Supplementary materials

Supplementary Methods.

Search strategies:

PubMed:

1: "COVID-19" OR "COVID 19" [MeSH Terms] OR COVID-2019 OR SARS-CoV-2 OR coronavirus OR 2019-nCoV OR 2019-SARS-CoV-2

2: survivor* OR recover* OR persistent OR follow up OR discharge* OR "long term" OR sequela* OR long Covid

3: breathless* OR dyspnoea OR dyspnea OR difficult* breath* OR short* breath*

4: #1 AND #2 AND #3 Filters: from 2020 – 2021

Embase:

1: exp coronavirus disease 2019/

2: (survivor* or recover* or persistent or follow up or discharge* or long term or sequela* or long Covid).tw.

3: (breathless* or dyspnoea or dyspnea or difficult* breath* or short* breath*).tw.

4: 1 and 2 and 3

5: limit 4 to (human and yr="2020 - 2021")

Two authors (B.Z. and Q.H.) independently screened the papers and performed data extraction and quality assessment. Any discrepancies were resolved following review of the corresponding papers by both authors.

Supplementary Table 1. Risk of bias assessments of 104 papers for meta-analysis.

First author	1. Sample frame appropriate to address the target population?	2. Were study participants sampled in an appropriate way?	3. Was the sample size adequate?	4. Were the study subjects and the setting described in detail?	5. Was the data analysis conducted with sufficient coverage of the identified sample?	6. Were valid methods used for the identification of the condition?	7. Was the condition measured in a standard, reliable way for all participants?	8. Was there appropriate statistical analysis?	9. Was the response rate adequate, and if not, was the low response rate managed appropriately?	Overall quality rating
Abdelrahman, M. M.	No	No	No	Yes	Unclear	No	No	No	Yes	Low
Anaya, J. M.	No	No	No	Yes	Unclear	No	Yes	Yes	Unclear	Low
Aparisi, Á.	No	No	No	Yes	Unclear	Yes	Yes	Yes	Unclear	Moderate
Ares-Blanco, S.	No	Yes	No	Yes	Unclear	No	Yes	Yes	Yes	Moderate
Armange, L.	No	No	No	Yes	Unclear	No	No	No	Yes	Low
Arnold, D. T.	No	No	No	Yes	Unclear	No	Yes	No	Yes	Low
Asadi-Pooya, A. A.	No	Yes	No	Yes	Unclear	No	Yes	Yes	No	Moderate
Augustin, M.	No	No	Yes	Yes	Unclear	No	Yes	Yes	No	Moderate
Aul, D. R.	No	Yes	Yes	Yes	Unclear	No	Yes	Yes	Yes	High
Aydin, S.	No	No	No	No	Unclear	No	No	Yes	Unclear	Low
Baldini, M.	No	Yes	No	Yes	Unclear	No	Yes	No	Unclear	Low
Bell, M. L.	Yes	Yes	Yes	Yes	Unclear	No	Yes	Yes	Yes	High
Blomberg, B.	Yes	Yes	Yes	Yes	Unclear	No	Yes	Yes	Yes	High
Boari, G. E. M.	No	No	No	No	Unclear	No	Yes	Yes	No	Low

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Çalik Kütükcü, E.	No	No	No	Yes	Unclear	No	Yes	Yes	Unclear	Low
Carfì, A.	No	Yes	No	Yes	Unclear	No	Yes	No	Yes	Moderate
Carvalho-Schneider, C.	No	Yes	No	Yes	Unclear	Yes	No	Yes	Yes	Moderate
Cheng, D.	No	No	No	No	Unclear	Yes	Yes	No	Yes	Moderate
Cortés-Telles, A.	No	Yes	No	Yes	Unclear	No	Yes	No	Unclear	Low
Damanti, S.	No	Yes	No	Yes	Unclear	Yes	Yes	Yes	Yes	Moderate
Dankowski, R.	No	Yes	No	Yes	Unclear	No	Yes	No	Unclear	Low
Darcis, G.	No	Yes	No	No	Unclear	No	Yes	Yes	Unclear	Low
Daynes, E.	No	No	No	Yes	Unclear	Yes	No	No	Unclear	Low
D'Cruz, R. F.	No	Yes	No	Yes	Unclear	Yes	Yes	Yes	Yes	High
de Graaf, M. A.	No	No	No	Yes	Unclear	Yes	Yes	Yes	No	Moderate
Diaz-Fuentes, G.	No	Yes	No	Yes	Unclear	No	Yes	No	Unclear	Low
Dreyer, N.	Yes	No	Yes	Yes	Unclear	No	No	Yes	NA	Moderate
Erol, N.	No	Yes	No	Yes	Unclear	No	Yes	No	Unclear	Low
Evans, R. A.	Yes	Yes	Yes	Yes	Unclear	No	Yes	Yes	Unclear	High

