Bijlage Evidence tabellen

Evidence tabel module 4.2 Beleid - Niet-medicamenteuze behandeling

VRAAG: WAT IS HET EFFECT VAN NIET-MEDICAMENTEUZE INTERVENTIES OP DYSPNEU BIJ MENSEN MET DYSPNEU IN DE PALLIATIEVE FASE MET ILD/LONGFIBROSE, COPD, HARTFALEN, KANKER EN ALS?

Systematische reviews

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
Ahmadi 2025	• Design: systematic review + meta-analysis • Funding: Swedish Research Council (Dnr: 2019–02081), Swedish Heart-Lung foundation (ID: 20200295), Swedish government funding of clinical research (ALF).; CoI: see article • Search date: June 2022 • Databases: Embase, Medline and CENTRAL • Study designs: RCTs • N included studies: N=37 RCTs, of which 35 were relevant (28 on COPD, 7 on interstitial lung disease)	• Eligibility criteria: adults with serious respiratory illness (asthma, bronchiectasis, COPD, cystic fibrosis, interstitial lung diseases, other obstructive lung diseases and pulmonary arterial hypertension) • Exclusion: studies where study participants were treated with supplemental oxygen at the time of randomisation or met the criteria for long-term oxygen or ambulatory oxygen therapy; trials of short-burst oxygen therapy delivered only before or after exertion; if comparator was other types of oxygen therapy (eg high-flow nasal cannulae); if intervention data were not provided or could not be calculated	Oxygen	CRITICAL OUTCOMES • Dyspnoea: ○ At iso-time: 12 laboratory-based exercise studies (N=245), SMD -0.75, 95%CI -1.23 to -0.28, I^2 66% ○ Daily life setting: 1 study, SMD -0.08, 95%CI -0.41 to 0.26 • Quality of life: 14 studies (N=1062), SMD -0.08, 95%CI -0.17 to 0.05, I^2 0% • Exercise tolerance: not reported IMPORTANT OUTCOMES • Physical functioning: not reported	• Selection process by independent reviewers • Unclear if data extraction was done by independent reviewers • Language restrictions unclear • Quality appraisal with RoB1 • Included relevant RCTs on COPD published since 2019: Alison 2019, Lacasse 2020 • Included other relevant RCTs published since 2015: Arizono 2020, Dipla 2021, Khor 2020, Schaeffer 2017, Visca 2018 • No separate analyses per disease type
Ammous 2023	• Design: systematic review + meta-analysis • Funding: National Institute for Health and	• Eligibility criteria: patients with COPD at any stage	Inspiratory muscle training, with or without concomitant pulmonary rehabilitation	CRITICAL OUTCOMES <u>Inspiratory muscle training + pulmonary rehabilitation vs. pulmonary rehabilitation alone</u> • Dyspnoea:	• Review process by independent reviewers • No language restrictions

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
	Care Research (NIHR); CoI: none • Search date: Oct 2022 • Databases: Cochrane Airways trials register, CENTRAL, MEDLINE, Embase, PsycINFO, CINAHL, PEDro ClinicalTrials.gov, WHO International Clinical Trials Registry Platform • Study designs: RCTs • N included studies: N=55 RCTs			○ Borg: 2 studies, MD 0.19, 95%CI -0.42 to 0.79; I² 0% ○ mMRC: 2 studies, MD -0.12, 95%CI -0.39 to 0.14; I² 0% ○ BDI-TDI: no difference ○ MDP: no difference • Quality of life: ○ SGRQ: 7 studies, MD 0.13, 95%CI -0.93 to 1.20; I² 0% ○ CRQ: dyspnoea, 3 studies, MD -0.30, 95%CI -1.90 to 1.29; fatigue, 3 studies, MD 0.28, 95%CI -0.76 to 1.31; emotion, 2 studies, MD -0.63, 95%CI -2.53 to 1.26; mastery, 2 studies, MD -0.05, 95%CI -1.18 to 1.08 ○ CAT: 2 studies, MD 0.13, 95%CI -0.80 to 1.06; I² 50% • Exercise tolerance: ○ 6MWD: 12 studies, MD 5.95, 95%CI -5.73 to 17.63; I² 61% ○ 12MWD: 3 studies, MD 155.77, 95%CI -84.53 to 396.08; I² 79% ○ Wmax: 5 studies, MD -1.01, 95%CI -6.96 to 4.94; I² 25% ○ Exercise time: 3 studies, MD 58.62, 95%CI -25.09 to 142.32; I² 0% ○ VO_2 max: 5 studies, MD -0.01, 95%CI -0.05 to 0.03; I² 0%	• Quality appraisal with RoB2 • Included relevant RCTs published since 2019: Abedi Yekta 2019, Fanfa Bordin 2020, Tounsi 2021, Saka 2021, Saher 2021

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
				<u>Inspiratory muscle training vs. sham or no inspiratory muscle training</u> • Dyspnoea: ○ Borg: 6 studies, MD -0.94, 95%CI -1.36 to -0.51, I² 0% ○ BDI-TDI 'Focal Score': 8 studies, MD 2.98, 95%CI 2.07-3.89; I² 65% ○ mMRC: 4 studies, MD -0.59, 95%CI -0.76 to -0.43; I² 17% • Quality of life: ○ CRQ: dyspnoea, 5 studies, MD 1.63, 95%CI 0.23-3.03; fatigue, 5 studies, MD 1.32, 95%CI 0.08-2.55; emotion, 4 studies, MD 2.64, 95%CI 0.82-4.46; mastery, 4 studies, MD 1.57, 95%CI 0.07-3.06 ○ CAT: 2 studies, MD -2.97; 95%CI -3.85 to -2.10 ○ SF-36: significant difference ○ CCQ: significant difference ○ SGRQ: 6 studies, MD -3.85, 95%CI -8.18 to 0.48; I² 66% • Exercise tolerance: ○ 6MWD: 16 studies, MD 35.71, 95%CI 25.68-45.74; I² 16% ○ VO_2 max: 11 studies, SMD 0.31, 95%CI 0.05-0.57; I² 14% ○ 12MWD: 3 studies, MD -33.31, 95%CI -158.10 to 91.48; I² 59%	

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
				○ Wmax: 7 studies, MD 0.66, 95%CI -6.44 to 7.76; I^2 42% ○ SWT: 2 studies, MD -7.45, 95%CI -92.74 to 77.83 IMPORTANT OUTCOMES • Physical functioning: not reported	
Archontakis Barakakis 2024	• Design: systematic review + meta-analysis • Funding: Hoshi Iryo-Sanki Co. Ltd, NPO Central Japan Lung Study Group, American Thoracic Society, Fisher & Paykel; CoI: none • Search date: June 2023 • Databases: Medline, Embase • Study designs: RCTs • N included studies: N=15 RCTs (11 on COPD, 4 on interstitial lung disease) • Protocol: CRD42022372935	• Eligibility criteria: adult patients with chronic and primary pulmonary disorders causing exertion-induced desaturation • Exclusion: participants with chronic but not primarily pulmonary parenchymal disorders	Oxygen	CRITICAL OUTCOMES <u>COPD</u> • Dyspnoea: ○ Exercise dyspnoea: ▪ Immediate effect: 5 studies (N=200), SMD -0.40, 95%CI -0.76 to -0.04, I^2 31% ▪ During cardiopulmonary rehabilitation for post-rehabilitation dyspnoea: 3 studies (N=139), SMD -0.32, 95%CI -0.66 to 0.01, I^2 0% ▪ Short-term, ambulatory effect: 3 studies (N=382), SMD -0.12, 95%CI -0.52 to 0.27, I^2 66% ○ Baseline dyspnoea: ▪ During cardiopulmonary rehabilitation for post-rehabilitation dyspnoea: 3 studies (N=168), SMD 0.12, 95%CI -0.18 to 0.43, I^2 0% ▪ Short-term, ambulatory effect: 1 study, no significant difference • Quality of life: ○ During cardiopulmonary rehabilitation for post-rehabilitation quality of life: 3 studies	• Review process by independent reviewers • Restricted to English literature • Quality appraisal with RoB2 • Included relevant RCTs published since 2019 for COPD: Alison 2019 • Included other relevant RCTs published since 2015: Visca 2018, Arizono 2020, Dipla 2021

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
				(N=166), SMD 0.03, 95%CI -0.28 to 0.33, I^2 0% ○ Short-term, ambulatory effect: 2 studies (N=323), SMD -0.06, 95%CI -0.28 to 0.15, I^2 0% • Exercise tolerance: ○ Immediate effect on exercise capacity: 6 studies (N=232), SMD 0.42, 95%CI 0.15-0.69, I^2 3%; 6MWD: MD 54.6, 95%CI 19.5-89.7 ○ During cardiopulmonary rehabilitation for post-rehabilitation exercise capacity: 5 studies (N=231), SMD 0.15, 95%CI -0.27 to 0.57, I^2 56%; 6MWD 18.3, 95%CI -33 to 69.7 ○ Short-term, ambulatory effect: 5 studies (N=474), SMD 0.21, 95%CI -0.10 to 0.53, I^2 59%; 6MWD 23.3, 95%CI -11.1 to 58.9 <u>Interstitial lung disease</u> • Dyspnoea: ○ Exercise dyspnoea: ▪ Immediate effect: 4 studies (N=396), SMD -0.17, 95%CI -0.59 to 0.24, I^2 52% ○ Baseline dyspnoea: ▪ Short-term, ambulatory effect: 1 study, significant difference • Quality of life: ○ Short-term, ambulatory effect: 1 study, no significant difference	

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
				• Exercise tolerance: ○ Immediate effect on exercise capacity: 4 studies (N=396), SMD 0.42, 95%CI 0.08-0.75, I^2 57%; 6MWD: MD 48.2, 95%CI 5.5-91 IMPORTANT OUTCOMES • Physical functioning: not reported	
Asano 2020	• Design: systematic review • Funding: not reported; CoI: none • Search date: 2001 – Jan 2019 • Databases: PubMed, Embase, CINAHL, and Web of Science • Study designs: all • N included studies: N=2 RCTs	• Eligibility criteria: patients with chronic heart failure • Exclusion: children, LVAD or ICD populations, sleep disordered and sleep apnea populations	Oxygen	CRITICAL OUTCOMES <u>Long-term oxygen therapy</u>: Clark 2015 • Dyspnoea: better in treatment group at 3 months • Quality of life: MLHFQ, lower in treatment group at 3 months, no significant difference at 6 months • Exercise tolerance: no significant difference <u>Acute oxygen therapy</u>: Park 2010: only patients with NYHA I-II IMPORTANT OUTCOMES • Physical functioning: not reported	• Unclear if review process was done by independent reviewers • Quality appraisal not reported • Restricted to English literature • Included relevant RCTs published since 2015: Clark 2015
Azambuja 2020	• Design: systematic review + meta-analysis • Funding: Coordenação de Aperfei.oamento de Pessoal de Nivel Superior; CoI: none • Search date: Sep 2019 • Databases: MEDLINE, EMBASE, CENTRAL, Physiotherapy Evidence	• Eligibility criteria: patients with heart failure in both decompensation and outpatient care	Inspiratory muscle training	CRITICAL OUTCOMES <u>Isolated inspiratory muscle training</u> • Dyspnoea: 2 studies, MD -1.11, 95%CI -2.97 to 0.75; I^2 70% • Quality of life: 2 studies, MD -20.68, 95%CI -29.03 to -12.32; I^2 0% • Exercise tolerance:	• Review process by independent reviewers • No language restrictions • Quality appraisal with RoB1 • Included relevant RCTs published since 2015: Kawauchi 2017, Moreno 2017, Palau 2018

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
	Database, and LILACS database • Study designs: RCTs • N included studies: N=14 RCTs • Protocol: CRD42017080339			○ 6MWD, 3 studies, mean change from baseline, MD 81.18, 95%CI 9.73-152.63; I^2 47% ○ VO_2 max: 5 studies, MD 2.21, 95%CI -0.10 to 0.45; I^2 88% <u>Inspiratory muscle training combined with another intervention</u> • Dyspnoea: 1 study, significant difference • Quality of life: 4 studies, MD -5.04, 95%CI -11.78 to 1.70; I^2 0% • Exercise tolerance: ○ 6MWD, 2 studies, mean change from baseline, MD 42.5, 95%CI -17.91 to 102.92; I^2 0% ○ VO_2 max: 3 studies, MD -0.00, 95%CI -0.32 to 0.31, I^2 0% IMPORTANT OUTCOMES • Physical functioning: not reported	
Bell 2017	• Design: systematic review + meta-analysis • Funding: not reported; CoI: none • Search date: March 2016 • Databases: Medline, Embase and Cochrane Library • Study designs: all	• Eligibility criteria: adults with any type of interstitial lung disease • Exclusion: case studies	Oxygen	CRITICAL OUTCOMES • Dyspnoea ○ Modified Borg scale at the end of exercise: short-term treatment, 2 studies, MD -0.06, 95%CI -0.24 to 0.13 ○ At rest: VAS, 1 study, 30.2 vs. 48.1, p<0.05 • Quality of life: not reported • Exercise tolerance: ○ Peak work capacity, 1 study, MD 17, 95%CI 10.60-23.40	• Selection process by independent reviewers • Unclear if data extraction was done by independent reviewers • Restricted to English literature • Quality appraisal with RoB1 • Included relevant RCTs published since 2015: -

