

SARS-CoV-2 post-acute sequelae in previously hospitalised patients: SLR and meta-analysis

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*At time of study

SUPPLEMENTARY APPENDIX

SUPPLEMENTARY TABLES AND FIGURES**Table S1. All symptoms extracted from the 52 studies identified by the SLR**

Category	Symptom	Number of Reporting Studies	Reported Frequency Range (Minimum, Maximum)	Prioritised for Meta-Analysis
Percentage of patients with at least 1 symptom		21	(0, 92.8)	Y
General/systemic	Fatigue	38	(0, 78.9)	Y
	Fever	12	(0, 7.5)	N
	Dizziness	11	(0.1, 48.4)	N
	Weakness/asthenia	7	(0, 67.0)	N
	Sweat	6	(0, 36.2)	N
	Malaise	2	(4.3, 18.7)	N
	Pain	2	(19, 36.8)	N
	Shivering	2	(0.1, 0.5)	N
Cardiopulmonary	Dyspnea/breathlessness	42	(0, 77.7)	Y
	Cough	34	(0, 61.3)	Y
	Chest pain	24	(0, 31.5)	Y
	Palpitations	11	(0.3, 25.5)	N
	Sputum	10	(0, 44.3)	N
	Pedal edema	7	(0.2, 28.3)	N
	General	4	(2.6, 56.0)	N

Category	Symptom	Number of Reporting Studies	Reported Frequency Range (Minimum, Maximum)	Prioritised for Meta-Analysis
	Syncope	4	(0.1, 2.3)	N
	Hypertension	2	(0.4, 1.3)	N
	Flushing	1	(4.8, 4.8)	N
	Tachycardia	1	(35.4, 40.8)	N
Upper respiratory/ENT	Sore throat	7	(0, 7.2)	N
	Swallowing difficulties	5	(0, 13.3)	N
	General	3	(1.1, 37)	N
	Dysarthria	3	(1.6, 16.7)	N
	Nasal congestion/rhinitis	2	(0, 12.7)	N
	Rhinorrhea/runny nose	2	(0, 10.9)	N
	Laryngeal sensitivity	1	(16.0, 16.0)	N
	Dry mouth	1	(24.0, 24.0)	N
	Sneezing	1	(0.5, 0.5)	N
Gastrointestinal	Diarrhea	19	(0, 17.0)	Y
	General	9	(1.6, 44.7)	N
	Loss of appetite	9	(0.2, 26.9)	N
	Stomach/abdominal pain	6	(0, 15.4)	N
	Nausea	5	(0.1, 18.0)	N
	Weight loss	6	(0.2, 37.7)	N

Category	Symptom	Number of Reporting Studies	Reported Frequency Range (Minimum, Maximum)	Prioritised for Meta-Analysis
	Vomiting	5	(0, 9.0)	N
	Constipation	4	(0.2, 36.9)	N
	Bloody stool	1	(2.0, 2.0)	N
	Ulcer	1	(20.0, 20.0)	N
	Bowel control problem	1	(3.0, 3.0)	N
	Cramps	1	(15.0, 17.7)	N
	Acid reflux	1	(18.0, 18.0)	N
	Belching	1	(10.0, 10.0)	N
	Abdominal distension	1	(14.0, 14.0)	N
Neurological/ neuromuscular/ cognitive	Smell disturbance/anosmia	29	(0, 44.6)	Y
	Taste disturbance/dysgeusia/ageusia	25	(0, 42.0)	Y
	Combined anosmia and ageusia	7	(0, 28.8)	Y
	Headache	21	(0, 39.0)	Y
	Insomnia/sleep disorder	17	(0.5, 76)	N
	Memory loss/impairment	16	(0, 53.8)	N
	Inability to concentrate	12	(7.1, 40.7)	N
	Tingling/numbness/paresthesia	10	(0, 46.9)	N
	Abnormal walking/gait	5	(2.7, 35.6)	N
	Tremors	5	(0.1, 13.9)	N