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Faverio, P.	Yes	No	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	High
Fernández-de-Las-Peñas, C.	No	Yes	Yes	Yes	Unclear	No	Yes	Yes	Yes	Moderate
Fortini, A.	No	Yes	No	Yes	Unclear	No	Yes	Yes	No	Moderate
Froidure, A.	No	No	No	Yes	Unclear	Yes	Yes	Yes	Yes	Moderate
Gaber, T. A. K.	No	Yes	No	No	Unclear	No	No	No	No	Low
Galván-Tejada, C. E.	No	Unclear	No	Yes	Unclear	No	Unclear	Yes	Unclear	Low
Gamberini, L.	Yes	Yes	No	Yes	Unclear	Yes	Yes	Yes	Yes	High
Garrigues, E.	No	Yes	No	Yes	Unclear	Yes	No	Yes	Yes	Moderate
Gautam, N.	No	Unclear	No	Yes	Unclear	Yes	Yes	Yes	Yes	Moderate
Ghosn, J.	Yes	Yes	Yes	Yes	Unclear	No	Yes	No	No	Moderate
González, J.	No	No	No	Yes	Unclear	Yes	Yes	Yes	Yes	Moderate
Halpin, S. J.	No	Yes	No	Yes	Unclear	Yes	Yes	No	No	Moderate
Horwitz, L. I.	No	Yes	No	Yes	Unclear	Yes	No	Yes	No	Moderate
Huang, C.	No	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	High
Huang, L.	No	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	High

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Huang, Y.	No	Yes	Yes	No	Unclear	No	No	No	NA	Low
Italia, L.	No	No	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	High
Jacobs, L. G.	No	Yes	No	Yes	Unclear	No	No	Yes	No	Low
Karaarslan, F.	No	Yes	Yes	Yes	Unclear	Yes	No	Yes	Unclear	Moderate
Klein, H.	No	No	No	Yes	Unclear	No	No	Yes	Yes	Low
Landi, F.	No	Yes	No	Yes	Unclear	No	Yes	Yes	Yes	Moderate
Lerum, T. V.	Yes	No	No	Yes	Unclear	Yes	Yes	Yes	Unclear	Moderate
Liang, L.	No	Yes	No	Yes	Unclear	Yes	Yes	Yes	No	Moderate
Lindahl, A.	No	Yes	No	Yes	Unclear	Yes	No	Yes	No	Moderate
Lund, L. C.	Yes	Yes	Yes	Yes	Unclear	Yes	No	Yes	NA	High
Maestre-Muñiz, M. M.	No	Yes	Yes	Yes	Unclear	Yes	No	Yes	Yes	High
Mahmud, R.	No	No	Yes	Yes	Unclear	No	No	Yes	Yes	Moderate
Mallia, P.	No	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	Unclear	High
Mandal, S.	No	Yes	Yes	Yes	Unclear	No	No	Yes	Yes	Moderate
Mechi, A.	No	No	No	No	Unclear	No	Yes	Yes	Unclear	Low

First author	1. Sample frame appropriate to address the target population?	2. Were study participants sampled in an appropriate way?	3. Was the sample size adequate?	4. Were the study subjects and the setting described in detail?	5. Was the data analysis conducted with sufficient coverage of the identified sample?	6. Were valid methods used for the identification of the condition?	7. Was the condition measured in a standard, reliable way for all participants?	8. Was there appropriate statistical analysis?	9. Was the response rate adequate, and if not, was the low response rate managed appropriately?	Overall quality rating
Meije, Y.	No	Yes	No	Yes	Unclear	No	Yes	Yes	Yes	Moderate
Menges, D.	Yes	Yes	Yes	Yes	Unclear	Yes	No	Yes	No	High
Moradian, S. T.	No	No	No	Yes	Unclear	No	No	Yes	Yes	Low
Morin, L.	No	Yes	Yes	Yes	Unclear	No	No	Yes	Yes	Moderate
Motiejunaite, J.	No	Yes	No	No	Unclear	No	Yes	Yes	Unclear	Low
Mumoli, N.	No	No	No	Yes	Unclear	No	Yes	Yes	Unclear	Low
Munblit, D.	Yes	Yes	Yes	Yes	Unclear	No	Yes	Yes	Yes	High
Naik, S.	No	No	Yes	Yes	Unclear	No	No	Yes	No	Low
Nehme, M.	No	Yes	Yes	Yes	Unclear	Yes	No	Yes	Yes	High
O'Keefe, J. B.	No	Yes	No	Yes	Unclear	No	No	Yes	No	Low
O'Sullivan, O.	No	Yes	No	No	Unclear	No	Yes	Yes	Unclear	Low
Peluso, M. J.	No	No	No	Yes	Unclear	No	Yes	No	Unclear	Low
Qin, W.	No	Yes	Yes	Yes	Unclear	No	Yes	Yes	Yes	High
Raman, B.	No	Yes	No	Yes	Unclear	Yes	Yes	Yes	Unclear	Moderate
Righi, E.	No	Yes	Yes	Yes	Unclear	No	No	Yes	Yes	Moderate
Riou, M.	No	Yes	No	No	Unclear	No	Yes	Yes	Unclear	Low

