2	2	2	2	NA	13
72	2	2	1	1	1	2	2	NA	11
73	2	2	1	2	2	2	2	NA	13
74	2	0	1	1	1	2	2	NA	9
75	2	2	1	2	2	2	2	NA	13
76	2	2	1	1	1	2	2	NA	11
77	2	2	2	2	2	2	2	NA	14
78	2	2	1	2	2	2	0	NA	11
79	2	1	1	1	1	2	2	NA	10
80	2	0	0	1	1	2	2	NA	8
81	2	2	2	2	2	2	2	NA	14
82	2	1	0	1	1	2	2	NA	9
83	2	0	1	2	2	2	2	NA	11
84	2	2	0	1	1	2	2	NA	10
85	2	2	0	1	1	2	2	NA	10
86	2	0	0	1	1	2	2	NA	8
87	2	2	1	2	2	2	2	NA	13
88	2	2	1	2	2	2	2	NA	13
89	2	2	2	2	2	2	2	NA	14
90	2	2	2	1	1	2	2	NA	12
91	2	2	2	1	1	2	2	NA	12

92	2	2	0	2	2	2	2	NA	12
93	2	0	1	2	2	2	2	NA	11
94	2	2	2	2	2	2	2	NA	14
95	2	2	1	2	2	2	2	NA	13
96	2	2	2	2	2	2	2	NA	14
97	2	2	1	1	1	2	2	NA	11
98	2	0	1	2	2	2	2	NA	11
99	2	1	1	1	1	2	2	NA	10
100	2	1	2	1	1	2	2	NA	11
101	2	2	0	2	2	2	2	NA	12
102	2	1	2	1	1	2	2	NA	11
103	2	2	1	1	1	2	2	NA	11
104	2	2	1	2	2	2	2	NA	13
105	2	2	1	1	1	2	2	NA	11
106	2	2	2	2	2	2	2	NA	14
107	2	2	1	2	2	2	2	NA	13
108	2	2	2	1	1	2	2	NA	12
109	2	2	1	1	1	2	2	NA	11
110	2	0	0	2	2	2	2	NA	10
111	2	2	1	2	2	2	2	NA	13
112	2	2	1	1	1	2	2	NA	11
113	2	0	1	1	1	2	2	NA	9
114	2	0	0	1	1	2	2	NA	8
115	2	2	1	2	2	2	2	NA	13
116	2	0	2	1	1	2	2	NA	10
117	2	2	2	1	1	2	2	NA	12
118	2	2	1	2	2	2	2	NA	13
119	2	2	2	2	2	2	2	NA	14
120	2	2	2	1	1	2	2	NA	12
121	2	2	0	2	2	2	2	NA	12
122	2	2	1	2	2	2	2	NA	13
123	2	2	1	2	2	2	2	NA	13
124	2	2	2	1	1	2	2	NA	12
125	2	2	1	1	1	2	2	NA	11
126	2	2	2	1	1	2	2	NA	12
127	2	2	2	1	1	2	2	NA	12
128	2	2	1	2	2	2	2	NA	13
129	2	2	1	2	2	2	2	NA	13
130	2	2	1	1	1	2	2	NA	11