Category	Symptom	Number of Reporting Studies	Reported Frequency Range (Minimum, Maximum)	Prioritised for Meta-Analysis
	General	4	(15.0, 61.0)	N
	Confusion	3	(0.1, 43.2)	N
	Facial palsy and asymmetry	3	(0, 5.9)	N
	Reduced sensation/sensibility	3	(7.5, 26.0)	N
	Seizures	2	(0.1, 1.1)	N
Musculoskeletal	Muscle pain/myalgia	22	(0, 57.2)	Y
	Joint pain/arthralgia	12	(0, 54.7)	Y
	Combined arthralgia and myalgia	4	(12.6, 51.0)	Y
	Impaired or altered mobility	8	(0, 53.1)	N
	General	2	(38.5, 40.4)	N
	Myoclonus/muscle jerks	2	(0, 0.4)	N
	Masticatory muscle weakness	2	(0, 3.8)	N
	Arthritis	1	(26.1, 26.1)	N
	Abnormal muscle tone	1	(5.5, 5.5)	N
Skin/ integumentary	Alopecia/hair loss	9	(0.2, 28.6)	N
	Cutaneous manifestation/rash	8	(0.2, 16.0)	N
Reproductive/ sexual function	Urinary dysfunction	5	(0.1, 13.8)	N
	Sexual dysfunction	2	(13.8, 21.5)	N
	Changes in menstruation	1	(0.2, 0.2)	N

Category	Symptom	Number of Reporting Studies	Reported Frequency Range (Minimum, Maximum)	Prioritised for Meta-Analysis
Vision/hearing	Visual disturbance	7	(0.4, 38.5)	N
	General	4	(3.0, 7.1)	N
	Difficulty hearing	2	(0.2, 7.0)	N
	Eye irritation	1	(42.9, 42.9)	N
	Tinnitus	1	(3.1, 4.4)	N
	Otalgia	1	(0.5, 0.5)	N
Composite symptoms	Other systemic symptoms: dizziness; weakness/asthenia	16	(0.1, 9.7)	N
	Other cardiopulmonary symptoms: palpitations; syncope; tachycardia	12	(0.1, 9.5)	N
	Other neurological symptoms: insomnia/sleep disorder; memory loss/impairment; inability to concentrate; tingling/numbness/paraesthesia; confusion	29	(0.1, 9.5)	N

Footnote: Ranges of symptom frequency provide an indication as to the extent of variation in the percentage of patients experiencing each symptom.

Table S2. Search terms used in MEDLINE (searched via the OvidSP platform)

Date searched: 16 Nov.,2021 Records retrieved: 1,461			
Term group	#	Search terms	Results 16 Nov., 2021
Disease Area: Long COVID-19	1	exp coronavirus/ or exp coronavirus infections/	46596
	2	SARS-CoV-2.ti,ab,kf.	64255
	3	(coronavirus\$ or corona virus\$).ti,ab,kf.	86116

Date searched: 16 Nov.,2021 Records retrieved: 1,461			
Term group	#	Search terms	Results 16 Nov., 2021
	4	(Covid-19 or Covid19).ti,ab,kf.	173614
	5	nCoV.ti,ab,kf.	2385
	6	or/1-5	207013
	7	(long-term or long-haul or post-acute or long-COVID or post-COVID or chronic-COVID).ti,ab,kf.	885659
	8	6 and 7	8675
	9	((long or longer or hauler\$ or post or persistent or persistence or prolong\$ or extend\$ or protract\$ or sequelae or chronic) adj2 (SARSCOV2 or SAR-CoV2 or COVID or COVID19 or COVID-19 or "Sars Covid" or 2019ncov or 19ncov or ncov or n-cov or coronavirus or SARS-CoV-2 or sarscov2 or sarsCov-2 or sars-cov2 or "novel Cov" or "wuhan virus")).ti,ab.	4201
	10	8 or 9	10030
Study Design: RCTs and Clinical Trials	11	randomized controlled trials as topic/	150175
	12	randomized controlled trial/	550319
	13	random allocation/	106182
	14	double blind method/	168318
	15	single blind method/	31185
	16	Placebos/	35764
	17	exp Clinical Trials as Topic/	366447
	18	Clinical Trial/	532273
	19	Clinical Trial, Phase II/ or Clinical Trial, Phase III/ or Clinical Trial, Phase IV/	56446
	20	Controlled Clinical Trial/ or Adaptive Clinical Trial/	94572
	21	randomized controlled trial.pt.	550319