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
	• N included studies: N=3 RCTs (on short-term treatment)			○ VO_2 max: 1 study, 1.58 vs. 1.32, p<0.05 ○ Cycle endurance time: 1 study, MD 6, 95%CI 3.64-8.26 ○ 6MWD: 1 study, MD 13, 95%CI -24 to 50 IMPORTANT OUTCOMES • Physical functioning: not reported	
Brighton 2019 Maddocks 2019	• Design: systematic review • Funding: part of a project funded by an NIHR Health Services and Delivery research grant (NIHR HSDR 16/02/18); CoI: none • Search date: Jun 2017 • Databases: British Nursing Index, CINAHL, Cochrane Database, DARE, Embase, Medline, PsycInfo, Science Citation Index expanded • Study designs: all • N included studies: N=37; 11 RCTs included in quantitative synthesis • Protocol: CRD42017057508	• Eligibility criteria: adults experiencing breathlessness related to advanced disease, including cancer (advanced local or metastatic), chronic respira- tory disease (GOLD stage III–IV/grade C–D), heart failure (New York Heart Association stage III–IV) or progressive neurological conditions	Holistic breathlessness studies: services where patients are enrolled due to their breathlessness (not their diagnosis); drawing on skills from multiple specialties and disciplines; using a holistic approach encompassing non-pharmacological and pharmacological interventions as indicated; and supporting self-management	CRITICAL OUTCOMES • Dyspnoea: ○ Best dyspnoea: ▪ VAS, 2 studies: difference in median change 5.7 [p=0.0334] and 1.0 [p=0.02], respectively ▪ Unspecified instrument: 1 study with significant difference (p=0.009), 2 studies with no difference ○ Worst dyspnoea: ▪ VAS: 1 study with significant difference (difference in median change 3.5, p=0.05), 1 study with no difference (difference in median change 3.8, p=0.14) ▪ NRS: 2 studies with no difference (MD -0.35 [p=0.61] and 0.41 [p=0.53], respectively) ▪ Unspecified instrument: 1 study with no difference ○ Average dyspnoea: ▪ Unspecified instrument: 1 study with difference (MD 1.2)	• Review process by independent reviewers • No language restrictions • Quality appraisal with RoB1

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
				▪ NRS: 2 studies with no difference (MD -0.33 [p=0.49] and 0.65 [p=0.26], respectively) ○ Dyspnoea on exertion: ▪ NRS: 1 study with no difference (MD -0.73, p=0.13) ▪ Borg: 1 study with no difference ○ Distress due to dyspnoea: NRS, 5 studies, MD -2.30, 95%CI -4.43 to -0.16, p=0.03; I^2 90% ○ Mastery over dyspnoea: CRQ, 4 studies, MD 0.23, 95%CI -0.10 to 0.55, p=0.17; I^2 0% ○ Dyspnoea-12: 1 study, MD 5.19, p=0.026 • Quality of life: 7 studies, no significant difference • Exercise tolerance: not reported IMPORTANT OUTCOMES • Physical functioning: ○ Functional Capacity Scale: 1 study, MD 1.25, p<0.02 ○ WHO Performance Scale: 1 study, difference in median change-2, p=0.02 ○ 3 studies with no difference	
Cai 2024	• Design: systematic review + network meta-analysis	• Eligibility criteria: adults with COPD	Breathing exercises	CRITICAL OUTCOMES <u>Chinese traditional fitness exercises</u>: • Dyspnoea: indirect meta-analysis SMD 0.51, 95%CI -5.19 to 6.20	• Review process by independent reviewers • Limited to English literature

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
	• Funding: none; CoI: none • Search date: October 2022 • Databases: PubMed, Web of Science, Embase, Cochrane Library • Study designs: RCTs • N included studies: N=43 RCTs			• Quality of life: direct meta-analysis, SGRQ, 3 studies, SMD 0.93, 95%CI 0.16-1.71; indirect meta-analysis MD 17.87, 95%CI 7.98-30.00 • Exercise tolerance: direct meta-analysis, 6MWD, 7 studies, SMD 0.80, 95%CI 0.28-1.33; indirect meta-analysis MD 40.87, 95%CI 12.02-69.89 <u>Yoga</u>: • Dyspnoea: direct meta-analysis, Borg, 2 studies, SMD 1.17, 95%CI -0.41 to 2.75; indirect meta-analysis SMD 2.65, 95%BI -1.29 to 6.83 • Quality of life: indirect meta-analysis MD 23.47, 95%CI 4.82-40.92 • Exercise tolerance: direct meta-analysis, 6MWD, 5 studies, SMD 0.48, 95%CI 0.11-0.84; indirect meta-analysis MD 25.56, 95%CI -8.65 to 59.94 <u>Diaphragm breathing</u>: • Dyspnoea: not reported • Quality of life: indirect meta-analysis SMD 11.02, 95%CI -40.71 to 61.59 • Exercise tolerance: direct meta-analysis, 6MWD, 2 studies, SMD -0.13, 95%CI -0.69 to 0.43; indirect meta-analysis MD -51.71, 95%CI -178.34 to 77.29 <u>Diaphragm breathing + pursed-lip breathing</u>: • Dyspnoea: indirect meta-analysis SMD -3.66, 95%CI -9.24 to 2.04	• Quality appraisal with RoB1 • Included relevant RCTs published since 2019: Abedi 2019, Cutrim 2019, Yekefallah 2019, Yudhawati 2019, Kantatong 2020, Yeh 2020, Hasanpour 2021, Jayasheela 2021, Ittinirundorn 2022

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
				• Quality of life: indirect meta-analysis SMD 9.43, 95%CI -8.08 to 26.99 • Exercise tolerance: direct meta-analysis, 6MWD, 4 studies, SMD 1.04, 95%CI 0.24-1.85; indirect meta-analysis MD 28.16, 95%CI -6.19 to 61.21 <u>Pursed-lip breathing</u>: • Dyspnoea: indirect meta-analysis SMD 1.16, 95%CI -4.63 to 7.00 • Quality of life: not reported • Exercise tolerance: not reported <u>Inspiratory muscle training</u>: • Dyspnoea: direct meta-analysis, Borg, 2 studies, SMD 0.51, 95%CI -0.25 to 1.27; indirect meta-analysis SMD -2.44, 95%CI -7.21 to 2.30 • Quality of life: direct meta-analysis, SGRQ, 4 studies, SMD 0.52, 95%CI -0.12 to 1.15; indirect meta-analysis SMD 2.55, 95%CI -6.53 to 11.85 • Exercise tolerance: direct meta-analysis, 6MWD, 10 studies, SMD 0.77, 95%CI 0.25-1.29; indirect meta-analysis MD -35.92, 95%CI -80.52 to 10.26 <u>Singing</u>: • Dyspnoea: not reported • Quality of life: direct meta-analysis, SGRQ, 2 studies, SMD 0.10, 95%CI -0.40 to 0.61; indirect meta-analysis MD 0.88, 95%CI -11.31 to 12.64	

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
				• Exercise tolerance: not reported IMPORTANT OUTCOMES • Physical functioning: not reported	
Cardoso 2020	• Design: systematic review + meta-analysis • Funding: Fundo de Incentivo à Pesquisa of Hospital de Clínicas de Porto Alegre (FIPE/HCPA); CoI: none • Search date: Dec 2019 • Databases: PubMed, EMBASE, PeDRO, and Cochrane databases • Study designs: RCTs • N included studies: N=7 RCTs	• Eligibility criteria: patients with stable mild to very severe COPD and dynamic hyperinflation • Exclusion: CPAP or NIV	Expiratory positive airway pressure	CRITICAL OUTCOMES • Dyspnoea: Borg, 5 studies, MD 0.04, 95%CI -1.33 to 1.42; I^2 86% • Quality of life: not reported • Exercise tolerance: ○ Tolerable limit in an endurance CEPT: 2 studies, MD -214.8, 95%CI -400.2 to -29.4, p=0.02; I^2 0% ○ 6MWD: 3 studies, MD 1.72, 95%CI -35.74 to 39.19, p=0.93; I^2 38% IMPORTANT OUTCOMES • Physical functioning: not reported	• Review process by independent reviewers • Restricted to English and Portuguese literature • Quality appraisal with RoB1 • Included relevant RCTs published since 2019: -
Cramer 2019	• Design: systematic review + meta-analysis • Funding: Erich Rothenfußer Stiftung; CoI: none • Search date: June 219 • Databases: Medline/PubMed, Scopus, and CENTRAL • Study designs: RCTs	• Eligibility criteria: adult patients with COPD	Yoga	CRITICAL OUTCOMES <u>Yoga in general</u>: • Dyspnoea: 3 studies, SMD -0.23, 95%CI -0.69 to 0.23, p=0.33; I^2 43% • Quality of life: 5 studies, SMD 0.57, 95%CI -0.12 to 1.25, p=0.10; I^2 79% • Exercise tolerance: 8 studies, SMD 0.54, 95%CI 0.32-0.77, p<0.00001; I^2 9% <u>Yoga-breathing</u>: (subgroup analysis) • Dyspnoea: 2 studies, SMD -0.43, 95%CI -0.81 to -0.05, I^2 0%	• Review process by independent reviewers • No language restrictions • Quality appraisal with RoB1 • Included relevant RCTs published since 2019: -

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
	• N included studies: N=11 RCTs			• Quality of life: not reported • Exercise tolerance: 4 studies, MD 22.74, 95%CI 7.01-38.48, I^2 0% IMPORTANT OUTCOMES • Physical functioning: not reported	
Da Silva 2025	• Design: systematic review + meta-analysis • Funding: none; CoI: none • Search date: Jan 2023 • Databases: PubMed, CENTRAL, Embase, LILACS, SciELO, and CINAHL • Study designs: RCTs • N included studies: N=7 RCTs • Protocol: CRD42022367746	• Eligibility criteria: adult patients with heart failure • Exclusion: COPD or sleep disorders associated with heart failure	Non-invasive ventilation before and/or during exercise	CRITICAL OUTCOMES • Dyspnoea: ○ Short-term effects: Borg, 2 studies, MD -1.95, 95%CI -2.88 tot -1.01, I^2 0% • Quality of life: ○ Long-term treatment: MLHFQ, 3 studies, MD -8.94, 95%CI -20.38 to 2.51; p=0.13, I^2 74% • Exercise tolerance: ○ Short-term effects: 6MWD, 2 studies, MD 68.61, 95%CI 5.69-131.54; p=0.03, I^2 34% ○ Long-term treatment: 6MWD, 2 studies; MD 41.72, 95%CI 2.15-81.29; p=0.04, I^2 0% IMPORTANT OUTCOMES • Physical functioning: not reported	• Review process by independent reviewers • No language restrictions • Quality appraisal with RoB2 • Included relevant RCTs published since 2015: Araujo 2019, Bittencourt 2017, Di Leone 2023, Gomes Neto 2018
Dy 2020 Gupta 2021	• Design: systematic review + meta-analysis • Funding: AHRQ; CoI: none • Search date: May 2020 • Databases: PubMed, Embase, Cinahl, ISI	• Eligibility criteria: adult patients with advanced cancer (unlikely to be cured or unlikely to be controlled with treatment) and breathlessness • Exclusion: studies with fewer than 10 patients enrolled in each arm, studies with mixed populations in which the	Fan vs. usual care or sham 3 RCTs, N=118	CRITICAL OUTCOMES • Dyspnoea: ○ SMD -2.09, 95%CI -3.81 to -0.37, I^2 94.3% • Quality of life: not reported • Exercise tolerance: not reported IMPORTANT OUTCOMES	• Review process by independent reviewers • Limited to English literature • Quality appraisal with RoB2 • Included relevant RCTs published since 2015: Wong 2017, Kako 2018, Ting 2020