First author	1. Sample frame appropriate to address the target population?	2. Were study participants sampled in an appropriate way?	3. Was the sample size adequate?	4. Were the study subjects and the setting described in detail?	5. Was the data analysis conducted with sufficient coverage of the identified sample?	6. Were valid methods used for the identification of the condition?	7. Was the condition measured in a standard, reliable way for all participants?	8. Was there appropriate statistical analysis?	9. Was the response rate adequate, and if not, was the low response rate managed appropriately?	Overall quality rating
Sathyamurthy, P.	No	Yes	No	Yes	Unclear	No	Yes	Yes	Yes	Moderate
Seeßle, J.	No	Yes	No	Yes	Unclear	No	Yes	Yes	Unclear	Moderate
Shah, A. S.	Yes	No	No	Yes	Unclear	Yes	Yes	Yes	Yes	Moderate
Shang, Y. F.	No	No	Yes	No	Unclear	No	No	Yes	Yes	Low
Shendy, W.	No	Yes	No	Yes	Unclear	Yes	Yes	No	Unclear	Moderate
Shoucri, S. M.	No	Yes	Yes	Yes	Unclear	No	No	Yes	NA	Moderate
Sigfrid, L.	Yes	No	Yes	Yes	Unclear	Yes	No	Yes	No	Moderate
Skjorten, I.	Yes	No	No	Yes	Unclear	Yes	Yes	Yes	Unclear	Moderate
Sonnweber, T.	No	Yes	No	Yes	Unclear	Yes	Yes	Yes	Yes	High
Stavem, K.	No	Yes	Yes	Yes	Unclear	No	No	Yes	No	Moderate
Suárez-Robles, M.	No	Yes	No	No	Unclear	No	No	Yes	Unclear	Low
Sultana, S.	No	Yes	Yes	Yes	Unclear	No	Yes	Yes	Yes	Moderate
Sun, L. L.	No	Yes	Yes	Yes	Unclear	Yes	No	Yes	Yes	High
Szekely, Y.	No	Yes	No	Yes	Unclear	No	Yes	Yes	No	Moderate
Tawfik, H. M.	No	No	No	Yes	Unclear	No	No	Yes	Unclear	Low
Taylor, R. R.	No	Yes	Yes	No	Unclear	Yes	No	Yes	Unclear	Moderate

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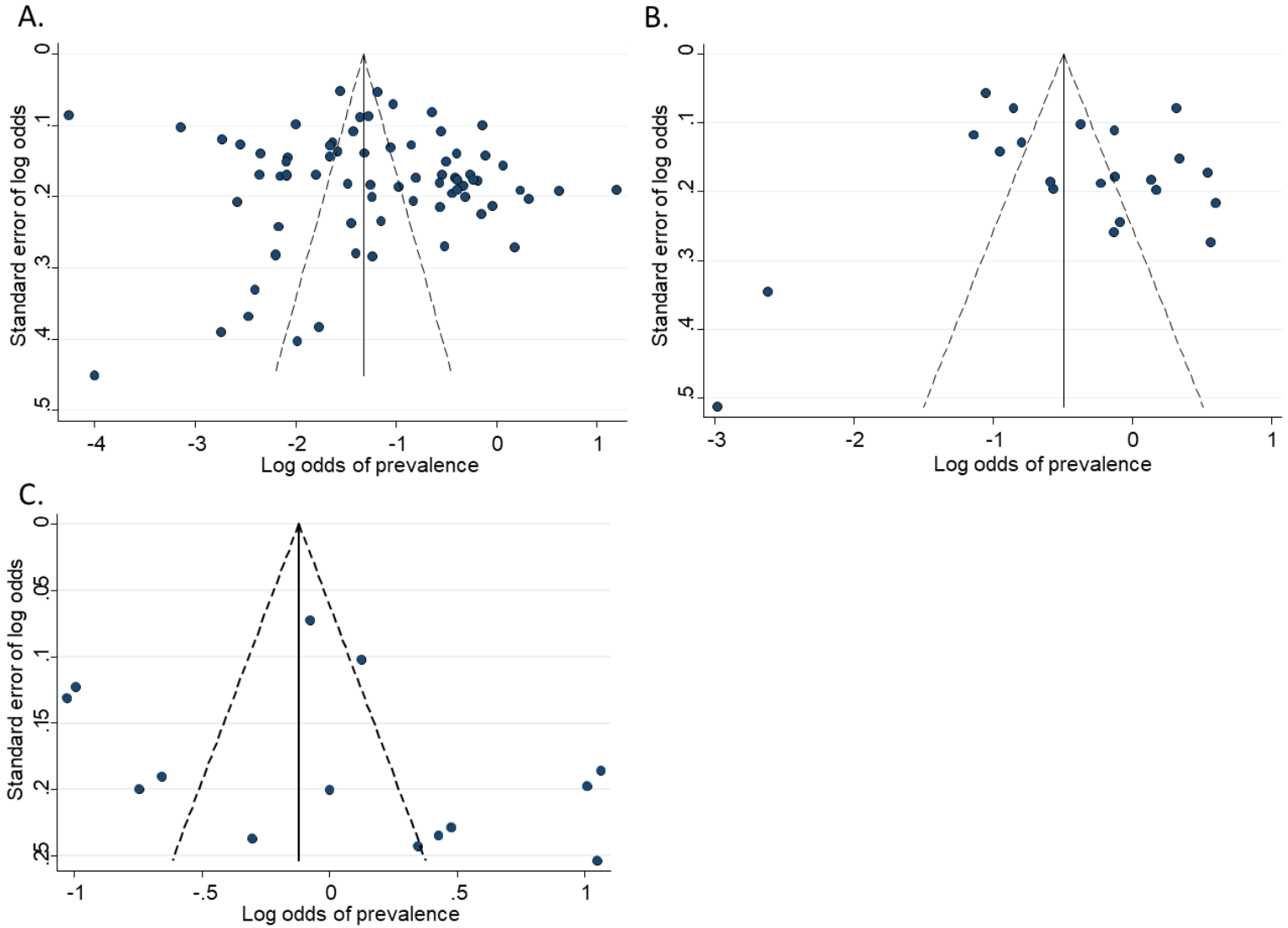
Todt, B. C.	No	Yes	No	Yes	Unclear	Yes	No	Yes	No	Moderate
Tosato, M.	No	Yes	No	Yes	Unclear	No	Yes	No	Yes	Moderate
Varghese, J.	No	No	No	Yes	Unclear	No	Yes	No	Unclear	Low
Venturelli, S.	No	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	No	High
Vijayakumar, B.	No	No	No	Yes	Unclear	Yes	Yes	Yes	No	Moderate
Weerahandi, H.	No	Yes	No	Yes	Unclear	Yes	No	Yes	No	Moderate
Wu, Q.	No	Yes	No	No	Unclear	Yes	Yes	Yes	No	Moderate
Wu, X.	No	Yes	No	Yes	Unclear	Yes	Yes	Yes	Yes	High
Yin, X.	No	No	Yes	Yes	Unclear	Yes	Yes	Yes	Unclear	Moderate
Yomogida, K.	Yes	Yes	Yes	Yes	Unclear	No	Yes	Yes	No	High
Zayet, S.	No	Yes	Yes	Yes	Unclear	No	No	Yes	Unclear	Moderate
Zhang, X.	No	Yes	Yes	Yes	Unclear	No	Yes	Yes	Yes	High
Zhao, Y. M.	No	Yes	No	Yes	Unclear	No	Yes	Yes	Yes	Moderate