Date searched: 16 Nov.,2021 Records retrieved: 1,461			
Term group	#	Search terms	Results 16 Nov., 2021
	22	clinical trial.pt.	532273
	23	(clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase iv).pt.	56446
	24	(controlled clinical trial or multicenter study).pt.	399110
	25	(clinical adj trial\$).ti,ab,kf.	427313
	26	((singl\$ or doubl\$ or treb\$ or tripl\$) adj (blind\$3 or mask\$3)).ti,ab,kf.	184351
	27	placebo\$.ti,ab,kf.	231288
	28	(allocat\$ adj2 random\$).ti,ab,kf.	39059
	29	Randomi?ed adj2 trial\$.ti,ab,kf.	369805
	30	rct.ti,ab,kf.	27854
	31	or/11-30	1870024
	Observational Studies	32	Epidemiologic Studies/
33		Observational Study/	114118
34		Cohort Studies/	298712
35		exp Case-Control Studies/	1249513
36		Cross-Sectional Studies/	398257
37		Clinical Study/	4293
38		Follow-Up Studies/	675244
39		Longitudinal Studies/	152284
40		Retrospective Studies/	964740
41		Prospective Studies/ not Randomised Controlled Trials as Topic/	596526

Date searched: 16 Nov.,2021 Records retrieved: 1,461			
Term group	#	Search terms	Results 16 Nov., 2021
	42	(observational adj (study or studies)).ti,ab,kf.	131980
	43	(cohort adj (study or studies)).ti,ab,kf.	257418
	44	cohort analy\$.ti,ab,kf.	10465
	45	case control.ti,ab,kf.	139609
	46	cross sectional.ti,ab,kf.	423377
	47	(follow up adj (study or studies)).ti,ab,kf.	54091
	48	longitudinal.ti,ab,kf.	283228
	49	retrospective.ti,ab,kf.	626726
	50	(prospective adj (study or studies)).ti,ab,kf.	191030
	51	(epidemiologic\$ adj (study or studies)).ti,ab,kf.	89760
	52	or/32-51	3502808
Standard exclusion filter	53	exp animals/ not exp humans/	4914943
	54	(comment or editorial or "case reports" or "historical article").pt.	3896432
	55	(case stud\$ or case report\$).ti.	331874
	56	historical article/	366481
	57	case reports/ or comment/ or editorial/	3548986
	58	or/53-57	8800666
Combination	59	10 and (31 or 52)	2588
	60	59 not 58	2484
	61	limit 60 to yr="2019-current"	2470

Databases: Ovid MEDLINE(R) and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations and Daily 1946 to 15 Nov., 2021.

Abbreviations: COVID-19, coronavirus 2019; RCT, randomised controlled/clinical trial.

Table S3. Search terms used in Embase (searched via the OvidSP platform)

Date searched: 16 Nov., 2021			
Records retrieved: 587			
Term group	#	Search terms	Results 16 Nov., 2021
Disease Area: Long COVID-19	1	coronavirinae/ or coronavirus infection/	15341
	2	SARS-CoV-2.ti,ab,kf.	63732
	3	(coronavirus\$ or corona virus\$).ti,ab,kf.	84983
	4	(Covid-19 or Covid19).ti,ab,kf.	175512
	5	nCoV.ti,ab,kf.	2394
	6	or/1-5	208442
	7	(long-term or long-haul or post-acute or long-COVID or post-COVID or chronic-COVID).ti,ab,kf.	1221393
	8	6 and 7	9166
	9	((long or longer or hauler\$ or post or persistent or persistence or prolong\$ or extend\$ or protract\$ or sequelae or chronic) adj2 (SARSCOV2 or SAR-CoV2 or COVID or COVID19 or COVID-19 or "Sars Covid" or 2019nCoV or 19ncov or nCoV or n-cov or coronavirus or SARS-CoV-2 or sarscov2 or sarsCov-2 or sars-cov2 or "novel Cov" or "wuhan virus")).ti,ab.	4558
	10	8 or 9	10688
Study Design: RCTs or interventional studies	11	"randomized controlled trial (topic)"/	214585
	12	randomized controlled trial/	683614
	13	randomization/	92195
	14	double blind procedure/	189553
	15	single blind procedure/	44334
	16	crossover procedure/	68676