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
	Web of Science, CENTRAL • Study designs: RCTs and observational studies • N included studies: N=48 RCTs (29 on non-pharmacological interventions)	percentage of patients with cancer was less than 50%		• Physical functioning: not reported	
			Compressed air vs. standard supplemental oxygen 4 RCTs, N=136	CRITICAL OUTCOMES • Dyspnoea: ○ Booth 1996: VAS (0-100), no between group difference (p value not reported) ○ Bruera 1993: VAS (0-100), MD 20.5, 95%CI 13.5-27.6, in favour of oxygen ○ Bruera 2003: NRS (0-10), no statistically significant difference in breathlessness between groups (p=0.52) ○ Philip 2006: VAS (0-100), SMD -0.23, 95%CI -0.79 to 0.31 • Quality of life: not reported • Exercise tolerance: ○ 6MWD: 1 study, N=33, no statistically significant between groups differences (p=0.95) IMPORTANT OUTCOMES • Physical functioning:	• Included relevant RCTs published since 2015: -

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
				○ Physical function subscale (0-100): 1 study, N=33, no statistically significant between group differences (p=0.64)	
			Bi-level ventilation vs. high-flow nasal cannula 1 RCT, N=30	CRITICAL OUTCOMES • Dyspnoea: ○ NRS (0-10): SMD 0.37, 95%CI -0.34 to 1.10 ○ Modified Borg scale (0-10): SMD -0.18, 95%CI -0.90 to 0.53 ○ Proportion of patients who reported improvement in breathlessness: RR 0.85, 95%CI 0.59-1.23 • Quality of life: not reported • Exercise tolerance: not reported IMPORTANT OUTCOMES • Physical functioning: not reported	• Included relevant RCTs published since 2015: -
			Bi-level ventilation vs. standard supplemental oxygen 1 RCT, N=200	CRITICAL OUTCOMES • Dyspnoea: ○ Borg scale (0-10): significant improvement in favour of bi-level ventilation, p=0.0012; estimated slope difference -0.58 (95%CI -0.92 to -0.23) over the study period of 48 hours • Quality of life: not reported • Exercise tolerance: not reported IMPORTANT OUTCOMES • Physical functioning: not reported	• Included relevant RCTs published since 2015: -
			Psychological interventions	CRITICAL OUTCOMES • Dyspnoea:	• Included relevant RCTs published since 2015: -

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
			2 RCTs, N=543	○ Bordeleau 2003: EORTC QLQ-C30 at 12m, SMD -0.02, 95%CI -0.30 to 0.27; p=0.96 ○ McMillan 2007: Dyspnea Intensity Scale, p=0.771 • Quality of life: ○ Bordeleau 2003: EORTC QLQ-C30 at 12m, SMD 0.15, 95%CI -0.13 to 0.44; p= 0.84 ○ McMillan 2007: Hospice Quality of Life Index [HQLI]; p=0.246 • Exercise tolerance: not reported IMPORTANT OUTCOMES • Physical functioning: ○ Bordeleau 2003: EORTC QLQ-C30 at 12m, SMD -0.22, 95%CI -0.51 to 0.07, p=0.83	
			Respiratory training 1 RCT, N=47	CRITICAL OUTCOMES • Dyspnoea: not reported • Quality of life: CRDQ at 8 weeks, change from baseline 8.8 vs. 6.8 • Exercise tolerance: not reported IMPORTANT OUTCOMES • Physical functioning: not reported	• Included relevant RCTs published since 2015: Molassiotis 2015
			Music therapy 1 RCT, N=40	CRITICAL OUTCOMES • Dyspnoea: ○ ESAS (0-10): statistically significant improvement in music group (p=0.042), but not in control group; no between group differences reported	• Included relevant RCTs published since 2015: Ramirez 2018

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
				• Quality of life: not reported • Exercise tolerance: not reported IMPORTANT OUTCOMES • Physical functioning: not reported	
Fan 2024	• Design: systematic review + meta-analysis • Funding: Jilin Province Health Special Project Discipline Talent Development Project [grant number-2020SCZT055] and the Jilin Province Health Science and Technology Capability Improvement Project [grant number2021JC041]; CoI: none • Search date: Feb 2024 • Databases: PubMed, Web of Science, Medline, Embase, Cochrane Library, CINAHL, China National Knowledge Infrastructure (CNKI), WanFang Data, and China Science and Technology Journal Database (CQVIP) • Study designs: RCTs	• Eligibility criteria: adult patients with interstitial lung diseases • Exclusion: patients who have undergone lung transplants	Breathing exercises	CRITICAL OUTCOMES • Dyspnoea: ○ MRC or mMRC, 7 studies, MD -0.50, 95%CI -0.77 to -0.22 ▪ Compared to usual care: 5 studies, MD -0.36, 95%CI -0.60 to -0.12 ▪ Compared to exercise therapy: 2 studies, MD -0.91, 95%CI -2.04 to 0.23 ○ Borg: 3 studies compared to usual care, MD -0.13, 95%CI -1.42 to 1.16 • Quality of life: SGRQ, 13 studies, MD -6.53, 95%CI -8.72 to -4.34 ○ Compared to usual care: 11 studies, MD -7.46, 95%CI -9.66 to -5.27 ○ Compared to exercise therapy: 2 studies, MD 0.51, 95%CI -9.07 to 10.09 • Exercise tolerance: 6MWD, 14 studies, MD 32.65, 95%CI 14.77-50.53 ○ Compared to usual care: 12 studies, MD 32.55, 95%CI 13.18-51.92 ○ Compared to exercise therapy: 2 studies, MD 34.36, 95%CI -20.73 to 89.46 IMPORTANT OUTCOMES	• Review process by independent reviewers • Restricted to English or Chinese articles • Quality appraisal with RoB1 • Included relevant RCTs published since 2015: Bassi 2023, Cao 2023, Ding 2018, Essam 2022, Hun Kim 2023, Jarosch 2020, Jiang 2022, Li 2015, Liu 2017, Ma 2016, Ma 2017, Parisien – La Salle 2019, Shang 2022, Shen 2021, Wang 2020, Wang 2023, Wei 2023, Xiao 2019, Zaki 2023, Zuo 2016

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
	• N included studies: N=25 RCTs • Protocol: CRD42022320912			• Physical functioning: not reported	
Farver-Vestergaard 2022	• Design: systematic review + meta-analysis • Funding: not reported; CoI: see article • Search date: Feb 2020 • Databases: PubMed, PsycINFO, Embase,Web of Science, Cochrane Library, and CINAHL • Study designs: RCTs • N included studies: N=35 RCTs • Protocol: CRD42020170083	• Eligibility criteria: adult patients with COPD • Exclusion: patients with comorbid physical conditions	Individual or group-based psychosocial interventions	CRITICAL OUTCOMES • Dyspnoea: 16 studies; effect size 0.19, 95%CI -0.02 to 0.40; I^2 68% • Quality of life: not reported • Exercise tolerance: 12 studies; effect size 0.27, 95%CI 0.03-0.50; I^2 63% IMPORTANT OUTCOMES • Physical functioning: not reported	• Review process by independent reviewers • Limited to English literature • Quality appraisal with Jadad instrument • Included relevant RCTs published since 2019: Lopez-Lopez 2019, Tan 2019
Feng 2024	• Design: systematic review + meta-analysis • Funding: National Natural Science Foundation of China under Grant number 72071004, number 72471006 and number 71601004, National Key R&D Program of China under Grant number 2020YFC2008805 and number No.	• Eligibility criteria: patients with stable COPD • Exclusion: unstable clinical status, serious organic diseases, or complications; patients with hearing impairment, severe cognitive dysfunction, etc., who could not cooperate	Music therapy	CRITICAL OUTCOMES <u>Active music therapy</u>: singing • Dyspnoea: 3 studies; MD -0.08, 95%CI -0.31 to 0.16; p=0.52, I^2 0% • Quality of life: 4 studies, SMD -1.17, 95%CI -2.37 to 0.02; p=0.05, I^2 95% • Exercise tolerance: 3 studies, SMD 0.10, 95%CI -0.48 to 0.68; p=0.73, I^2 74% <u>Passive music therapy</u>: listening to music	• Unclear if selection process was done by independent reviewers • Data extraction by two independent reviewers • Quality appraisal with RoB2 • Restricted to English or Chinese articles • Included relevant RCTs published since 2019: Liu 2019, Guo 2020, Xiao Jie

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
	2020YFC2008800; CoI: none • Search date: June 2024 • Databases: Cochrane Library, Web of Science, PubMed, Embase, CINAHL, CNKI, CBM, WanFang Data and VIP databases • Study designs: RCTs • N included studies: N=11 RCTs • Protocol: CRD42022369531			• Dyspnoea: 3 studies, SMD -0.15, 95%CI -0.95 to 0.64; p=0.70, I^2 75% • Quality of life: 3 studies, SMD -0.83, 95%CI -1.23 to -0.44; p<0.001, I^2 0% • Exercise tolerance: 3 studies, SMD 1.54, 95%CI 0.55 to 2.54; p=0.002, I^2 78% IMPORTANT OUTCOMES • Physical functioning: not reported	2021, Kaasgaard 2022, Cai 2022
Filipe 2024	• Design: systematic review • Funding: none; CoI: none • Search date: 2011-2022 • Databases: PubMed, Cochrane Library, and Web of Science • Study designs: all • N included studies: N=1 RCT	• Eligibility criteria: adults with ALS or motor neuron disease experiencing breathlessness	Interventions for controlling dyspnoea	CRITICAL OUTCOMES • Dyspnoea: significant effect, no data reported • Quality of life: significant effect, no data reported • Exercise tolerance: not reported IMPORTANT OUTCOMES • Physical functioning: not reported	• Review process by independent reviewers • Limited to English literature • Quality appraisal with RoB2 • Included relevant RCTs published since 2015: Veronese 2017
Franco de Macedo 2024	• Design: systematic review + meta-analysis • Funding: not reported; CoI: none	• Eligibility criteria: patients with mild to very severe COPD and hyperinflation	Expiratory positive airway pressure	CRITICAL OUTCOMES • Dyspnoea: 6 studies, SMD -1.17, 95%CI -1.68 to -0.66; I^2 75% • Quality of life: not reported	• Review process by independent reviewers • No language restrictions

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
	• Search date: Jan 2023 • Databases: PubMed, Embase, CENTRAL, Physiotherapy Evidence Database, Literatura Latino-Americana e do Caribe em Ciências da Saude, ScienceDirect, and Scopus • Study designs: (quasi) RCTs • N included studies: N=7 RCTs • Protocol: CRD42020190667			• Exercise tolerance: 6MWD, 5 studies, MD 30.1, 95%CI 19.2-41.0; I^2 73% IMPORTANT OUTCOMES • Physical functioning: not reported	• Quality appraisal with RoB1 • Included relevant RCTs published since 2019: -
Hanada 2020	• Design: systematic review + meta-analysis • Funding: none; CoI: none • Search date: Jan 2019 • Databases: MEDLINE, Embase, CENTRAL, SPORTDiscus, PubMed and PEDro • Study designs: RCTs, prospective studies with pre-post design • N included studies: N=4 RCTs • Protocol: CRD42018091411	• Eligibility criteria: patients with idiopathic pulmonary fibrosis • Exclusion: connective tissue disorders, extraparenchymal causes of restriction	Aerobic and breathing exercises (diaphragmatic or pursed lip)	CRITICAL OUTCOMES • Dyspnoea: ○ Aerobic exercise + breathing exercise vs. control: 1 study, MD -5.30, 95%CI -7.67 to -2.93 • Quality of life: ○ Aerobic exercise + breathing exercise vs. control: 1 study, MD -9.70, 95%CI -13.41 to -5.99 • Exercise tolerance: ○ Aerobic exercise + breathing exercise vs. control: ▪ 6MWD: 1 study, MD 81.00, 95%CI 38.56-123.44	• Review process done by independent reviewers • Limited to English and Japanese literature • Downs and Black checklist for quality appraisal • Included relevant RCTs published since 2015: Dowman 2017

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
				▪ Peak work rate: 1 study, MD 22.10, 95%CI 15.39-28.81 ○ Aerobic exercise + inspiratory muscle training vs. control: ▪ 6MWD: 1 study, MD 47.70, 95%CI 42.33-53.07 ▪ Peak work rate: 1 study, MD 9.40, 95%CI 8.26-10.54 ▪ Endurance time: 1 study, MD 624, 95%CI 433.82-814.18 IMPORTANT OUTCOMES • Physical functioning: not reported	
Hasegawa 2023	• Design: systematic review + meta-analysis • Funding: Japanese Society for Palliative Medicine; CoI: one author with several conflicts • Search date: Sep 2019 • Databases: CENTRAL, Medline, Embase, Ichushi-Web of the Japan Medical Abstracts Society • Study designs: RCTs • N included studies: N=43 RCTs	• Eligibility criteria: adults with any type of advanced progressive illness with dyspnea • Exclusion: RCTs wherein acute respiratory failure was involved in the development of dyspnea and those exploring dyspnea in the emergency department and/or intensive care unit; high-flow nasal cannula oxygen therapy and non-invasive ventilation	Non-invasive supplemental oxygen therapy (nasal cannula, medium concentration, or fixed concentration Venturi or non-rebreather masks)	CRITICAL OUTCOMES • Dyspnoea: ○ Supplemental oxygen during exercise: 16 studies (N=902), SMD -0.57, 95%CI -0.77 to -0.38, I² 43% ○ Supplemental oxygen during daily activities: 2 studies (N=191), MD 1.34, 95%CI -0.35 to 3.04, I² 0% ○ Supplemental oxygen during rehabilitation: 4 studies (N=168), MD 0.16, 95%CI -0.75 to 1.06, I² 52% • Quality of life: ○ Supplemental oxygen during exercise: 2 studies (N=287), SMD 0.17, 95%CI -0.06 to 0.40, I² 0% ○ Supplemental oxygen during daily activities: 2 studies (N=227), SMD 0.12, 95%CI -0.14 to 0.38, I² 0%	• Review process done by independent reviewers • Unclear if language restriction was applied • Quality appraisal with RoB1 • Included relevant RCTs published since 2015: Alison 2019, Visca 2018, Dowman 2017, Jarosch 2017, Neunhäuserer 2016, Clark 2015, Spielmanns 2015