Note: The risk of bias assessment was conducted based on the "Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Studies Reporting Prevalence Data" (https://jbi.global/critical-appraisal-tools) [1].

Supplementary Figure 1. Funnel plots for meta-analyses of studies with no scale (A), MRC/mMRC dyspnoea scale (B) and other scales (C).



Supplementary Table 2. Sensitivity analyses for studies not using scales for breathlessness measurement.

Sensitivity analyses	No. of eligible studies	Overall pooled prevalence (95% CI)	Hospitalisation		Follow-up time	
			Hospitalised	Non-hospitalised	1-6 months	7-12 months
Exclude studies with any children or adolescents (<18 years old)	63	28% (25-31)	29% (24-33)	19% (12-25)	29% (26-33)	20% (15-26)
Exclude studies with any follow-up data ≤28 days	66	27% (24-30)	27% (23-31)	19% (14-24)	29% (25-33)	20% (15-26)
Exclude studies based on electronic health record data	68	27% (24-30)	28% (24-32)	19% (13-25)	28% (25-32)	20% (15-26)
Exclude studies rated as low quality	40	22% (19-25)	23% (19-27)	13% (6-20)	25% (21-29)	19% (13-25)
Use prevalence estimates after logit transformation	71	23% (19-27)	24% (19-29)	14% (7-27)	25% (22-30)	18% (13-25)
Use prevalence estimates after Freeman-Tukey double arcsine transformation	71	25% (21-29)	25% (20-31)	16% (7-28)	27% (23-31)	19% (13-26)

Supplementary Table 3. Influential analysis by removing each study from the meta-analysis.

	No scale	MRC/mMRC dyspnoea scale	Other scales
No. of eligible studies	71	22	14
Range of overall pooled prevalence of post-COVID breathlessness	25%-27%	40%-43%	49%-53%

Supplementary Table 4. Characteristics of 46 papers qualitatively synthesised for risk factors or mechanisms of post-COVID breathlessness.