Date searched: 16 Nov., 2021			
Records retrieved: 587			
Term group	#	Search terms	Results 16 Nov., 2021
	17	placebo/	373463
	18	exp "clinical trial (topic)"/	373392
	19	clinical trial/	1019104
	20	phase 2 clinical trial/ or phase 3 clinical trial/ or phase 4 clinical trial/	145208
	21	controlled clinical trial/ or adaptive clinical trial/ or multicenter study/	708519
	22	(clinical adj trial\$.ti,ab,kf.	618520
	23	((singl\$ or doubl\$ or treb\$ or tripl\$) adj (blind\$3 or mask\$3)).ti,ab,kf.	257244
	24	placebo\$.ti,ab,kf.	334814
	25	(allocat\$ adj2 random\$).ti,ab,kf.	48298
	26	Randomi?ed adj2 trial\$.ti,ab,kf.	499475
	27	rct.ti,ab,kf.	46607
	28	or/11-27	2608679
Observational Studies	29	epidemiology/	223752
	30	observational study/	252727
	31	cohort analysis/	774305
	32	exp case control study/	198237
	33	cross-sectional study/	445094
	34	clinical study/	156642
	35	follow up/	1762139
	36	longitudinal study/	163621
	37	retrospective study/	1160312

Date searched: 16 Nov., 2021 Records retrieved: 587			
Term group	#	Search terms	Results 16 Nov., 2021
	38	prospective study/ not "randomized controlled trial (topic)"/	717723
	39	(observational adj (study or studies)).ti,ab,kf.	205127
	40	(cohort adj (study or studies)).ti,ab,kf.	374155
	41	cohort analy\$.ti,ab,kf.	15724
	42	case control.ti,ab,kf.	183634
	43	cross sectional.ti,ab,kf.	554369
	44	(follow up adj (study or studies)).ti,ab,kf.	71168
	45	longitudinal.ti,ab,kf.	382874
	46	retrospective.ti,ab,kf.	1039709
	47	(prospective adj (study or studies)).ti,ab,kf.	288690
	48	(epidemiologic\$ adj (study or studies)).ti,ab,kf.	116243
	49	or/29-48	5276416
Standard exclusion filter	50	exp animals/ not exp humans/	4860764
	51	(comment or editorial or case reports or historical article).pt.	708217
	52	case report/ or editorial/	3355456
	53	(case stud\$ or case report\$).ti.	405562
	54	or/50-53	8305199
Combination	55	10 and (28 or 49)	4447
	56	55 not 54	4048
	57	limit 56 to yr="2019-current"	4013

Databases: Embase 1974 to 15 Nov., 2021.

Abbreviations: COVID-19, coronavirus disease 2019; RCT, randomised controlled/clinical trial.

Table S4. Search terms used in the Cochrane Library databases (searched simultaneously via the Wiley platform)

Date searched: 16 Nov., 2021 Records retrieved: CENTRAL, 153; CDSR, 3			
Term group	#	Search terms	Results 16 Nov., 2021
Disease Area: Long COVID-19	1	[mh ^"coronavirus"] OR [mh ^"coronavirus infections"]	668
	2	SARS-CoV-2:ti,ab,kw	315
	3	(coronavirus* OR (corona NEXT virus*)):ti,ab,kw	4911
	4	("Covid-19" OR Covid19):ti,ab,kw	7918
	5	nCoV:ti,ab,kw	189
	6	[12-#5]	8364
	7	("long term" OR "long haul" OR "post acute" OR "long COVID" OR "post COVID" OR "chronic COVID"):ti,ab,kw	104386
	8	#6 AND #7	433
	9	((long OR longer OR hauler* OR post OR persistent OR persistence OR prolong* OR extend* OR protract* OR sequelae OR chronic) NEAR/2 (SARSCOVID OR SAR-CoV2 OR COVID OR COVID19 OR COVID-19 OR "Sars Covid" OR 2019nCoV OR 19ncov OR nCoV OR n-cov OR coronavirus OR SARS-CoV-2 OR sarscov2 OR sarsCov-2 OR sars-cov2 OR "novel Cov" OR "wuhan virus")):ti,ab	218
	10	#8 AND #9	159
	11	#10 with publication date 2019-2021, in Trials	153
	12	#10 with publication date 2019-2021, in Cochrane Reviews and Cochrane Protocols	3

Databases: Cochrane Central Register of Controlled Trials Issue 10 of 12, October 2021; Cochrane Database of Systematic Reviews Issue 10 of 12, October 2021.

Abbreviations: COVID-19, coronavirus disease 2019; CDSR, Cochrane Database of Systematic Reviews; CENTRAL, Cochrane Central Register of Controlled Trials.

