

Supplement

Neuromuscular electrical stimulation for early mobilization in critically ill patients: a systematic review of applied protocols

Short Title: NMESinICU

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Table A1. Systematic search strategy for the databases used in each case.

Medline and Cochrane Library	Search #1 (Positioning)	(„positioning“ [Title/Abstract] OR „prone position“ [Title/Abstract] OR „prone positioning“ [Title/Abstract] OR „pronation“ [Title/Abstract] OR „proning“ [Title/Abstract] OR „prone“ [Title/Abstract] OR „self-proning“ [Title/Abstract] OR „conscious proning“ [Title/Abstract] OR „conscious prone positioning“ [Title/Abstract] OR „proning in non-intubated“ [Title/Abstract] OR „PINI“ [Title/Abstract] OR „prone ventilation“ [Title/Abstract] OR „face down“ [Title/Abstract] OR „ventral position“ [Title/Abstract] OR „awake proning“ [Title/Abstract] OR „supine position“ [Title/Abstract] OR „supine positioning“ [Title/Abstract] OR „supination“ [Title/Abstract] OR „supine“ [Title/Abstract] OR „lateral position“ [Title/Abstract] OR „lateral positioning“ [Title/Abstract] OR „sitting position“ [Title/Abstract] OR „semisitting position“ [Title/Abstract] OR „horizontal position“ [Title/Abstract] OR „horizontal positioning“ [Title/Abstract] OR „semi-recumbent position“ [Title/Abstract] OR „rotation“ [Title/Abstract] OR „body position“ [Title/Abstract] OR „body positioning“ [Title/Abstract] OR „patient positioning“ [Title/Abstract] OR „positioning therapy“ [Title/Abstract] OR „kinetic therapy“ [Title/Abstract] OR „continuous lateral rotation“ [Title/Abstract] OR „continuous passive motion therapy“ [Title/Abstract] OR „backrest elevation“ [Title/Abstract] OR „axial position change“ [Title/Abstract] OR „body position change“ [Title/Abstract] OR „facedown position“ [Title/Abstract] OR „side position“ [Title/Abstract] OR „posture“ [Title/Abstract] OR „thorax angulation“ [Title/Abstract] OR „kinetics“ OR "prone position"[MeSH Terms] OR "pronation"[MeSH Terms] OR "supine position"[MeSH Terms] OR "supination"[MeSH Terms] OR "sitting position"[MeSH Terms] OR "rotation"[MeSH Terms] OR "patient positioning"[MeSH Terms] OR "posture"[MeSH Terms] OR "kinetics"[MeSH Terms])
	Search #2 (Mobilization)	(„mobilisation“ [Title/Abstract] OR „mobilization“ [Title/Abstract] OR „early mobilisation“ [Title/Abstract] OR „early mobilization“ [Title/Abstract] OR „early goal-directed mobilization“ [Title/Abstract] OR „early ambulation“ [Title/Abstract] OR „early exercise“ [Title/Abstract] OR „early activity“ [Title/Abstract] OR „early activities“ [Title/Abstract] OR „early goal-directed therapy“ [Title/Abstract] OR „early goal-directed therapies“ [Title/Abstract] OR „accelerated ambulation“ [Title/Abstract] OR „occupational therapy“ [Title/Abstract] OR „occupational therapies“ [Title/Abstract] OR „occupational therapist“ [Title/Abstract] OR „physiotherapy“ [Title/Abstract] OR „physical therapy“ [Title/Abstract] OR „physical therapies“ [Title/Abstract] OR „physical therapist“ [Title/Abstract] OR „physical therapy modality“ [Title/Abstract] OR „physical therapy modalities“ [Title/Abstract] OR „physical fitness“ [Title/Abstract] OR „mobility therapy“ [Title/Abstract] OR „exercise therapy“ [Title/Abstract] OR „exercise therapies“ [Title/Abstract] OR „movement therapy“ [Title/Abstract] OR „movement therapies“ [Title/Abstract] OR „myofunctional therapy“ [Title/Abstract] OR „myofunctional therapies“ [Title/Abstract] OR „kinesiotherapy“ [Title/Abstract] OR „motion therapy“ [Title/Abstract] OR „mobility intervention“ [Title/Abstract] OR „motor activity“ [Title/Abstract] OR „motor activities“ [Title/Abstract] OR „rehabilitation“ [Title/Abstract] OR „muscle training“ [Title/Abstract] OR „muscle strength“ [Title/Abstract] OR „muscle strengthening“ [Title/Abstract] OR „musculoskeletal manipulations“ [Title/Abstract] OR „resistance training“ [Title/Abstract] OR „strength training“ [Title/Abstract] OR „endurance training“ [Title/Abstract] OR „fitness training“ [Title/Abstract] OR „high-intensity interval training“ [Title/Abstract] OR „physical conditioning“ [Title/Abstract] OR „physical medicine“ [Title/Abstract] OR „physical endurance“ [Title/Abstract] OR „physical strength“ [Title/Abstract] OR „walking“ [Title/Abstract] OR „exercise“ [Title/Abstract] OR „exercises“ [Title/Abstract] OR „exercising“ [Title/Abstract] OR „exercise tolerance“ [Title/Abstract] OR „functional status“ [Title/Abstract] OR „load bearing“ [Title/Abstract] OR „loadbearing“ [Title/Abstract] OR „weight bearing“ [Title/Abstract] OR „weightbearing“ [Title/Abstract] OR „locomotion“ [Title/Abstract] OR „locomotor activity“ [Title/Abstract] OR „locomotor activities“ [Title/Abstract] OR „muscle strength“ [Title/Abstract] OR „muscle strengthening“ [Title/Abstract] OR „recovery of