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
	• Protocol: CRD42020161838			○ Supplemental oxygen during rehabilitation: 2 studies (N=121), SMD 0.06, 95%CI -0.29 to 0.42, I² 0% • Exercise tolerance: ○ Supplemental oxygen during exercise: 12 studies (N=934), SMD 0.23, 95%CI 0.10 to 0.36, I² 0% ○ Supplemental oxygen during daily activities: 2 studies (N=191), SMD 0.01, 95%CI -0.28 to 0.29, I² 0% ○ Supplemental oxygen during rehabilitation: 3 studies (N=155), SMD -0.07, 95%CI -0.54 to 0.40, I² 45% IMPORTANT OUTCOMES • Physical functioning: not reported	
Kako 2023	• Design: systematic review • Funding: JSPS KAKENHI (grant number 21H03236); CoI: none • Search date: Jan 2022 • Databases: PubMed, Cinahl, CENTRAL, Ichushi-Web of the Japan Medical Abstract Society Databases • Study designs: RCTs, prospective studies	• Eligibility criteria: adult patients with cancer (at least 18y) • Exclusion: papers involving more than 20% of participants without cancer	Fan 4 RCTs, N=106	CRITICAL OUTCOMES • Dyspnoea: ○ Wong 2017: mean NRS scores changed by -1.53 ± 1.06 in the experimental group vs. -0.13 ± 1.06 in the control group (p = 0.001) ○ Kako 2018: mean NRS score reduction changed by -1.35 (95%CI -1.86 to 0.84) in the fan-to-face group vs. -0.1 (95%CI -0.53 to 0.33) in the fan-to-legs group ($p < 0.001$) ○ Ting 2020: mean change in the MBS score was significantly higher in the intervention group than in the placebo group (2.79 vs. 0.15; p<0.0001). ○ Kocatepe 2021: MBS scores of the experimental group on days 1, 7, and 14 of handheld fan use were statistically	• Review process by independent reviewers • Limited to English and Japanese literature • No quality appraisal reported • Included relevant RCTs published since 2015: Wong 2017, Kako 2018, Ting 2020, Kocatepe 2021

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
	• N included studies: N=27 RCTs			significantly lower than those of the control group (p<0.01) • Quality of life: not reported • Exercise tolerance: not reported IMPORTANT OUTCOMES • Physical functioning: not reported	
			Respiratory training 2 RCTs, N=68	CRITICAL OUTCOMES • Dyspnoea: ○ Barton 2010: mean NRS score reduction changed by 3.0 in the three-session arm vs. 1.0 in the single-session arm ○ Molassiotis 2015: modified Borg, comparing the scores at each time point between the two groups, the Borg score in the no-IMT group was significantly higher (p=0.029) than that in the IMT group (2.5 ± 1.0) at week 8 • Quality of life: not reported • Exercise tolerance: not reported IMPORTANT OUTCOMES • Physical functioning: not reported	• Included relevant RCTs published since 2015: Molassiotis 2015
			Yoga 1 RCT, N=92	CRITICAL OUTCOMES • Dyspnoea: EORTC QLQ-C30, no significant differences were observed between both groups • Quality of life: not reported • Exercise tolerance: not reported IMPORTANT OUTCOMES	• Included relevant RCTs published since 2015: Lötzke 2016

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
				• Physical functioning: not reported	
			Abdominal massage 1 RCT, N=80	CRITICAL OUTCOMES • Dyspnoea: NRS, no change • Quality of life: not reported • Exercise tolerance: not reported IMPORTANT OUTCOMES • Physical functioning: not reported	• Included relevant RCTs published since 2015: Wang 2015
			Education 2 RCTs, N=163	CRITICAL OUTCOMES • Dyspnoea: ○ Choratas 2020: the intervention group showed an improvement in breathlessness (modified Borg) between baseline and final assessments; however, no significant difference was found in the control group ○ Yates 2020: for the primary outcome of worst breathlessness, no significant difference was observed in change over time between the groups (p=0.70); however, analysis of secondary outcomes revealed significant differences between the groups in average breathlessness; breathlessness, on average, improved only for the intervention group (p=0.018) • Quality of life: not reported • Exercise tolerance: not reported IMPORTANT OUTCOMES • Physical functioning: not reported	• Included relevant RCTs published since 2015: Choratas 2020, Yates 2020
			Psychosocial support 1 RCT, N=119	CRITICAL OUTCOMES • Dyspnoea: breathlessness as a subscale of EORTC QLQ-C30 worsened over time in both	• Included relevant RCTs published since 2015: -

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
				groups; however, during follow-up, patients in the INS (individual nurse support) group had lower levels of problems concerning 'breathlessness' (p=0.001) at the 1-month assessment than those in the standard care group • Quality of life: not reported • Exercise tolerance: not reported IMPORTANT OUTCOMES • Physical functioning: not reported	
Kwekkeboom 2016	• Design: systematic review • Funding: National Institute of Nursing Research of the National Institutes of Health under awards number R01NR013468 (Kwekkeboom, PI) and R00NR012773 (Bratzke, PI); CoI: not reported • Search date: Dec 2014 • Databases: Medline, Cinahl, PsycINFO • Study designs: all • N included studies: N=13, of which 6 RCTs (2 relevant)	Eligibility criteria: adults with heart failure	Cognitive-behavioural therapy	CRITICAL OUTCOMES • Dyspnoea: ○ Swanson 2009: biofeedback-assisted relaxation vs. attention control, no significant difference ○ Beniaminovitz 2002: guided imagery vs. exercise, no significant difference • Quality of life: ○ Swanson 2009: biofeedback-assisted relaxation vs. attention control, no significant difference ○ Beniaminovitz 2002: guided imagery vs. exercise, no significant difference • Exercise tolerance: not reported IMPORTANT OUTCOMES • Physical functioning: not reported	• Review process done by independent reviewers • Restricted to English language • Yates' rating scale for quality appraisal • Included relevant RCTs published since 2015: -
Li H 2022	• Design: systematic review + meta-analysis	• Eligibility criteria: adults with heart failure	Inspiratory muscle training	CRITICAL OUTCOMES • Dyspnoea: (narrative)	• Review process by independent reviewers

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
	• Funding: Huangpu District Science and Technology Project (HKW201414); CoI: none • Search date: Jan 2022 • Databases: PubMed, EMBASE, Cochrane Library, CNKI, Wanfang and VIP databases • Study designs: RCT • N included studies: N=17 RCTs			○ Borg: 4 studies, significant differences ○ mMRC: 2 studies with discordant results • Quality of life: ○ MLHFQ: 7 studies, MD -13.34, 95%CI -20.42 to -6.26; I^2 91% ○ SF-36: 3 studies, no significant differences ○ Self-made scale: 1 study, no significant difference • Exercise tolerance: ○ 6MWD: 4 studies, MD 74.45, 95%CI -12.88 to 161.79; I^2 84% ○ VO_2 max: 9 studies, MD 2.53, 95%CI 1.54-3.51; I^2 74% IMPORTANT OUTCOMES • Physical functioning: not reported	• Unclear language restriction • Quality appraisal with RoB1 • Included relevant RCTs published since 2015: Cheng 2015, Kinugasa 2020, Palau 2018, Palau 2019
Li JY 2025	• Design: systematic review and network meta-analysis • Funding: Construction and Practice of Exercise Rehabilitation Programme for Patients With Chronic Heart Failure Based on HAPA Model (No. HLZD202407); CoI: none • Search date: May 2024	• Eligibility criteria: adults with heart failure	Exercise treatment	CRITICAL OUTCOMES <u>Inspiratory muscle training</u> • Dyspnoea: ○ Inspiratory muscle training alone: MD -0.87, 95%CI -1.27 to -0.47 ○ Inspiratory muscle training + high-intensity interval training: MD -1.58, 95%CI -2.64 to -0.52 ○ Inspiratory muscle training + high-intensity interval training + resistance training: MD -1.29, 95%CI -2.34 to -0.24 • Quality of life:	• Review process by independent reviewers • Quality appraisal with RoB1 • Limited to English literature • Included relevant RCTs published since 2015: Tanriverdi 2023, Trevizan 2021, Sadek 2022, Gaikar 2023, Laoutaris 2021, Hossein Pour 2020, Sadek 2024, Palau 2019, Sadek 2023, Jain 2022, Hägglund 2017

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
	• Databases: PubMed, Embase and the Cochrane Library • Study designs: RCTs • N included studies: N=60 RCTs			○ Inspiratory muscle training alone: MD -12.83, 95%CI -18.62 to -7.04 ○ Inspiratory muscle training + high-intensity interval training: MD -19.28, 95%CI -26.42 to -12.14 ○ Inspiratory muscle training + aerobic training: MD -17.72, 95%CI -22.98 to -12.47 ○ Inspiratory muscle training + aerobic + resistance training: MD -16.07, 95%CI -21.08 to -11.07 • Exercise tolerance: ○ 6MWD: ▪ Inspiratory muscle training alone: MD 65.55, 95%CI 10.75-120.34 ▪ Inspiratory muscle training + high-intensity interval training: MD 107.81, 95%CI 15.18-200.43 ▪ Inspiratory muscle training + aerobic + resistance training: MD 88.36, 95%CI 7.87-168.84 ○ VO_2 max: ▪ Inspiratory muscle training alone: MD 3.51, 95%CI 1.09-5.93 ▪ Inspiratory muscle training + aerobic + resistance training: MD 3.75, 95%CI 0.47-7.03 <u>Tai Chi</u> • Dyspnoea: not reported	

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
				• Quality of life: MLHFQ, MD -10.87, 95%CI -21.49 to -0.25 • Exercise tolerance: ○ 6MWD: MD -9.08, 95%CI -108.10 to 89.94 ○ VO_2 max: MD -0.70, 95%CI -4.70 to 3.30 <u>Yoga</u> • Dyspnoea: not reported • Quality of life: MLHFQ, MD -3.90, 95%CI -8.18 to 0.37 • Exercise tolerance: not reported IMPORTANT OUTCOMES • Physical functioning: not reported	
Lin 2024	• Design: systematic review and meta-analysis • Funding: grant of the Taipei Medical University (TMU112-AE1-B10) in Taiwan; CoI: none • Search date: April 2024 • Databases: PubMed, EMBASE, Scopus, and Cochrane Library • Study designs: RCTs • N included studies: N=14 RCTs	• Eligibility criteria: patients with fibrotic interstitial lung disease	Oxygen therapy	CRITICAL OUTCOMES • Dyspnoea: 11 studies, MD -0.75, 95%CI -1.07 to -0.42; I^2 15% • Quality of life: not reported • Exercise tolerance: ○ Exercise duration: 5 studies, MD 122.15, 95%CI 61.40-182.89; I^2 0% ○ Exercise distance: 5 studies, 15.17, 95%CI -4.30 to 34.64; I^2 0% IMPORTANT OUTCOMES • Physical functioning: not reported	• Unclear if selection process was done by independent reviewers • Data extraction by two independent reviewers • Unclear language restriction • Quality appraisal with RoB1 • Included relevant RCTs published since 2015: Visca 2018, Badenes-Bonet 2021, Harada 2022, Suzuki 2020, Arizono 2020, Cournoyer 2020, Dipla 2021, Dowman 2017, Khor 2020, Kim 2023, Marillier 2021, Ventura 2023, Yanagita 2024