First author	Sample size	Country	Mean/median age, year	Male proportion	Exposure/measurement	Scale for breathlessness	Hospitalisation	Follow-up method	Follow-up period, month	Main results
Anaya, J. M. [2]	100	Colombia	49	0.47	COVID-19 severity		mixed	visit	7-12	No significant association between COVID-19 severity and persistent breathlessness.
Arnold, D. T. [3]	67	UK	55	0.63	KL-6 level		hosp	visit	1-6	No significant difference in the 12-week KL-6 level and presence of subjective breathlessness.
Aparisi, Á. [4]	70	Spain	55	0.36	sex, age, obesity, comorbidities, transthoracic echocardiogram, pulmonary function test, cardiopulmonary exercise testing, predicted peak VO2 consumption, total distance in the six-minute walking test	NYHA functional class ≥ 2	mixed	visit	1-6	Patients with dyspnoea had higher proportion of females (p=0.065), significant decline in predicted peak VO2 consumption, total distance in the six-minute walking test and abnormalities in cardiopulmonary exercise testing. No significant differences in age, prevalence of cardiovascular risk factors and transthoracic echocardiogram and pulmonary function test.
Aydin, S. [5]	116	Turkey	49	0.48	CT severity index, CRP		hosp	phone	1-6	Persistent shortness of breath was significantly correlated with high CT severity index and CRP values.
Baldini, M. [6]	55	Argentina	55	0.73	gas transfer		hosp	visit	1-6	Patients with dyspnoea had DLCO and KCO values lower than those who did not have this symptom.
Cortés-Telles, A. [7]	186	Mexico	47	0.61	spirometry, gas transfer, six-minute walk distance, end-exercise oxygen saturation		mixed	visit	1-6	Patients with persistent dyspnoea had significantly lower FVC, FEV1, DLCO, 6-minute walk distance, end-exercise oxygen saturation.
D'Cruz, R. F. [8]	115	UK	59	0.62	age, sex, obesity, smoking, comorbidities, hospital length of stay, ICU, CT, exertional desaturation, mood symptoms, anxiety, post-traumatic stress disorder	mMRC increase, numerical rating scale ≥ 4	hosp	visit	1-6	Pre-morbid obstructive lung disease, mood symptoms, anxiety and post-traumatic stress disorder was significantly associated with persistent breathlessness, but not for age, sex, obesity, smoking, other/overall comorbidities, hospital length of stay, ICU-admission, CT and exertional desaturation.
de Graaf, M. A. [9]	81	Netherlands	61	0.63	spirometry, gas transfer, echocardiogram	NYHA functional class ≥ 2	hosp	visit	1-6	Patients with higher NYHA class had significantly lower DLCOc values, but no significant difference in spirometry or echocardiogram.
Dreyer, N. [10]	977	USA	42	0.12	use of medications for autoimmune disease		mixed	online	1-6	Around day 30 a higher proportion of participants reporting use of medications for

First author	Sample size	Country	Mean/median age, year	Male proportion	Exposure/measurement	Scale for breathlessness	Hospitalisation	Follow-up method	Follow-up period, month	Main results
										autoimmune disease remained symptomatic compared to all other participants.
Faverio, P. [11]	283	Italy	62	0.73	COVID-19 severity	mMRC ≥ 1	hosp	visit	1-6	mMRC scale had no difference between severity groups.
Fernández-de-Las-Peñas, C. [12]	1142	Spain	61	0.52	sex, comorbidities, number of symptoms at hospitalisation, ICU, number of days at hospital		hosp	phone	7-12	Risk factors associated with dyspnoea included female gender, number of pre-existing comorbidities, number of symptoms at hospitalisation, and number of days at hospital.
Fernández-de-Las-Peñas, C. [13]	435	Spain	70	0.62	diabetes		hosp	phone	7-12	No differences were observed in the presence of dyspnoea on exertion between patients with or without diabetes.
Fernández-de-Las-Peñas, C. [14]	264	Spain	52	0.60	obesity		hosp	phone	7-12	No significant difference in the prevalence of dyspnoea was observed between people with and without obesity.
Fortini, A. [15]	59	Italy	68	0.53	age, sex, comorbidities, clinical severity of COVID-19 during hospitalisation, lung ultrasound abnormalities, gas transfer		hosp	visit	1-6	Age, gender, Charlson Comorbidity Index, presence of Chronic Obstructive Pulmonary Disease, and clinical severity of COVID-19 during hospitalisation did not predict the persistence of dyspnoea. Exertional dyspnoea was significantly associated with the persistence of lung ultrasound abnormalities and diffusing capacity alterations.
Froidure, A. [16]	126	Belgium	60	0.59	age, sex, severity, HRCT, spirometry, gas transfer	mMRC ≥ 1	hosp	visit	1-6	None of the factors tested (age, sex, severity, HRCT, spirometry, gas transfer) were able to explain the persistence of dyspnoea at follow-up.
Gamberini, L. [17]	178	Italy	64	0.73	spirometry, gas transfer, respiratory system compliance, PaO2/FiO2, length of IMV	mMRC ≥ 1	hosp	visit	7-12	Persistent dyspnoea was weakly but significantly correlated with both DLCO and length of IMV, but not with PaO2/FiO2 or spirometry.
Garrigues, E. [18]	120	France	63	0.63	ICU	mMRC ≥ 1, no	hosp	phone	1-6	No significant difference regarding persistent symptoms between ward patients versus ICU patients.
Gautam, N. [19]	144	UK	57	0.63	obesity, comorbidities, abnormal chest X-ray, spirometry, severity, ICU, CRP	mMRC ≥ 1	hosp	visit	-	Patients with breathlessness had significantly higher rate of comorbidities, abnormal residual chest X-ray and spirometry. No significant difference