	function" [Title/Abstract] OR „function recovery" [Title/Abstract] OR „functional recoveries" [Title/Abstract] OR „functional recovery" [Title/Abstract] OR „functional training" [Title/Abstract] OR „joint mobilization" [Title/Abstract] OR „joint mobilization" [Title/Abstract] OR „movement" [Title/Abstract] OR „physical stimulation" [Title/Abstract] OR „stimulation" [Title/Abstract] OR „cycle" [Title/Abstract] OR „cycling" [Title/Abstract] OR „leg-cycle" [Title/Abstract] OR „leg-cycling" [Title/Abstract] OR „bicycle" [Title/Abstract] OR „bicycling" [Title/Abstract] OR „in-bed cycling" [Title/Abstract] OR „ergometer" [Title/Abstract] OR „ergometry" [Title/Abstract] OR „electrostimulation" [Title/Abstract] OR „electric stimulation" [Title/Abstract] OR „electrical stimulation" [Title/Abstract] OR „electrotherapy" [Title/Abstract] OR „electrotherapies" [Title/Abstract] OR „electric stimulation therapy" [Title/Abstract] OR „electrical stimulation therapy" [Title/Abstract] OR „electrical stimulation therapies" [Title/Abstract] OR „neuromuscular stimulation" [Title/Abstract] OR „neuromuscular electric stimulation" [Title/Abstract] OR „neuromuscular electrical stimulation" [Title/Abstract] OR „transcutaneous electric stimulation" [Title/Abstract] OR „transcutaneous electrical stimulation" [Title/Abstract] OR „muscle stimulation" [Title/Abstract] OR „muscular stimulation" [Title/Abstract] OR „muscle excitation" [Title/Abstract] OR „electromyostimulation" [Title/Abstract] OR „functional electrical stimulation" [Title/Abstract] OR „TENS" [Title/Abstract] OR „NMES" [Title/Abstract] OR „EMS" [Title/Abstract] OR „FES" [Title/Abstract] OR „assistive technology devices" [Title/Abstract] OR "early ambulation"[MeSH Terms] OR "early goal-directed therapy"[MeSH Terms] OR "occupational therapy"[MeSH Terms] OR "physical therapy modalities"[MeSH Terms] OR "physical fitness"[MeSH Terms] OR "exercise therapy"[MeSH Terms] OR "myofunctional therapy"[MeSH Terms] OR "motor activity"[MeSH Terms] OR "rehabilitation"[MeSH Terms] OR "muscle strength"[MeSH Terms] OR "musculoskeletal manipulations"[MeSH Terms] OR "resistance training"[MeSH Terms] OR "endurance training"[MeSH Terms] OR "high-intensity interval training"[MeSH Terms] OR "physical endurance"[MeSH Terms] OR "walking"[MeSH Terms] OR "exercise"[MeSH Terms] OR "exercise tolerance"[MeSH Terms] OR "functional status"[MeSH Terms] OR "weight bearing"[MeSH Terms] OR "locomotion"[MeSH Terms] OR "muscle strength"[MeSH Terms] OR "recovery of function"[MeSH Terms] OR "movement"[MeSH Terms] OR "physical stimulation"[MeSH Terms] OR "bicycling"[MeSH Terms] OR "ergometry"[MeSH Terms] OR "electric stimulation"[MeSH Terms] OR "electric stimulation therapy"[MeSH Terms])
Search #3 (Critical Care)	(„critically ill" [Title/Abstract] OR „critical illness" [Title/Abstract] OR „catastrophic illness" [Title/Abstract] OR „critical care" [Title/Abstract] OR „critical care unit" [Title/Abstract] OR „critical care units" [Title/Abstract] OR „intensive care" [Title/Abstract] OR „intensive care unit" [Title/Abstract] OR „intensive care units" [Title/Abstract] OR „respiratory care unit" [Title/Abstract] OR „respiratory care units" [Title/Abstract] OR „intensive treatment unit" [Title/Abstract] OR „intensive therapy unit" [Title/Abstract] OR „special care unit" [Title/Abstract] OR „ICU" [Title/Abstract] OR „ITU" [Title/Abstract] OR „MICU" [Title/Abstract] OR „controlled ventilation" [Title/Abstract] OR „intensive care patient" [Title/Abstract] OR „invasive ventilation" [Title/Abstract] OR „invasive respiration" [Title/Abstract] OR „artificial respiration" [Title/Abstract] OR „mechanical ventilation"[Title/Abstract]) OR "critical illness"[MeSH Terms] OR "catastrophic illness"[MeSH Terms] OR "critical care"[MeSH Terms] OR "intensive care units"[MeSH Terms] OR "respiratory care units"[MeSH Terms])
Final Search (#1 OR #2) AND #3	
Pedro	Abstract & Title: mob* critical* Abstract & Title: mob* ICU Abstract & Title: mob* intensive