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
	• Protocol: 42023410696				
Liu 2019	• Design: systematic review and meta-analysis • Funding: unclear; CoI: none • Search date: Apr 2018 • Databases: Cochrane Library, Web of Science, Embase, PubMed, Weipu, Wanfang, and Chinese National Knowledge Infrastructure • Study designs: RCTs • N included studies: N=15 RCTs	• Eligibility criteria: patients were diagnosed with lung cancer, or a mixed cancer cohort that included lung cancer	Breathing exercises	CRITICAL OUTCOMES • Dyspnoea: 1 study, N=36, SMD -0.72, 95%CI -1.40 to -0.05 • Quality of life: not reported • Exercise tolerance: not reported IMPORTANT OUTCOMES • Physical functioning: not reported	• Review process by independent reviewers • Limited to English and Chinese literature • Quality appraisal with RoB1 • Included relevant RCTs published since 2015: Molassiotis 2015

Liu 2021	• Design: systematic review and meta-analysis
	• Funding: National Key Research and Development Program of China (No. 2018YFC1313600), the National Natural Science Foundation of China (Nos. 81570081 and 81770083), and the Natural Science Foundation of Fujian Province (No. 2017J01140); CoI: none
		• Eligibility criteria: patients with COPD	Tai Chi	CRITICAL OUTCOMES
				
				<u>Tai Chi vs. usual care</u>
				• Dyspnoea: not reported
				• Quality of life:
				  ○ SGRQ: 3 studies, MD -9.22, 95%CI -14.67 to -3.77, p=0.009; I^2 64%
				  ○ CRQ: 2 studies, MD 1.60, 95%CI 0.89-2.30, p<0.00001; I^2 0%
				  ○ CAT: 4 studies, MD -3.66, 95%CI -4.55 to -2.78, p<0.00001; I^2 18%
				• Exercise tolerance: 6MWD, 8 studies, MD 19.25, 95%CI 14.71-23.80, p<0.00001; I^2 79%
					• Unclear if selection process was done by independent reviewers
					• Data extraction by two independent reviewers
					• No language restrictions
					• Quality appraisal with RoB1
					• Included relevant RCTs published since 2019: -

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
	• Search date: Sep 2019 • Databases: PubMed, CENTRAL, Embase, CNKI, China Biology Medicine, Wangfang Data • Study designs: RCTs • N included studies: N=23 RCTs			<u>Tai Chi vs. experimental control</u> • Dyspnoea: not reported • Quality of life: SGRQ, 4 studies, MD -1.82, 95%CI -4.29 to 0.66, p=0.15; I^2 0% • Exercise tolerance: 6MWD, 5 studies, MD 14.15, 95%CI 3.76-24.53, p=0.008; I^2 0% <u>Tai Chi vs. other therapy</u> • Dyspnoea: not reported • Quality of life: SGRQ, 2 studies, MD -5.31, 95%CI -9.13 to -1.48, p=0.007; I^2 0% • Exercise tolerance: 6MWD, 3 studies, MD 16.72, 95%CI -2.13 to 35.58, p=0.08; I^2 54% IMPORTANT OUTCOMES • Physical functioning: not reported	
Lopez-Lois 2021	• Design: systematic review • Funding: SEPAR (Spanish Society of Chest Diseases and Thoracic Surgery); CoI: none • Search date: 2018 • Databases: PubMed, PsycInfo • Study designs: all • N included studies: N=12, of which 4 RCTs on COPD	• Eligibility criteria: adults with asthma or COPD • Exclusion: other pulmonary diseases	Mindfulness	CRITICAL OUTCOMES • Dyspnoea: ○ Mularski 2009: no significant effect of mindfulness-based breathing exercise (Dyspnea Rest Visual Analog Scale p=0.81, Dyspnea Activity Visual Analog Scale p=0.82) ○ Perkins-Porras 2018: no significant effect • Quality of life: ○ Chan 2015: CRQ – emotional function, no significant effect of mindfulness-based stress reduction (p=0.06) • Exercise tolerance: not reported	• One reviewer did the selection and discussed this with the other reviewers • Data extraction was done by pairs of reviewers • Unclear language restriction • No quality appraisal reported • Narrative discussion • Included relevant RCTs published since 2019: -

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
				IMPORTANT OUTCOMES • Physical functioning: not reported	
Marjanovic 2024	• Design: systematic review and meta-analysis • Funding: not reported; CoI: Fisher and Paykel society (one author) • Search date: Mar 2024 • Databases: MEDLINE, Web of Science, and the Cochrane Library • Study designs: RCTs, observational studies • N included studies: N=3 RCTs • Protocol: CRD42024514051	• Eligibility criteria: adult patients with acute respiratory failure due to suspected or confirmed acute heart failure	High-flow oxygen vs. standard oxygen treatment or non-invasive ventilation	CRITICAL OUTCOMES • Dyspnoea: 2 studies, MD -0.13, 95%CI -1.25 to 0.99 • Quality of life: not reported • Exercise tolerance: not reported IMPORTANT OUTCOMES • Physical functioning: not reported	• Review process by independent reviewers • Restricted to English or French literature • Quality appraisal with RoB2 • Included relevant RCTs published since 2015: Haywood 2019, Osman 2021, Marjanovic 2024

McNamara 2017	• Design: systematic review and meta-analysis
	• Funding: none; CoI: none
	• Search date: Aug 2017
	• Databases: CENTRAL, Medline, Embase, PsycINFO, CINAHL, AMED
	• Study designs: RCTs
		• Eligibility criteria: adults with stable COPD	Singing	CRITICAL OUTCOMES
				• Dyspnoea: BDI, 1 study, MD 0.40, 95%CI -0.65 to 1.45
				• Quality of life:
				  ○ SGRQ: 2 studies, MD -0.82, 95%CI -4.67 to 3.02; p=0.68, I^2 0%
				  ○ SF-36 MCS: 2 studies, MD5.42, 95%CI -3.90 to 14.74; p=0.25, I^2 31%
				  ○ SF-36 PCS: 2 studies, MD 12.64, 95%CI 5.50 to 19.77; p=0.0005, I^2 0%
					• Review process by independent reviewers
					• No language restrictions
					• Quality appraisal with RoB1
					• Included relevant RCTs published since 2019: -

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
	• N included studies: N=3 RCTs			• Exercise tolerance: ISWT, 2 studies, MD -9.26, 95%CI -43.10 to 24.57; p=0.59, I^2 24% IMPORTANT OUTCOMES • Physical functioning: not reported	
Moya-Gallardo 2024	• Design: systematic review and meta-analysis • Funding: Physiotherapy Program, Department of Health Sciences Pontificia Universidad Católica de Chile (grant number 4); CoI: none • Search date: April 2023 • Databases: CENTRAL, PubMed, Embase, Epistemonikos, Lilacs, PEDro, ICTRP, ClinicalTrials.gov • Study designs: RCTs • N included studies: N=17 RCTs • Protocol: CRD42022336263	• Eligibility criteria: adults with chronic respiratory diseases that affected the respiratory system; that met the criteria for admission or were already admitted to pulmonary rehabilitation according to international guidelines	High-flow oxygen during exercise	CRITICAL OUTCOMES • Dyspnoea: mMRC, 2 studies on COPD, WMD 0.06, 95%CI -0.00 to 0.11, p=0.06, I^2 0% • Quality of life: CAT, 2 studies on COPD, WMD -0.06, 95%CI -0.65 to 0.53, p=0.84, I^2 0% • Exercise tolerance: ○ Exercise time during Constant Work Rate Exercise Test (CWRET) after multiple training sessions, all disease types: 2 studies, WMD 170.94, 95%CI 54.71-287.17, p=0.004, I^2 0% ○ Exercise time during CWRET after a single exercise session, all disease types: 10 studies, WMD 72.10, 95%CI 28.96-115.24, p=0.001, I^2 0% ○ Exercise time during CWRET, COPD: 6 studies, WMD 81.46, 95%CI 22.46-140.47, p=0.007, I^2 0% ○ Exercise time during CWRET, interstitial lung diseases: 3 studies, WMD 72.29, 95%CI -30.36 to 174.93, p=0.17, I^2 0% ○ 6MWD after multiple training sessions: 2 studies, WMD 37.28, 95%CI -0.47 to 75.03, p=0.05, I^2 0% IMPORTANT OUTCOMES	• Review process by independent reviewers • No language restrictions • Quality appraisal with RoB2 • Included relevant RCTs on COPD published since 2019: Bitos 2021, Carlucci 2021, Chao 2021, Chen 2021, Dell'Era 2019, Fang 2020, Sanguanwong 2020, Vitacca 2020 • Included other relevant RCTs published since 2015: Badenes 2021, Chihara 2022, Harada 2022, Hui 2020, Prieur 2019, Suzuki 2020

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
				• Physical functioning: not reported	
Nolan 2023	• Design: systematic review and meta-analysis • Funding: see article; CoI: see article • Search date: Feb 2023 • Databases: Cochrane Database of Systematic Reviews, Central, Embase, PsycINFO, CINAHL (EBSCO), Wanfang database, Chinese National Knowledge Infrastructure, SinoMed • Study designs: RCTs • N included studies: N=17 RCTs • Protocol: CRD42021271421	• Eligibility criteria: adult patients diagnosed with advanced disease(s) with a high prevalence of breathlessness • Exclusion: paediatric populations	Meditative movement (yoga, tai chi, qi gong)	CRITICAL OUTCOMES • Dyspnoea: ○ All disease types: 14 studies, SMD 0.10, 95%CI -0.15 to 0.34, I^2 57% ○ COPD: 12 studies, SMD 0.35, 95%CI -0.23 to 0.94, I^2 91% ○ Cancer: 4 studies, SMD -0.05, 95%CI -0.65 to 0.56, I^2 68% • Quality of life: ○ All disease types: 10 studies, SMD 0.16, 95%CI -0.03 to 0.35, I^2 41% • Exercise tolerance: ○ All disease types: 11 studies, MD 17.25, 95%CI -6.06 to 41.06, I^2 72% IMPORTANT OUTCOMES • Physical functioning: 3 studies, no significant differences	• Review process by independent reviewers • No language restrictions • Quality appraisal with RoB1 • Included relevant RCTs on COPD published since 2019: Siqin 2019, Moy 2021, Yanchan 2019, Malik 2022 • Included other relevant RCTs published since 2015: Vanderbyl 2017, Molassiotis 2021, Cheung 2021 • Results of Vanderbyl 2017 wrongly included in meta-analysis for COPD
Oltra 2024	• Design: systematic review and meta-analysis • Funding: not reported; CoI: none • Search date: Sep 2022 • Databases: CENTRAL, PubMed, Embase, Cinahl	• Eligibility criteria: adults with stable COPD • Exclusion: studies with mixed populations	High-flow oxygen during exercise training	CRITICAL OUTCOMES • Dyspnoea: mMRC, 4 studies, MD -0.07, 95%CI -0.40 to 0.26; p=0.69, I^2 63% • Quality of life: 4 studies, MD 0.17, 95%CI -1.20 to 1.54; p=0.81, I^2 50% • Exercise tolerance: 6MWD, 3 studies, MD 18.73, 95%CI -20.49 to 57.94; p=0.35, I^2 56% IMPORTANT OUTCOMES • Physical functioning: not reported	• Review process by independent reviewers • No language restrictions • Quality appraisal with RoB1 • Included relevant RCTs published since 2019: Fang 2020, Tung 2020, Vitacca 2020, Volpi 2022

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
	• Study designs: RCTs • N included studies: N=5 RCTs • Protocol: CRD42022330929				
Priego-Jimenez 2025	• Design: systematic review and network meta-analysis • Funding: FEDER funds; CoI: none • Search date: Dec 2023 • Databases: PubMed, SCOPUS, WoS, Physiotherapy Evidence Database, Central, Cochrane Database of Systematic Reviews, and Web of Science databases • Study designs: RCTs • N included studies: N=54 RCTs • Protocol: CRD42023393463	• Eligibility criteria: patients with COPD • Exclusion: another respiratory pathology other than COPD	Exercise therapy	CRITICAL OUTCOMES • Dyspnoea: not reported • Quality of life: ○ Active mind-body movement therapy: effect size 0.87, 95%CI 0.65-1.09 ○ Active mind-body movement therapy + exercise treatment: effect size 0.44, 95%CI -0.25 to 1.14 • Exercise tolerance: not reported IMPORTANT OUTCOMES • Physical functioning: not reported	• Review process by independent reviewers • No language restrictions • Quality appraisal with RoB2 • Included relevant RCTs published since 2019: Liu 2023, Jiang 2023, Kantatong 2020, Yudhawati 2019
Prieur 2022	• Design: systematic review and meta-analysis • Funding: Havrais Group to Help Those with Respiratory Disability	• Eligibility criteria: patients with COPD • Exclusion: studies with a mixed population if the proportion of participants with COPD was less than 95%	Nasal high-low oxygen therapy	CRITICAL OUTCOMES • Dyspnoea: ○ After singe session: Borg, 5 studies, MD -0.22, 95%CI -0.74 to 0.31; p=0.42, I^2 75%	• Review process by independent reviewers • Restricted to English and French literature • Quality appraisal with RoB2