First author	Sample size	Country	Mean/median age, year	Male proportion	Exposure/measurement	Scale for breathlessness	Hospitalisation	Follow-up method	Follow-up period, month	Main results
										between patients managed on hospital wards and on ITU groups, in blood markers for inflammation or organ injury, nor the state of their acute illness.
Horwitz, L. I. [20]	126	USA	62	0.60	follow-up time	PROMIS® Dyspnea Characteristics instrument ≥ 1	hosp	online/phone	7-12	A trend of decreased prevalence in 6 months vs 1 month (p=0.06).
Huang, C. [21]	1615	China	57	0.52	COVID-19 severity	mMRC ≥ 1	hosp	visit	1-6	The risk of an mMRC score greater than 1 was significantly higher in participants with COVID-19 disease severity scale 5–6 than those with scale 3.
Huang, L. [22]	1271	China	59	0.53	follow-up time	mMRC ≥ 1	hosp	visit	7-12	The proportion of patients with dyspnoea slightly increased from 26% at 6-month visit to 30% at 12-month visit (p=0.014).
Italia, L. [23]	123	Italy	62	0.68	myocardial injury	NYHA functional class ≥ 2	hosp	visit	1-6	Patients with myocardial injury were more frequently symptomatic for dyspnoea.
Lerum, T. V. [24]	103	Norway	59	0.52	age, sex, ICU	mMRC ≥ 1	hosp	visit	1-6	No significant associations between ICU admission or age and dyspnoea scores. Females tend to have higher prevalence of the symptom (p=0.069).
Liang, L. [25]	76	China	41	0.28	spirometry, gas transfer	0-4 grade ≥ 1	hosp	visit	1-6	Dyspnoea scores correlated well with pulmonary function parameters for FEV1, FVC, FEV1/FVC, TLC.
Lindahl, A. [26]	93	Finland	60	0.53	sex	mMRC ≥ 1	hosp	online/printed	1-6	Women reported more frequently dyspnoea than men.
Mechi, A. [27]	112	Iraq	51	0.66	diabetes		mixed	visit	7-12	Diabetes group reported persistent shortness of breath more frequently compared to non-diabetes group.
Meije, Y. [28]	294	Spain	69	0.57	PaO2/FiO2 <200 during hospitalisation		hosp	visit	1-6	PaO2/FiO2 <200 during hospitalisation as an independent predictor of persistent dyspnoea.
Menges, D. [29]	384	Switzerland	47	0.50	age, sex, hospitalisation, BMI, comorbidities, initial symptom severity, ICU, smoking status, follow-up time	mMRC ≥ 1	mixed	online	7-12	Significant association of dyspnoea with female sex, initial hospitalisation, higher BMI and presence of comorbidities, but not for initial symptom severity, smoking status or presence of chronic respiratory condition.

First author	Sample size	Country	Mean/median age, year	Male proportion	Exposure/measurement	Scale for breathlessness	Hospitalisation	Follow-up method	Follow-up period, month	Main results
Milanese, M. [30]	135	Italy	59	0.67	COVID-19 severity	mMRC ≥ 2	hosp	visit	1-6	No significant association between COVID-19 severity and persistent breathlessness.
Motiejunaite, J. [31]	114	France	57	0.67	gas transfer		mixed	visit	1-6	No significant association between DLCO and persistent breathlessness.
Naik, S. [32]	1234	India	41	0.69	hospitalisation		mixed	visit/phone	1-6	Hospitalised patients had significantly higher prevalence of the symptom than non-hospitalised patients.
Qin, W. [33]	647	China	58	0.44	COVID-19 severity		hosp	visit	1-6	Prevalence of dyspnoea in patients with severe COVID-19 was markedly higher than that in the non-severe patients (12% vs 7%, p=0.014).
Raman, B. [34]	58	UK	55	0.59	mood symptoms, anxiety, severity	MRC ≥ 2	hosp	visit	1-6	A moderate correlation was seen between extent of mood symptoms and anxiety and ongoing breathlessness. Hospitalised patients with more severe disease were more likely to experience persistent breathlessness.
Riou, M. [35]	81	France	61	0.73	COVID-19 severity		hosp	visit	1-6	No significant association between COVID-19 severity and persistent breathlessness.
Seeßle, J. [36]	96	Germany	57	0.49	age, follow-up time		mixed	visit	1-6, 7-12	Between 5 months and 12 months after symptom onset, the reported symptom frequency increased for dyspnoea. Younger patients (<60 years) reported dyspnoea significantly more often than the group of patients aged 60 years and older.
Shah, A. S. [37]	73	Canada	65	0.60	age, sex, follow-up time, smoking status, comorbidities, spirometry, gas transfer, echocardiogram, mood symptoms	UCSD-SOBQ > 10	hosp	Visit	1-6	Patients with dyspnoea had greater impairments in spirometry and DLCO and mood symptoms compared to patients without dyspnoea. No significant change in median dyspnoea score over time. No difference in age, smoking status, comorbidities or echocardiogram.
Shang, Y. F. [38]	796	China	62	0.51	age, sex, severity		hosp	phone	1-6	No association between shortness of breath and disease severity or age; females tend to have higher prevalence of the symptom (p=0.072).
Sigfrid, L. [39]	327	UK	60	0.59	age, sex, comorbidities	MRC increase	hosp	post/phone/visit	7-12	No association between new or persistent breathlessness and disease severity or age.