131	2	2	1	1	1	2	2	NA	11
132	2	2	1	2	2	2	2	NA	13
133	2	2	2	2	2	2	2	NA	14
134	2	2	0	1	1	2	2	NA	10
135	2	2	2	1	1	2	2	NA	12
136	2	0	1	1	1	2	2	NA	9
137	2	2	0	2	2	2	2	NA	12
138	2	2	1	1	1	2	2	NA	11
139	2	0	1	1	1	2	2	NA	9
140	2	2	1	1	1	2	2	NA	11
141	2	2	1	2	2	2	2	NA	13
142	2	2	2	1	1	2	2	NA	12
143	2	2	1	2	2	2	2	NA	13
144	2	1	1	2	2	2	2	NA	12
145	2	2	1	1	1	2	2	NA	11
146	2	0	1	1	1	2	2	NA	9
147	2	2	1	2	2	2	2	NA	13
148	2	2	0	1	1	2	2	NA	10
149	2	1	0	1	1	2	2	NA	9
150	2	2	1	1	1	2	2	NA	11
151	2	2	1	1	1	2	2	NA	11
152	2	2	2	1	1	2	2	NA	12
153	2	2	1	2	2	2	2	NA	13
154	2	2	1	2	2	2	2	NA	13
155	2	2	1	2	2	2	2	NA	13
156	2	2	1	2	2	2	2	NA	13
157	2	2	1	1	1	2	2	NA	11
158	2	0	0	2	2	2	2	NA	10
159	2	2	1	1	1	2	2	NA	11
160	2	2	1	2	2	2	2	NA	13
161	2	2	1	1	1	2	2	NA	11
162	2	2	0	2	2	2	2	NA	12
163	2	2	0	1	1	2	2	NA	10
164	2	2	1	1	1	2	2	NA	11
165	2	2	1	1	1	2	2	NA	11
166	2	2	0	1	1	2	2	NA	10
167	2	2	1	1	1	2	2	NA	11
168	2	2	1	1	1	2	2	NA	11
169	2	2	0	2	2	2	2	NA	12

*MINORS score is a methodological index for non-randomized studies. The items are scored 0 if not reported; 1 when reported but inadequate; and 2 when reported and adequate. The global ideal score is 16 for non-comparative studies.
As low quality was considered a score of ≤ 8.
As intermediate quality was considered a score of 9-11.
As high quality was considered a score of ≥ 12.

Supplementary Table 4. Prevalence of organ dysfunctions in adult patients with COVID-19 in the Intensive Care Unit, as reported in included studies (N= 38239 patients).

Ref.	N of patients	Liver dysfunction, n (%)	ARDS, n (%)	Septic shock, n (%)	CNS dysfunction, n (%)	Coagulopathy, n (%)	Renal dysfunction, n (%)
22	52	15 (28.8)	52 (100.0)	18 (34.6)	NR	NR	15 (28.8)
24	117	29 (24.8)	117 (100.0)	65 (55.6)	NR	0 (0.0)	0 (0.0)
27	226	42 (18.6)	161 (71.2)	33 (14.6)	NR	66 (29.2)	70 (31.0)
38	31	0 (0.0)	31(100.0)	11 (35.5)	0 (0.0)	4 912.9)	9 (29.0)
39	257	0 (0.0)	222 (86.4)	170 (66.1)	23 (8.9)	64 (24.9)	128 (49.8)
42	103	NR	99 (96.1)	NR	NR	26 (25.2)	6 (5.8)
44	239	191 (79.9)	164 (68.6)	NR	NR	150 (62.8)	119 (49.8)
50	80	NR	80 (100.0)	NR	NR	13 (16.3)	20 (25.0)
51	90	23 (25.6)	68 (75.6)	23 (25.6)	NR	23 (25.6)	NR
52	51	4 (7.8)	NR	12 923.5)	NR	NR	5 (9.8)
53	244	0 (0.0)	153 (62.7)	NR	NR	11 (4.5)	NR
57	35	NR	35 (100.0)	NR	NR	0 (0.0)	9 (25.7)
59	60	41 (68.3)	16 (26.7)	NR	NR	8 (13.3)	NR
60	154	15 (9.7)	76 (49.4)	36 (23.4)	25 (16.2)	31 (20.1)	25 (16.2)
65	92	NR	NR	57 (62.0)	NR	4 (4.3)	NR
68	55	NR	NR	NR	NR	NR	NR
71	46	4 (8.7)	46 (100.0)	31 (67.4)	NR	3 (6.5)	10 (21.7)
73	379	NR	NR	165 (43.5)	NR	40 (10.6)	193 (50.9)
75	93	NR	NR	NR	NR	NR	NR
76	187	NR	187 (100.0)	NR	NR	NR	NR
77	59	NR	NR	NR	NR	NR	23 (39.0)
78	217	NR	165 (76.0)	143 (65.9)	NR	NR	NR
86	56	NR	56 (100.0)	NR	NR	NR	NR
87	146	NR	NR	NR	NR	NR	NR
88	199	NR	NR	NR	NR	50 (25.1)	NR
89	173	NR	173 (100.0)	1 (0.6)	NR	NR	6 (3.5)
93	80	NR	80 (100.0)	NR	NR	NR	NR
95	106	NR	NR	NR	NR	NR	20 (18.9)