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
	Association (Le Havre, France); CoI: see article • Search date: Feb 2021 • Databases: PubMed, Central, the Physiotherapy Evidence Database, ScienceDirect, the Web of Science, Open Grey, ClinicalTrials.gov, and European Respiratory Society and American Thoracic Society databases • Study designs: RCTs • N included studies: N=11 RCTs • Protocol: CRD42021221550			○ At iso-time: 3 studies, MD -1.77, 95%CI -3.96 to 0.42; p=0.11, I² 93% ○ During pulmonary rehabilitation: mMRC, 3 studies, MD -0.03, 95%CI -0.36 to 0.30; p=0.87, I² 74% • Quality of life: ○ During pulmonary rehabilitation: CAT at 4-12w, 3 studies, MD 1.51, 95%CI -1.36 to 4.39; p=0.30, I² 82% • Exercise tolerance: ○ After singe session: 5 studies, SMD 0.36, 95%CI 0.03-0.69; p=0.03, I² 83% ○ During pulmonary rehabilitation: 2 studies, SMD 0.34, 95%CI 0.00-0.68; p=0.05, I² 18% IMPORTANT OUTCOMES • Physical functioning: not reported	• Included relevant RCTs published since 2019: Fang 2020, Tung 2020, Dell'Era 2019, Bitos 2021, Prieur 2019, Vitacca 2020, Sanguanwong 2020, Chen 2021
Rafael Henriques 2024	• Design: systematic review • Funding: not reported; CoI: none • Search date: Dec 2023 • Databases: Medline, Scopus, Web of Science, CINAHL, Cochrane Database of Systematic Reviews (CDSR), and Joanna Briggs Institute (JBI) databases	• Eligibility criteria: adult patients with complex chronic conditions with chronic dyspnea • Exclusion: pediatric patients, acute dyspnoea	Interventions to promote self-management	• Very narrative reporting of data	• Review process by independent reviewers • Restricted to Portuguese, English, Spanish, and French literature • Quality appraisal with JBI checklist • Included relevant RCTs on COPD published since 2019: Cevime 2020

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
	• Study designs: all • N included studies: N=18 studies, of which 8 RCTs • Protocol: CRD42023456021				• Included other relevant RCTs published since 2015: -
Raveling 2021	• Design: systematic review and (individual patient data) meta-analysis • Funding: none; CoI: none • Search date: Dec 2020 • Databases: Cochrane Airways Register of Trials, MEDLINE, Embase, PsycINFO, CINAHL, AMED, proceedings of respiratory conferences, clinical trial registries • Study designs: RCTs • N included studies: N=21 RCTs	• Eligibility criteria: patients with COPD	Chronic non-invasive ventilation	CRITICAL OUTCOMES <u>Stable COPD</u> • Dyspnoea: ○ At 3m: ▪ TDI: 3 studies, adjusted MD 0.7, 95%CI -0.8 to 1.5 ▪ mMRC: 4 studies, MD -0.29, 95%CI -0.59 to 0.01 ○ At 12m: MRC, 2 studies, MD -0.49, 95%CI -0.90 to -0.08 • Quality of life: ○ At 3m: 3 studies, adjusted MD 0.39, 95%CI 0.15-0.62 ○ At 12m: 2 studies, adjusted MD 0.15, 95%CI -0.13 to 0.43 • Exercise tolerance: 6MWD ○ At 3m: 8 studies, adjusted MD 15.5, 95%CI -0.8 to 31.7 ○ At 12m: 3 studies, adjusted MD 26.4, 95%CI -7.6 to 60.5 <u>Post-exacerbation COPD</u>	• Review process by independent reviewers • No language restrictions • Quality appraisal with RoB1 • Included relevant RCTs published since 2019: Cui 2019, Ma 2019

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
				• Dyspnoea: not reported • Quality of life: ○ At 3m: 2 studies, adjusted MD 0.25, 95%CI -0.01 to 0.51 ○ At 12m: 2 studies, adjusted MD 0.25, 95%CI -0.06 to 0.55 • Exercise tolerance: not reported IMPORTANT OUTCOMES • Physical functioning: not reported	
Reychler 2019	• Design: systematic review • Funding: Institut de Recherche Expérimentale et Clinique (Université catholique de Louvain–Brussels–Belgium), from Vaincre la Mucoviscidose (France); CoI: none • Search date: Jan 2017 • Databases: PubMed, CINHAL, ScienceDirect • Study designs: all • N included studies: N=18, of which 17 RCTs	• Eligibility criteria: patients with COPD • Exclusion: studies about exacerbations or patients with concomitant diseases	Yoga, tai chi and qi gong	CRITICAL OUTCOMES • Dyspnoea: improvement was observed in all studies but the intergroup comparison was significantly different in only 50% of the studies • Quality of life: benefits on quality of life were observed in 60% of the studies within intervention group and between intervention and control groups • Exercise tolerance: the walked distance improved by more than 25 m for 6MWT in all except one study (+19 m); the ISWT (+39 m) and ESWT (+336 s) improved also significantly and the difference was significant between groups IMPORTANT OUTCOMES • Physical functioning: modified physical performance battery test showed a greater improvement in intervention group	• Review process by independent reviewers • Restricted to English and French literature • Quality appraisal with PEDro scale • Included relevant RCTs published since 2019: - • Narrative presentation of results

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
Sadek 2018	• Design: systematic review and meta-analysis • Funding: none; CoI: none • Search date: 1998-2016 • Databases: PubMed, Cochrane Library, Web of Science • Study designs: RCTs • N included studies: N=7 RCTs	• Eligibility criteria: patients with chronic heart failure	Inspiratory muscle training during rehabilitation	CRITICAL OUTCOMES • Dyspnoea: 5 studies, MD -1.369, 95%CI -1.888 to -0.850, I^2 85% • Quality of life: not reported • Exercise tolerance: 6MWD, 5 studies, mean change from baseline 71.042, 95%CI 29.018-113.066; I^2 96% IMPORTANT OUTCOMES • Physical functioning: not reported	• Unclear if review process was done by independent reviewers • Restricted to English literature • Quality appraisal with PEDro scale • Included relevant RCTs published since 2015: -
Sharp 2016	• Design: systematic review and meta-analysis • Funding: none; CoI: none • Search date: May 2016 • Databases: Cochrane Airways Group Specialised Register, CENTRA, MEDLINE and EMBASE • Study designs: RCTs • N included studies: N=3 RCTs	• Eligibility criteria: adults with a diagnosis of interstitial lung disease and exertional oxygen desaturation • Exclusion: resting hypoxaemia, combined pulmonary fibrosis and emphysema	Ambulatory or short-burst oxygen therapy	CRITICAL OUTCOMES • Dyspnoea: ○ Nishiyama 2013: Borg after 6MWT, MD -0.4, 95%CI -1.76 to 0.96 ○ Troy 2014: Borg after Shuttle test, no significant difference • Quality of life: not reported • Exercise tolerance: ○ Nishiyama 2013: 6MWD, MD 13.0, 95%CI -36.58 to 62.58 ○ Troy 2014: walking distance during Shuttle test, MD 265, 95%CI -58.39 to 588.39 ○ Arizono 2015: endurance time at constant load ergometry, MD 118.7, 95%CI 24.72-212.68 IMPORTANT OUTCOMES	• Review process by independent reviewers • No language restrictions • Quality appraisal with RoB1 • Included relevant RCTs published since 2015: Arizono 2015

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
				• Physical functioning: not reported	
Shaw 2020	• Design: systematic review and meta-analysis • Funding: NIHR Oxford Biomedical Research Centre; CoI: none • Search date: Apr 2019 • Databases: Medline, EMBASE, Cochrane Library, CINAHL, and the Science Citation Index • Study designs: RCTs • N included studies: N=13 RCTs • Protocol: CRD42019124232	• Eligibility criteria: patients with COPD	Mobile device application to support their COPD self-management	CRITICAL OUTCOMES • Dyspnoea: 5 studies, 4 without significant effect, 1 with significant effect (Wang 2018) • Quality of life: 8 studies, SMD -0.40, 95%CI -0.86 to 0.05, p=0.0; I^2 83% • Exercise tolerance: ○ 6MWD: 4 studies, MD 8.38, 95%CI -4.40 to 21.17, p=0.20; I^2 52% ○ ISWT: 1 study, no significant effect IMPORTANT OUTCOMES • Physical functioning: not reported	• Review process by independent reviewers • Unclear language restrictions • Quality appraisal with RoB1 • Included relevant RCTs published since 2019: -
Shnaigat 2021	• Design: systematic review • Funding: not reported; CoI: none • Search date: Feb 2020 • Databases: Science Citation Index, Academic Search Complete, Social Sciences Citation Index, CINAHL Plus, APA PsycInfo, MEDLINE,	• Eligibility criteria: patients with COPD in outpatient setting	Health literacy interventions	CRITICAL OUTCOMES • Dyspnoea: 5 studies, 2 with significant effect (Nguyen 2013, Wakabayashi 2011) • Quality of life: 8 studies, only one with significant effect (Efraimsson 2008) • Exercise tolerance: 4 studies, no significant effect IMPORTANT OUTCOMES • Physical functioning: not reported	• Review process by independent reviewers • Restricted to English literature • Quality appraisal with RoB1 • Included relevant RCTs published since 2019: Nyberg 2019 • Narrative presentation of results

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
	Scopus and ScienceDirect • Study designs: RCTs • N included studies: N=10 RCTs				
Steindal 2024	• Design: systematic review • Funding: none; CoI: none • Search date: Nov 2022 • Databases: AMED, CINAHL, Embase, MEDLINE, PEDro, and PsycInfo • Study designs: all • N included studies: N=6 RCTs	• Eligibility criteria: adult patients with severe or very severe COPD in need of palliative care	Non-invasive ventilation	CRITICAL OUTCOMES • Dyspnoea: ○ Borghi-Silva 2010: greater improvement with non-invasive ventilation ○ Casanova 2000: reduction at 6 months in non-invasive ventilation group • Quality of life: ○ Borghi-Silva 2010: SGRQ, significantly reduced in the non-invasive ventilation group only ○ McEvoy 2009: no significant difference • Exercise tolerance: ○ Borghi-Silva 2010: 6MWD, 122 vs. 47, p<0.05 ○ Funk 2011: 6MWD increased in the non-invasive ventilation group and decreased in the control group ○ Gloeckl 2019: increased cycle endurance time by 39% IMPORTANT OUTCOMES • Physical functioning: not reported	• Scoping review • Review process by independent reviewers • Restricted to Danish, English, German, Norwegian, Spanish, and Swedish literature • No quality appraisal reported • Included relevant RCTs published since 2019: Gloeckl 2019, Volpato 2022
Sunjaya 2022	• Design: systematic review	• Eligibility criteria: people with breathlessness as a symptom or as part of an associated	Mobile apps to promote self-	CRITICAL OUTCOMES <u>COPD</u>	• Review process by independent reviewers

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
	• Funding: Scientia PhD scholarship from UNSW Sydney; CoI: none • Search date: Jan 2022 • Databases: CENTRAL, Embase, Scopus, CINAHL, Cochrane Database of Systematic Reviews, and PubMed • Study designs: all • N included studies: N=16, of which 8 RCTs • Protocol: CRD42021246277	disease such as COPD, asthma, lung cancer, fibrotic lung disease, or heart failure • Exclusion: studies which assessed apps which only involve tracking/recording of health data without feedback; studies which evaluated apps that solely seek to market a particular pharmacotherapy; studies which solely report bench testing results	management for dyspnoea	• Dyspnoea: not reported • Quality of life: 1 study (Soo Kyung Park 2020), no significant effect • Exercise tolerance: not reported <u>Cancer</u> • Dyspnoea: mMRC, 1 study (Ji 2019), no significant differences • Quality of life: EQ-VAS, 1 study (Ji 2019), no significant differences • Exercise tolerance: 6MWD, 1 study (Ji 2019), no significant differences <u>Interstitial lung diseases</u> • Dyspnoea: 1 study (Moor 2020), no significant difference on K-BILD or VAS after 24w • Quality of life: not reported • Exercise tolerance: not reported <u>Heart failure</u> • Dyspnoea: 1 study (Schamaderer 2021), -2.18 vs. -3.55; Cohen's d effect size 0.6 • Quality of life: 1 study (Schamaderer 2021), no significant differences • Exercise tolerance: not reported IMPORTANT OUTCOMES • Physical functioning: not reported	• Restricted to English literature • Quality appraisal with RoB2 and Newcastle Ottawa Scale • Included relevant RCTs published since 2015: Crooks 2020, Ji 2019, Kwon 2018, Miler 2021, Moor 2020, Schamaderer 2021, Soo Kyung Park 2020 • Narrative presentation of results