First author	Sample size	Country	Mean/median age, year	Male proportion	Exposure/measurement	Scale for breathlessness	Hospitalisation	Follow-up method	Follow-up period, month	Main results
										Females had higher prevalence of breathlessness than males.
Skjorten, I. [40]	126	Norway	56	0.62	age, sex, obesity, diabetes, cardiopulmonary exercise testing, VO2 peak·kg^{-1}, ventilatory efficiency, heart rate, systolic blood pressure	mMRC ≥ 1	hosp	visit	1-6	Participants reporting dyspnoea had significantly lower VO2 peak·kg^{-1}, ventilatory efficiency, heart rate, systolic blood pressure, higher BMI, but no difference in age, sex or diabetes.
Sonnweber, T. [41]	133	Austria	57	0.55	CT, spirometry, gas transfer, follow-up time		mixed	visit	1-6	The CT severity score and lung function parameters including FVC, FEV1, TLC and DLCO demonstrated a weak but significant correlation to the severity of dyspnoea.
Szekely, Y. [42]	71	Israel	53	0.66	echocardiogram, cardiopulmonary exercise testing		mixed	visit	1-6	Patients with dyspnoea had attenuated changes in SV, HR, cardiac output, and lung tidal volume and decreased ventilatory efficiency.
Vijayakumar, B. [43]	80	UK	59	0.66	CT		hosp	visit	1-6	No difference in participant-reported breathlessness between those with and without CT abnormalities.
Wu, X. [44]	83	China	60	0.57	follow-up time	mMRC ≥ 1	hosp	visit	1-6, 7-12	The number of patients with various levels of dyspnoea symptoms progressively and significantly reduced at 6 months, 9 months, and 12 months.
Yin, X. [45]	337	China	54	0.50	CT, age, sex, follow-up time, comorbidities, smoking status, duration of hospital stays, receipt of hormone administration, receipt of immunoglobulin injections, severity, ICU admission, receipt of mechanical ventilation, CRP	0-4 grade ≥ 1	hosp	visit	7-12	Age, comorbidity score, duration of hospital stays, receipt of hormone administration, receipt of immunoglobulin injections, ICU admission, receipt of mechanical ventilation, laboratory parameters, and CT findings associated with lesion volume were significantly different between survivors with and without dyspnoea.
Yomogida, K. [46]	366	USA	39	0.43	ethnicity, age, sex, comorbidities		mixed	phone	1-6. 7-12	Risk of experiencing dyspnoea 2 months after testing were higher in Black people than in other racial/ethnic groups.
Zhang, X. [47]	2433	China	60	0.50	age, sex, follow-up time, smoking status, oxygen therapy, mechanical ventilation, comorbidities, ICU, days at hospital		hosp	phone	7-12	Age, oxygen therapy, mechanical ventilation and coexisting chronic liver diseases, but not sex, smoking or ICU admission, were risk factors for dyspnoea.

Note: "-" refers to information unclear or not applicable. hosp = hospitalised patients; non-hosp = non-hospitalised patients; NYHA = New York Heart Association; mMRC = modified Medical Research Council Dyspnoea Scale; MRC = Medical Research Council Dyspnoea Scale; UCSD-SOBQ = University of California San Diego–Shortness of Breath Questionnaire; KL-6 = Krebs von den Lungen 6; CT = computed tomography; CRP = C-reactive protein; ICU = intensive care unit; PaO2/FiO2 = ratio of arterial oxygen partial pressure to fractional inspired oxygen; IMV = invasive mechanical ventilation; BMI = body mass index.

Supplementary Table 5. Characteristics of 10 papers qualitatively synthesised for interventions or therapies of post-COVID breathlessness.