104	195	NR	162 (83.1)	35 (17.9)	NR	49 (25.1)	49 (25.1)
107	281	NR	NR	NR	NR	71 (25.3)	NR
110	50	NR	49 (98.0)	0 (0.0)	NR	NR	NR
111	204	NR	NR	NR	NR	NR	NR
115	30	NR	27 (90.0)	NR	NR	4 (13.3)	NR
117	317	NR	213 (67.2)	NR	NR	NR	NR
123	164	NR	164 (100.0)	NR	NR	NR	NR
126	9900	NR	7425 (75.0)	NR	NR	NR	2475 (25.0)
128	67	NR	51 (76.1)	NR	NR	NR	17 (25.4)
129	32	14 (43.8)	32 (100.0)	1 (3.1)	NR	8 (25.0)	8 (25.0)
130	147	NR	101 (68.7)	NR	NR	NR	NR
132	89	NR	NR	NR	NR	NR	NR
133	74	18 (24.3)	74 (100.0)	68 (91.9)	NR	17 (23.0)	35 (47.3)
134	4643	NR	2233 (48.1)	NR	NR	NR	979 (21.1)
135	3099	NR	NR	NR	681 (22.0)	NR	1330 (42.9)
140	2088	NR	2044 (97.9)	NR	NR	NR	NR
141	568	NR	521 (91.7)	102 (18.0)	26 (4.6)	NR	96 (16.9)
143	136	40 (29.4)	119 (87.5)	91 (66.9)	NR	NR	56 (41.2)
145	61	NR	37 (60.7)	NR	NR	NR	NR
147	158	NR	NR	NR	NR	NR	NR
153	57	NR	NR	19 (33.3)	NR	NR	NR
155	223	NR	NR	90 (40.4)	NR	NR	NR
156	671	NR	NR	NR	NR	NR	263 (39.2)
157	36	NR	36 (100.0)	NR	NR	NR	NR
158	77	17 (22.1)	75 (97.4)	NR	NR	NR	25 (32.5)
164	45	27 (60.0)	34 (75.6)	NR	NR	23 (51.1)	15 (33.3)
165	72	15 (20.8)	62 (86.1)	NR	NR	3 (4.2)	NR
168	10741	NR	NR	NR	NR	NR	5001 (46.6)

Abbreviations: ARDS, acute respiratory distress syndrome; CNS, central nervous system; NR, not reported.

Supplementary Table 5. Prevalence of specific organ dysfunctions in children hospitalized with COVID-19, as reported in included studies (N= 1213 patients).

Ref.	N of patients	ICU	Shock, n (%)	Liver dysfunction, n (%)	ARDS, n (%)	Coagulopathy, n (%)	CNS dysfunction, n (%)	Renal dysfunction, n (%)
35	81	No	2 (2.5)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
80	33	No	17 (51.5)	8 (24.2)	NR	8 (24.2)	NR	8 (24.2)
136	286	No	115 (40.2)	NR	NR	72 (25.2)	43 (15.0)	NR
142	191	No	NR	NR	NR	NR	NR	NR
146	106	No	NR	NR	NR	NR	13 (12.3)	NR
166	281	No	26 (9.3)	NR	27 (9.6)	NR	NR	37 (13.2)
83	45	Yes	42 (93.3)	NR	NR	21 (46.7)	NR	19 (42.2)
98	74	Yes	42 (56.8)	14 (18.9)	11 (14.9)	NR	5 (6.8)	12 (16.2)
116	116	Yes	14 (12.1)	NR	NR	NR	NR	32 (27.6)

Abbreviations: ARDS, acute respiratory distress syndrome; NR, not reported.