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
Tsai 2022	• Design: systematic review and meta-analysis • Funding: Taipei Medical University Hospital (107TMU-TMUH-25); CoI: none • Search date: June 2021 • Databases: PubMed, Cochrane Library, Embase, SCOPUS, Cinahl • Study designs: RCTs • N included studies: N=8 RCTs • Protocol: CRD42021128486	• Eligibility criteria: patients with cardiorespiratory diseases or cancer • Exclusion: (1) inclusion of patients with exercise-induced dyspnea, (2) clinical outcomes were not clearly stated, or (3) duplicate reporting of patient cohorts	Fan	CRITICAL OUTCOMES • Dyspnoea: ○ Fan to face vs. no fan: 6 studies, N=339, SMD -0.21, 95%CI -0.59 to 0.17, I^2 66% ○ Fan to face vs. fan to leg: 2 studies, N=89, SMD -0.43, 95%CI -0.87 to 0.01, I^2 9% ○ Long-term fan to face: 4 studies, N=267, SMD 0.07, 95%CI -0.17 to 0.31 ○ Short-term fan to face: 4 studies, N=210, SMD -0.86, 95%CI -1.17 to -0.55 • Quality of life: EQ-5D, 2 studies, MD 0.21, 95%CI -0.16 to 0.59 • Exercise tolerance: not reported IMPORTANT OUTCOMES • Physical functioning: not reported	• Unclear if selection was done by independent reviewers • Data extraction and quality appraisal done by independent reviewers • No language restriction • Quality appraisal with RoB2 • Important flaws in the meta-analyses: wrong data extracted from primary studies! • Included relevant RCTs published since 2015: Johnson 2016, Kako 2018, Puspawati 2017, Wong 2017
Vazquez-Gandullo 2022	• Design: systematic review • Funding: none; CoI: none • Search date: unclear • Databases: PubMed, Embase • Study designs: all • N included studies: N=16, unclear how many RCTs	• Eligibility criteria: patients with COPD	Inspiratory muscle training with mechanical devices	• Very narrative presentation of results	• Unclear if review process was done by independent reviewers • Unclear language restriction • No quality appraisal reported • Included relevant RCTs published since 2019: ?

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
Williams 2020	• Design: systematic review and meta-analysis • Funding: not reported; CoI: none • Search date: Oct 2019 • Databases: Medline, Scopus • Study designs: all • N included studies: N=21 RCTs • Protocol: CRD42016046415	• Eligibility criteria: adult patients with COPD • Exclusion: participants exclusively had a primary pulmonary condition other than COPD (asthma, interstitial lung disease, idiopathic fibrosis)	Cognitive behavioral therapy	CRITICAL OUTCOMES • Dyspnoea: 7 studies, SMD -0.24, 95%CI -0.47 to 0.00; I² 71% • Quality of life: ○ Mental wellbeing: 16 studies, SMD 0.28, 95%CI 0.15-0.42; I² 45% ○ Physical wellbeing: 17 studies, SMD 0.35, 95%CI 0.02-0.69; I² 92% • Exercise tolerance: 7 studies, SMD 0.16, 95%CI 0.02-0.35; I² 0% IMPORTANT OUTCOMES • Physical functioning: not reported	• Study selection by single reviewer, unclear for data extraction • Restricted to English literature • Quality appraisal with PEDro scale • Included relevant RCTs published since 2019: -
Wu 2018	• Design: systematic review and meta-analysis • Funding: Shanghai Municipal Education Commission-Gaoyuan Nursing Grant Support, Grant/Award Number: Hlgy1603gj; CoI: none • Search date: Nov 2016 • Databases: MEDLINE, EMBASE, Cochrane Library, CINHAL, and CBMdisc • Study designs: RCTs and non-RCTs	• Eligibility criteria: adult patients with chronic heart failure, NYHA I-III	Inspiratory muscle training	CRITICAL OUTCOMES • Dyspnoea: 4 studies, SMD -0.95, 95%CI -1.51 to -0.39; I² 56% • Quality of life: 6 studies, no meta-analysis, very narrative reporting • Exercise tolerance: 4 studies, no meta-analysis, very narrative reporting IMPORTANT OUTCOMES • Physical functioning: not reported	• Unclear if selection process was done by independent reviewers • Data extraction by independent reviewers • No language restriction • Quality appraisal with RoB1 • Included relevant RCTs published since 2015: -

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
	• N included studies: N=8 RCTs				
Xiang 2021	• Design: systematic review and meta-analysis • Funding: grants from The National Key Research and Development Program of China (No. 2018YFC1313600) and the National Natural Science Foundation of China (No. 82070094, 81570081, 81770083); CoI: none • Search date: May 2020 • Databases: PubMed, Embase, Cochrane Library, Web of Science, clinical trial registers and Wanfang • Study designs: RCTs • N included studies: N=15 RCTs • Protocol: CRD42020189474	• Eligibility criteria: adult patients with stable COPD, no other associated respiratory disorder, cardiovascular diseases, neuromuscular disorders, or other disease that would be inconvenient for individuals to exercise performance or use a nasal mask	Non-invasive ventilation intervention during exercise training	CRITICAL OUTCOMES • Dyspnoea: mMRC, 4 studies, SMD -0.07, 95%CI -0.46 to 0.33; p=0.74; I^2 0% • Quality of life: 7 studies, SMD -0.77, 95%CI -1.01 to -0.53; p<0.001, I^2 48% • Exercise tolerance: 6MWD, 7 studies, SMD 0.33, 95%CI 0.06-0.59; p=0.02; I^2 0% IMPORTANT OUTCOMES • Physical functioning: not reported	• Review process by independent reviewers • No language restriction • Quality appraisal with RoB1 • Included relevant RCTs published since 2019: Peng 2019, Shi 2020
Xie 2025	• Design: systematic review and network meta-analysis • Funding: none; CoI: none	• Eligibility criteria: adult patients with COPD	Exercise treatment	CRITICAL OUTCOMES <u>Qi gong</u> • Dyspnoea: not reported	• Study selection by independent reviewers, unclear for data extraction • No language restriction

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
	• Search date: June 2024 • Databases: PubMed, Cochrane, Embase, and Web of Science • Study designs: RCTs • N included studies: N=46 RCTs • Protocol: CRD42024568307			• Quality of life: SGRQ, MD -8.20, 95%CI -15.6 to -1.50 • Exercise tolerance: 6MWD, MD 33.3, 95%CI 10.4-58.1 <u>Yoga</u> • Dyspnoea: not reported • Quality of life: SGRQ, MD -28.3, 95%CI -48.1 to -8.61 • Exercise tolerance: 6MWD, MD -21.92, 95%CI -75.70 to 34.63 IMPORTANT OUTCOMES • Physical functioning: not reported	• Quality appraisal with RoB1 • Included relevant RCTs published since 2019: Liu 2023, Moy 2021, Dong 2021, Yudhawati 2019
Yan 2023	• Design: systematic review and meta-analysis • Funding: National Natural Science Foundation of China (grant number: 81900040), Liaoning Edication Division Scientific Foundation (grant number: QN2019014), National High Level Hospital Clinical Research Funding (grant number: 2022-NHLHCRF-LX-01), the Elite Medical Professionals project of China-Japan Friendship Hospital (grant number: ZRJY2021-BJ08), and	• Eligibility criteria: adult patients with acute heart failure who required oxygen therapy	Nasal high-low oxygen therapy	CRITICAL OUTCOMES • Dyspnoea: 4 studies, SMD 1.09, 95%CI -2.33 to 0.15 ○ Vs. BiPAP: 1 study, SMD -2.29, 95%CI -3.01 to -1.58 ○ Vs. CPAP: 2 studies, SMD -1.21, 95%CI -3.14 to 0.72 • Quality of life: not reported • Exercise tolerance: not reported IMPORTANT OUTCOMES • Physical functioning: not reported	• Study selection by independent reviewers, unclear for data extraction • Restricted to English and Chinese literature • Quality appraisal with RoB1 • Included relevant RCTs published since 2015: Ko 2020, Li 2021, Li 2022, Makdee 2017, Yang 2021, Li 2020, Liu 2022, Osman 2021, An 2018 Han 2019, Sun 2019, Xue 2019, Haywood 2019, Marjanovic 2020, Wang 2023, Yang 2019

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
	the Non-profit Central Research Institute Fund of Chinese Academy of Medical Sciences (grant number: 2020-PT320-001); CoI: none • Search date: Aug 2023 • Databases: PubMed, Embase, Web of Science, MEDLINE, the Cochrane Library, CNKI, Wanfang, and VIP databases • Study designs: RCTs • N included studies: N=16 RCTs • Protocol: CRD42022365611				
Yang 2022	• Design: systematic review and meta-analysis • Funding: not reported; CoI: none • Search date: Aug 2019 • Databases: PubMed, EMBASE, the Cochrane Library, China National Knowledge Infrastructure (CNKI), Wanfang database, and VIP database	• Eligibility criteria: patients with COPD	Pursed lip breathing combined with diaphragmatic breathing	CRITICAL OUTCOMES • Dyspnoea: not reported • Quality of life: not reported • Exercise tolerance: 6 studies, MD 29.09, 95%CI 19.35-38.83; p<0.001, I^2 2% IMPORTANT OUTCOMES • Physical functioning: not reported	• Review process by independent reviewers • Restricted to English and Chinese literature • Quality appraisal with RoB1 • Included relevant RCTs published since 2019: -

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
	• Study designs: RCTs • N included studies: N=15 RCTs				
Zhang 2023	• Design: systematic review and meta-analysis • Funding: Key Projects of Double First-Class and High-level University Subject Collaborative Innovation Team of Guangzhou University of Chinese Medicine (Project No. 2021XK16); The Construction Project of the National Clinical Medical Research Center (Project No. 2110200309) and the Innovative Training Program for College Students of Guangzhou University of Chinese Medicine (Project No. S202110572064); CoI: none • Search date: July 2021 • Databases: PubMed, Embase, Scopus, Web of Science and China National Knowledge Infrastructure • Study designs: RCTs	• Eligibility criteria: adult patients with chronic cardiopulmonary dyspnoea	Traditional mind–body movement therapy	CRITICAL OUTCOMES <u>Heart failure</u> • Dyspnoea: not reported • Quality of life: ○ Traditional mind–body movement therapy vs. exercise therapy: 3 studies, MD -9.19, 95%CI -11.05 to -7.32, p<0.00001; I^2 0% ○ Traditional mind–body movement therapy + exercise therapy vs. exercise therapy: 2 studies, MD -2.82, 95%CI -4.99 to -0.64, p=0.01; I^2 0% • Exercise tolerance: ○ Traditional mind–body movement therapy vs. exercise therapy: 5 studies, MD 43.65, 95%CI 7.91-79.38, p=0.02; I^2 0% ○ Traditional mind–body movement therapy + exercise therapy vs. exercise therapy: 3 studies, MD 13.77, 95%CI -1.01 to 28.54, p=0.07; I^2 65% <u>COPD</u> • Dyspnoea: not reported • Quality of life: ○ Traditional mind–body movement therapy vs. exercise therapy: 11 studies, SMD -0.31, 95%CI -0.62 to 0.01, p=0.06; I^2 78%	• Review process by independent reviewers • Language restrictions unclear • Quality appraisal with RoB1 • Included relevant RCTs on COPD published since 2019: Zhang 2019, Dong 2021, Chen 2021, Chen 2020, Zheng 2019, Zhou 2020 • Included other relevant RCTs published since 2015: Zheng 2017, Xu 2019, Ewa 2017, Redwine 2019, Yu 2018

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
	• N included studies: N=34 RCTs • Protocol: CRD42021241181			○ Traditional mind–body movement therapy + exercise therapy vs. exercise therapy: 9 studies, SMD -0.52, 95%CI -0.94 to -0.10, p=0.06; I^2 86% • Exercise tolerance: ○ Traditional mind–body movement therapy vs. exercise therapy: 14 studies, MD 12.22, 95%CI 5.94-18.50, p=0.0001; I^2 56% ○ Traditional mind–body movement therapy + exercise therapy vs. exercise therapy: 8 studies, MD 16.76, 95%CI 10.24-23.29, p<0.00001; I^2 0% IMPORTANT OUTCOMES • Physical functioning: not reported	

Abbreviations: 6MWD: Six-Minute Walking Distance; 95%CI: 95% confidence interval; ALS: amyotrophic lateral sclerosis; BDI-TDI: Baseline Dyspnea Index - Transition Dyspnea Index; CAT: COPD Assessment Test; CENTRAL: Cochrane Central Register of Controlled Trials; CoI: conflict of interest; COPD: chronic obstructive pulmonary disease; CRD: Chronic Respiratory Disease; CRDQ: Chronic Respiratory Disease Questionnaire; CRQ: Chronic Respiratory Questionnaire; EORTC-QLQ-C30: European Organisation for Research and Treatment of Cancer – Quality of Life Questionnaire – Core 30; ESWT: Endurance Shuttle Walk Test; ILD: Interstitial Lung Disease; ISWT: Incremental Shuttle Walk Test; MD: mean difference; MDP: Multidimensional Dyspnea Profile; MLHFQ: Minnesota Living with Heart Failure Questionnaire; mMRC: Modified Medical Research Council; NIHR: National Institute for Health and Care Research; NRS: Numeric Rating Scale; PEDro: Physiotherapy Evidence Database; RCT: randomised controlled trial; RoB: Risk of Bias; RR: relative risk; SGRQ: St. George's Respiratory Questionnaire; SMD: standardized mean difference; SWT: Shuttle Walk Test; VAS: Visual Analog Scale; VO2 max: Maximal Oxygen Uptake; NYHA: New York Heart Association.