Table S5. Search terms used in WHO ICTRP

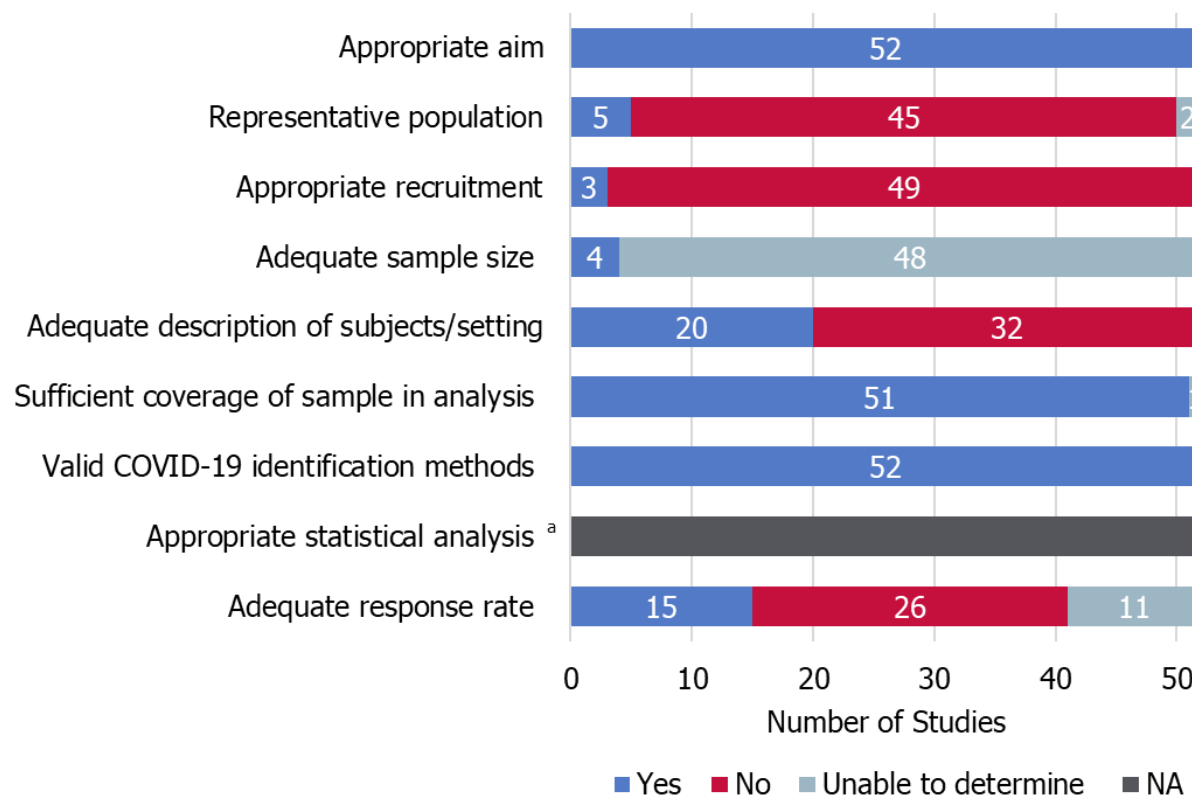
Term Group	Search Terms
Title	coronavirus infection OR covid-19 OR covid19 OR long-covid OR long covid OR post-covid OR post covid OR SARS-CoV-2 OR chronic covid OR long haul covid OR post-acute covid OR post acute covid OR post-discharge OR post discharge OR sequelae OR SARSCOV2 OR SAR-CoV2 OR COVID OR Sars Covid OR 2019ncov OR 19ncov OR ncov OR n-cov OR coronavirus OR sarsCov-2 OR novel Cov OR wuhan virus
Condition	coronavirus infection OR covid-19 OR covid19 OR long covid OR post covid OR SARS-CoV-2 OR chronic covid OR long haul covid OR SARSCOV2 OR COVID OR Sars Covid OR 2019ncov OR ncov OR n-cov OR coronavirus OR sarsCov-2 OR sars-cov2 OR novel Cov
Intervention	Blank
Recruitment Status	All
Primary Sponsor	Blank
Secondary ID	Blank
Countries Of Recruitment	Blank
Date of Registration	1 Jan., 2019 to 3 Dec., 2021
Phases	Phase 2, Phase 3, Phase 4

Platform: <https://www.who.int/clinical-trials-registry-platform> on 3 Dec., 2021

Abbreviations: COVID-19, coronavirus disease 2019; ICTRP, International Clinical Trials Registry Platform; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; WHO, World Health Organization.