First author	RCT	Population	Sample size	Country	Intervention	Results	Mean/ median age, year	Male proportion	Scale for breathlessness	Hospitalisation	Follow-up method	Follow-up time
Ahmed, I. [48]	No	post-discharge COVID-19 patients having below standard 6-min walk test and quality of life score at baseline	20	Pakistan	five weeks of moderate to high-intensity rehabilitation training (aerobic and breathing exercise), 3 sessions/week	After 5 weeks of exercise training, the Borg dyspnoea score has significantly improved ($p<0.001$).	40	0.65	Modified Borg Dyspnoea Scale	hosp	visit	23-28 days (baseline) + 5 weeks
Bouteleux, B. [49]	No	patients referred with COVID-19 sequelae	25	France	outpatient respiratory rehabilitation (aerobic exercise and strength training combined with specific controlled ventilation techniques when necessary), sessions of 1.5h three times a week	Over the course of rehabilitation, exertional dyspnoea significantly improved ($p<0.001$).	47	0.48	mMRC	mixed	visit	a median of 84 [35-154] days after disease onset (baseline) + 2 months rehabilitation
Cesarone, M. R. [50]	No	subjects with post-COVID-19 lung disease	18 (10 with Pycnogenol® Centellicum® combination; 8 with standard management)	Italy	the combination of Pycnogenol® (150 mg/day) and Centellicum® (3×225 mg/day), used before being diagnosed with COVID-19 and hospital admission	Shortness of breath and effort dyspnoea after 4 weeks were significantly improved with the supplement combination ($p<0.05$).	57	1.00		hosp	visit	4 weeks after hospital exit for COVID-19
Curci, C. [51]	No	post-intensive care unit COVID-19 patients referred to an Italian COVID-19 Rehabilitation Unit	39	Italy	patient-tailored inpatient rehabilitation (30 minutes/set, 2 times/day), aimed to improve gas exchanges, reduce dyspnoea, and improve muscle function	Dyspnoea in ADL was significantly reduced compared to baseline.	72	0.61	mMRC	hosp	visit	directly after ICU discharge (baseline) + mean of 32±9 days in the Rehabilitation Unit

First author	RCT	Population	Sample size	Country	Intervention	Results	Mean/ median age, year	Male proportion	Scale for breathlessness	Hospitalisation	Follow-up method	Follow-up time
Dalbosco-Salas, M. [52]	No	post-COVID-19 adult patients who had persistent dyspnoea at post-discharge follow-up	115	Chile	nine weeks of Primary Care Telerehabilitation Program, consisted of 24 sessions of supervised home-based exercise training	Dyspnoea improved significantly after the intervention (p<0.001).	56	0.45	mMRC	mixed	visit	30 (27-35) days after discharge of the acute COVID-19 phase (baseline) + 9 weeks
Hayden, M. C. [53]	No	still-symptomatic patients referred for Pulmonary Rehabilitation after overcoming acute COVID-19	105	Germany	three-week Inpatient Pulmonary Rehabilitation Program tailored to each patient's individual needs and with multiple components	At the end of Pulmonary Rehabilitation, we detected improvements with large effect sizes in exertional dyspnoea (NRS), with moderate effect sizes for the mMRC scores, and with small to moderate effect sizes in the intensity of dyspnoea at rest (NRS).	56	0.55	11-point numeric rating scale (NRS) to assess the present severity of dyspnoea sensation at rest and on exertion; mMRC	mixed	visit	mean of 69 (0-270) days after discharge from the clinic or acute COVID-19 undergone in an outpatient setting (baseline) + 3 weeks
Li, J. [54]	Yes	formerly hospitalised COVID-19 survivors with remaining dyspnoea complaints	120 (61 allocated to control and 59 to TERECO)	China	telerehabilitation programme for COVID-19 (TERECO), an unsupervised home-based 6-week exercise programme comprising breathing control and thoracic expansion, aerobic exercise and LMS exercise, delivered via smartphone, and remotely monitored with heart rate telemetry	A treatment effect for mMRC-dyspnoea was found immediately after the intervention period but not at the other time points.	51	0.45	mMRC	hosp	visit	mean (SD) 70 (17) days from hospital discharge (baseline) + 6 weeks (post-treatment) or 28 weeks (follow-up)
Roozbeh, F. [55]	Yes	outpatients with mild COVID-19	55 (27 vs 28 control)	Iran	a treatment arm receiving sofosbuvir/daclatasvir plus hydroxychloroquine vs a control arm receiving hydroxychloroquine alone	After one month of follow-up, the number of patients with dyspnoea was significantly lower in the sofosbuvir/daclatasvir group compared with control (p=0.035).	43	0.47		non-hosp	phone	30 days from enrolment

First author	RCT	Population	Sample size	Country	Intervention	Results	Mean/ median age, year	Male proportion	Scale for breathlessness	Hospitalisation	Follow-up method	Follow-up time
Stavrou, V. T. [56]	No	previously hospitalised COVID-19 patients	20	Greece	eight weeks unsupervised pulmonary rehabilitation exercise program (3 training sessions per week,100 min per session)	We observed differences before and after rehabilitation in dyspnoea at the end of 6-minute walking test (p=0.005).	64	0.75	Borg Scale	hosp	visit	two months after discharge from hospital (baseline) + 8 weeks
Zha, L. [57]	No	mild cases of COVID-19	60	China	a modified version of rehabilitation exercises retrieved from Chinese martial art Eight-section Brocade and acupressure, aimed to improve the pulmonary function of patients and ease the expectoration process	The pronounced decline in dyspnoea was recorded over time.	54	0.65		hosp	-	at admission, at discharge, 2 weeks after discharge, 4 weeks after discharge

Note: "-" refers to information unclear or not applicable. RCT = randomised controlled trial; hosp = hospitalised patients; non-hosp = non-hospitalised patients; mMRC = modified Medical Research Council Dyspnoea Scale; ICU = intensive care unit; ADL = activities of daily living; LMS = lower limb muscle strength.

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