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Evidence tabel module 4.3 Beleid - Medicamenteuze behandeling

VRAAG: WAT IS HET EFFECT VAN MEDICATIE OP DYSPNEU BIJ MENSEN MET DYSPNEU IN DE PALLIATIEVE FASE MET ILD/LONGFIBROSE, COPD, HARTFALEN, KANKER EN ALS?

Systematische reviews

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
Chitoran 2025	• Design: systematic review + meta-analysis • Funding: University of Medicine and Pharmacy "Carol Davila" through the institutional program "Publish not Perish"; CoI: none • Search date: Jan 2025 • Databases: PubMed, Medline, Embase, Cochrane Library • Study designs: RCTs • N included studies: N=13 RCTs	• Eligibility criteria: opioid-treated refractory dyspnea in adult cancer patients • Exclusion: 1. pediatric populations; 2. patients with other causes for dyspnea than cancer (chronic obstructive pulmonary disease—COPD, congestive heart failure); 3. non-randomized controlled trials (observational studies, single arm studies, case reports or case series, systematic reviews, and meta-analyses)	Opioids	CRITICAL OUTCOMES • Dyspnoea: 7 studies, N=164, SMD -0.44, 95%CI -0.75 to -0.12, p=0.007, I^2 0% ○ Morphine: 2 studies, N=38, SMD -0.78, 95%CI -1.45 to -0.10, p=0.02, I^2 0% ○ Fentanyl: 4 studies, N=86, SMD -0.37, 95%CI -0.81 to 0.06, p=0.09, I^2 17% ○ Hydromorphone: 1 study, N=40, SMD -0.27, 95%CI -0.89 to 0.35, p=0.40 • Quality of life: not reported • Exercise tolerance: not reported IMPORTANT OUTCOMES • Physical functioning: not reported	• Review process by independent reviewers • Limited to English and Spanish language • Included relevant RCTs published since 2015: Hui 2016, Hui 2017, Pinna 2015, Simon 2016, Yamaguchi 2018
Dy 2020 Feliciano 2021	• Design: systematic review + meta-analysis • Funding: AHRQ; CoI: none • Search date: May 2020 • Databases: PubMed, Embase, Cinahl, ISI Web of Science, CENTRAL	• Eligibility criteria: adult patients with advanced cancer (unlikely to be cured or unlikely to be controlled with treatment) and breathlessness • Exclusion: studies with fewer than 10 patients enrolled in each arm, studies with mixed populations in which the percentage of patients with cancer was less than 50%	Pharmacologic interventions	CRITICAL OUTCOMES • Dyspnoea: ○ Opioids vs. placebo: 6 studies, N=107, SMD -0.12, 95%CI -0.45 to 0.2, p=0.49, I^2 0% ○ Intranasal midazolam vs. placebo: 1 study, no statistically significant difference between groups (p=0.75) at 60 min	• Review process by independent reviewers • Limited to English literature • Included relevant RCTs published since 2015: Hui 2017, Hui 2016a, Hui 2016b, Simon 2016, Pinna 2015, Hui 2019, Hardy 2016, Aabom 2019

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
	• Study designs: RCTs and observational studies • N included studies: N=48 RCTs (17 RCTs on medication)			○ Corticosteroids vs. placebo: 1 study, N=28, SMD -0.06, 95%CI -0.7 to 0.58 ○ Opioids vs. opioids: 7 studies, N=132, SMD 0.15, 95%CI -0.22 to 0.52, I^2 4.8% ○ Morphine vs. midazolam: 2 studies, N=108: For breathlessness intensity: 1 study found midazolam was more effective than morphine at 5d (p<0.001); another study found no significant differences between groups at 24 or 48 h; for categorical variable of percentage not experiencing breathlessness relief: calculated RR 0.075, 95%CI 0.004-1.270; calculated RR 1.33, 95%CI 1.02-1.75 • Quality of life: ○ Corticosteroids vs. placebo: 1 study, N=28, EORTC-QLQ-C30, SMD -0.06, 95%CI -0.70 to 0.58 • Exercise tolerance: ○ Fentanyl vs. placebo: 3 studies, N=77, SMD 0.06, 95%CI -0.43 to 0.55, p=0.90, I^2 0% IMPORTANT OUTCOMES • Physical functioning: not reported	
Filipe 2024	• Design: systematic review • Funding: none; CoI: none • Search date: 2011-2022	• Eligibility criteria: adults with ALS or motor neuron disease experiencing breathlessness	Opioids	-	• Review process by independent reviewers • Limited to English language

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
	• Databases: PubMed, Cochrane Library, and Web of Science • Study designs: all • N included studies: N=0 RCTs				
Gaertner 2023	• Design: systematic review + meta-analysis • Funding: none; CoI: none • Search date: Jul 2021 • Databases: PubMed, Embase • Study designs: RCTs • N included studies: N=8 RCTs	• Eligibility criteria: adults (≥18 years) with heart failure and refractory breathlessness regardless of the underlying etiology	Opioids	CRITICAL OUTCOMES • Dyspnoea: 7 studies, N=271, SMD 0.03, 95%CI -0.21 to 0.28, I^2 0% ○ Dihydrocodeine: 1 study, N=12, SMD -0.13, 95%CI -0.94 to 0.67 ○ Morphine: 3 studies, N=101, SMD 0.15, 95%CI -0.24 to 0.55 ○ Oxycodone: 2 studies, N=106, SMD -0.04, 95%CI -0.44 to 0.36 ○ Fentanyl: 2 studies, N=40, SMD 0.00, 95%CI -0.62 to 0.62 • Quality of life: 4 studies, no significant differences ○ Johnson 2019: MD -2.7, 95%CI -9.7 to 4.3 • Exercise tolerance: not reported IMPORTANT OUTCOMES • Physical functioning: not reported	• Review process by independent reviewers • Limited to English and German language • Included relevant RCTs published since 2015: Ferreira 2018, Johnson 2019, Smith 2020
Haywood 2019	• Design: systematic review + meta-analysis • Funding: none; CoI: none • Search date: Jan 2018	• Eligibility criteria: participants with cancer with cancer-related dyspnoea, aged 18 years and above • Exclusion: studies assessing inhaled corticosteroids	Systemic corticosteroids at any dose, administered for the relief of cancer-related dyspnoea or other cancer-related symptoms (where dyspnoea was also	CRITICAL OUTCOMES • Dyspnoea: dexamethasone vs. placebo, 2 studies, N=114, MD -0.85, 95%CI -1.73 to 0.03, p=0.06, I^2 0% • Quality of life:	• Review process by independent reviewers • No language restrictions

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
	• Databases: CENTRAL, MEDLINE, Embase, CINAHL, Science Citation Index Web of Science, Latin America and Caribbean Health Sciences (LILACS) • Study designs: RCTs • N included studies: N=2 RCTs		measured), compared to placebo or any active comparator including supportive care or alternate non-pharmacological treatment	○ Hui 2016: EORTC QLQ-C30, in favour of dexamethasone at day 4 but not at day 7 ○ Yennurajalingam 2013: FACIT physical well-being scores showed significantly better improvement at days eight (p=0.007) and 15 (p=0.002) in the dexamethasone group compared with the control group; however, there were no significant changes for FACIT social/family, emotional or functional scales • Exercise tolerance: not reported IMPORTANT OUTCOMES • Physical functioning: not reported	• Included relevant RCTs: Hui 2016, Yennurajalingam 2013
Liu 2023	• Design: systematic review + meta-analysis • Funding: National Natural Science Foundation of China (Grants: 81870014 and 82174139 to JF); CoI: none • Search date: Dec 2022 • Databases: PubMed, Embase, CENTRAL • Study designs: RCTs • N included studies: N=24 RCTs	• Eligibility criteria: patients with COPD (FEV1/FVC ratio was less than 70%); vs. placebo; blinded trials	Opioids	CRITICAL OUTCOMES • Dyspnoea: 17 studies, N=898, SMD -0.31, 95%CI -0.46 to -0.16, I^2 59% ○ Cross-over studies: 13 studies, N=192, SMD -0.43, 95%CI -0.55 to -0.30, I^2 18% ○ Parallel studies: 4 studies, N=706, SMD -0.02, 95%CI -0.22 to 0.19, I^2 39% ○ Short-acting opioids: 11 cross-over studies, SMD -0.42, 95%CI -0.58 to -0.27, I^2 32% • Quality of life: 3 studies, N=595, SMD -0.04, 95%CI -0.21 to 0.13, I^2 0% • Exercise tolerance: 18 studies, N=458, SMD 0.19, 95%CI 0.01-0.36, I^2 68% ○ Cross-over studies : 16 studies, N=191, SMD 0.22, 95%CI 0.02-0.41, I^2 71% ○ Parallel studies: 2 studies, N=267, SMD 0.00, 95%CI -0.27 to 0.27	• Review process by independent reviewers • No language restrictions • Included relevant RCTs published since 2019: Currow 2020, Ekström 2022, Ferreira 2020, Verberkt 2020

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
				○ Short-acting opioids: 13 cross-over studies, SMD 0.25, 95%CI 0.05-0.46, I^2 71% IMPORTANT OUTCOMES • Physical functioning: not reported	
Pratama 2022	• Design: systematic review + meta-analysis • Funding: none; CoI: none • Search date: June 2022 • Databases: Medline, Scopus, Web of Science, EBSCO • Study designs: retrospective and prospective cohort studies, RCTs • N included studies: N=7 RCTs	• Eligibility criteria: adult patients with acute heart failure (i.e., patients with rapid or gradual onset of symptoms leading to hospitalization or an emergency department visit and those with clinical manifestations (first onset or de novo) including acute decompensation, acute pulmonary edema, isolated right ventricular failure, and cardiogenic shock) or chronic heart failure (i.e., patients who have established heart failure and are stable and those with gradual onset of symptoms not requiring hospitalization)	Opioids	CRITICAL OUTCOMES • Dyspnoea: ○ Acute heart failure: 1 study, breathlessness improvement at 3 h post treatment, MD -0.20, 95%CI -0.53 to 0.13 ○ Chronic heart failure: 4 studies, MD -0.77, 95%CI -1.72 to 0.19, I^2 71% • Quality of life: not reported • Exercise tolerance: exercise test duration, 3 studies, MD 69.24, 95%CI 10.11-128.37, I^2 89% IMPORTANT OUTCOMES • Physical functioning: not reported	• Review process by independent reviewers, although unclear for data extraction • No language restrictions • Included relevant RCTs published since 2015: Johnson 2019
Yamaguchi 2022	• Design: systematic review • Funding: Japan Agency for Medical Research and Development (AMED) under Grant Number 19dk0110038h0001, 20dk0110038h0002, and 21dk0110038s0303; CoI: see article • Search date: Oct 2020	• Eligibility criteria: patients with respiratory symptoms, primarily due to chronic respiratory diseases other than cancer • Exclusion: nebulized opioids; studies that exclusively involved respiratory symptoms due to cancer or chronic diseases of other organs, such as cardiac and neurological diseases	Oral or parenteral opioids	• Narrative overview	• Review process by independent reviewers • Limited to English language • Included relevant RCTs published since 2015 for non-COPD: Kronborg-White 2020 • Included relevant RCTs published since 2019 for COPD: Verberkt 2020, Currow 2020, Ferreira 2019

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
	• Databases: Medline, Cochrane Library • Study designs: RCTs, non-randomized, observational, and retrospective studies involving >5 patients • N included studies: N=15 RCTs				

Abbreviations: 95%CI: 95% confidence interval; ALS: amyotrophic lateral sclerosis; CoI: conflict of interest; COPD: chronic obstructive pulmonary disease; EORTC-QLQ-C30: European Organisation for Research and Treatment of Cancer – Quality of Life Questionnaire – Core 30; FACIT: Functional Assessment of Chronic Illness Therapy; IV: intravenous; MD: mean difference; RCT: randomised controlled trial; RR: relative risk; SC: subcutaneous; SMD: standardized mean difference.

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