Figure S1. Summary of study quality and risk of bias

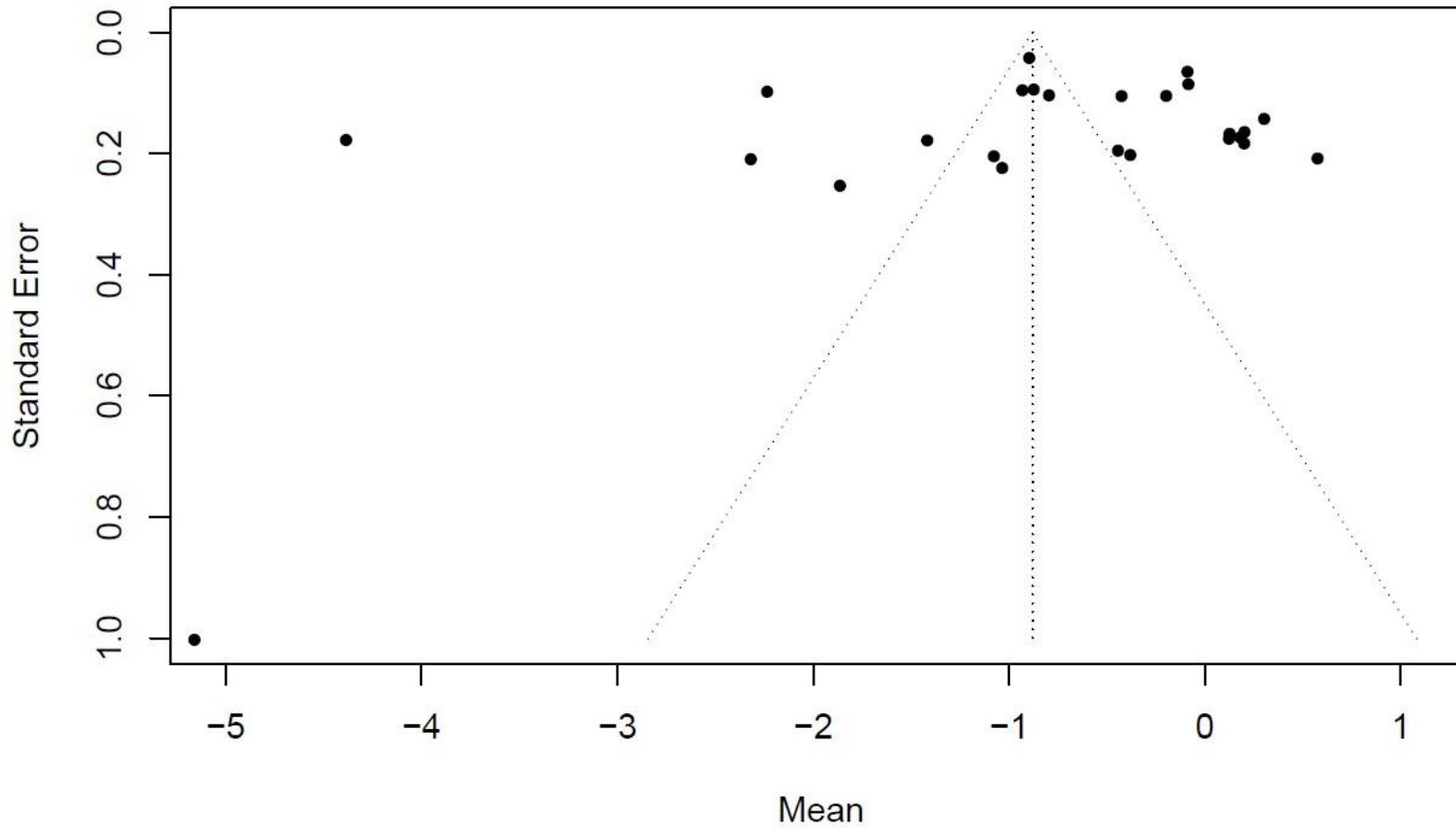
Modified JBI Prevalence Checklist



Footnotes: ^a Statistical analysis was not expected for outcomes of interest. All studies had appropriate aim and valid COVID-19 identification methods since these were inclusion criteria.

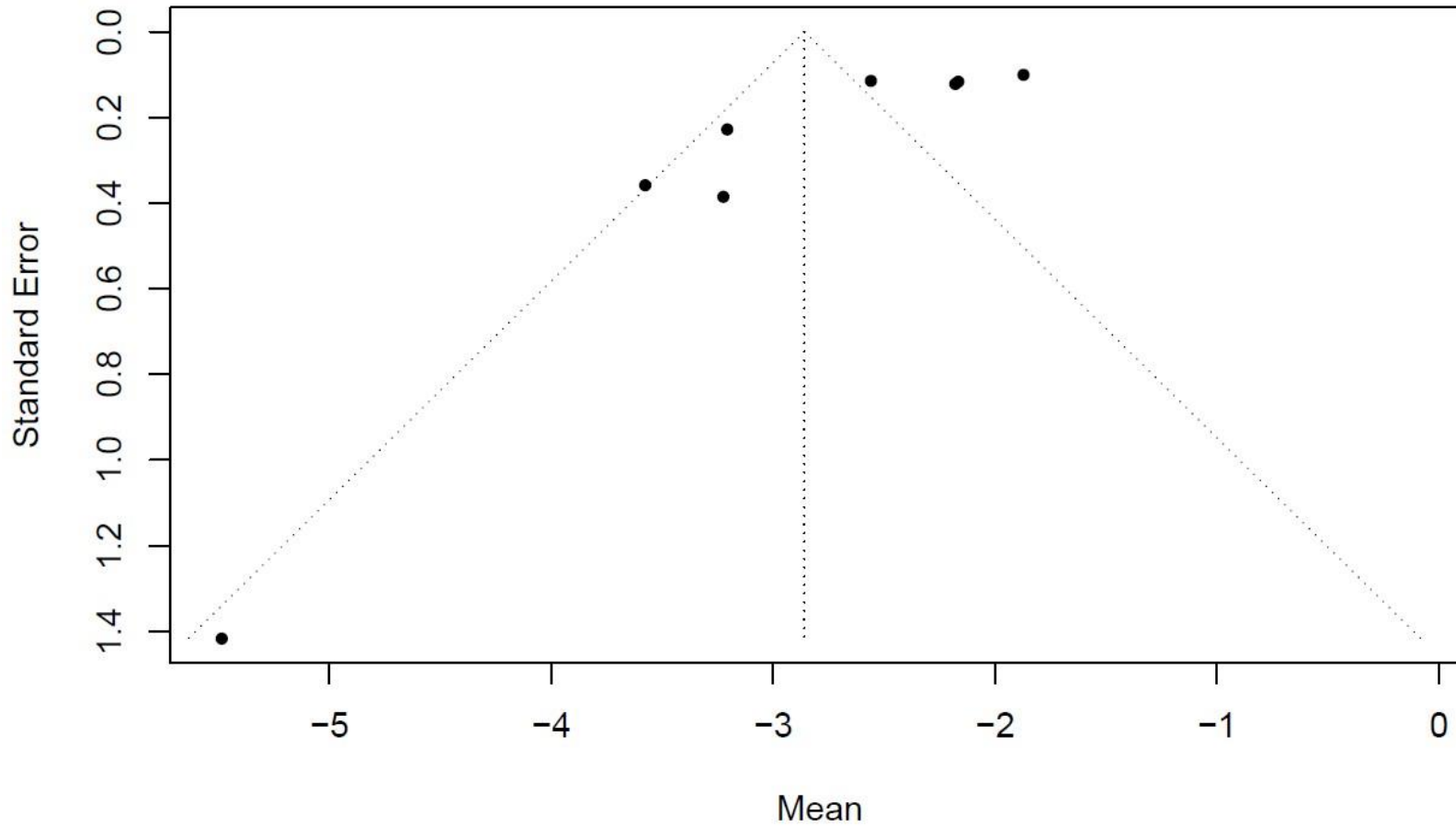
Abbreviations: COVID-19: coronavirus disease 2019; JBI: Joanna Briggs Institute.

Figure S2a. Funnel plot assessing risk of publication bias for fatigue at the ≥ 1 to < 4 months timepoint



*Egger's test: $p=0.7761$

Figure S2b. Funnel plot assessing risk of publication bias for diarrhoea at the ≥ 4 to < 8 months timepoint



*Egger's test: $p=0.0242$