		Abstract & Title: pron* critical*
		Abstract & Title: pron* ICU
		Abstract & Title: pron* intensive
		Abstract & Title: neuromusc* critical*
		Abstract & Title: neuromusc* ICU
		Abstract & Title: neuromusc* intensive
Cinahl	Search #1 (Positioning)	„positioning“ OR „prone position“ OR „prone positioning“ OR „pronation“ OR „proning“ OR „prone“ OR „self-proning“ OR „conscious proning“ OR „conscious prone positioning“ OR „proning in non-intubated“ OR „PINI“ OR „prone ventilation“ OR „face down“ OR „ventral position“ OR „awake proning“ OR „supine position“ OR „supine positioning“ OR „supination“ OR „supine“ OR „lateral position“ OR „lateral positioning“ OR „sitting position“ OR „semisitting position“ OR „horizontal position“ OR „horizontal positioning“ OR „semi-recumbent position“ OR „rotation“ OR „body position“ OR „body positioning“ OR „patient positioning“ OR „positioning therapy“ OR „kinetic therapy“ OR „continuous lateral rotation“ OR „continuous passive motion therapy“ OR „backrest elevation“ OR „axial position change“ OR „body position change“ OR „facedown position“ OR „side position“ OR „posture“ OR „thorax angulation“ OR „kinetics“
	Search #2 (Mobilization)	„mobilisation“ OR „mobilization“ OR „early mobilisation“ OR „early mobilization“ OR „early goal-directed mobilisation“ OR „early goal-directed mobilization“ OR „early ambulation“ OR „early exercise“ OR „early activity“ OR „early activities“ OR „early goal-directed therapy“ OR „early goal-directed therapies“ OR „accelerated ambulation“ OR „occupational therapy“ OR „occupational therapies“ OR „occupational therapist“ OR „physiotherapy“ OR „physical therapy“ OR „physical therapies“ OR „physical therapist“ OR „physical therapy modality“ OR „physical therapy modalities“ OR „physical fitness“ OR „mobility therapy“ OR „mobility therapies“ OR „exercise therapy“ OR „exercise therapies“ OR „movement therapy“ OR „movement therapies“ OR „myofunctional therapy“ OR „myofunctional therapies“ OR „kinesiotherapy“ OR „kinesiotherapies“ OR „motion therapy“ OR „mobility intervention“ OR „motor activity“ OR „motor activities“ OR „rehabilitation“ OR „muscle training“ OR „muscle strength“ OR „muscle strengthening“ OR „musculoskeletal manipulations“ OR „resistance training“ OR „strength training“ OR „endurance training“ OR „fitness training“ OR „high-intensity interval training“ OR „physical conditioning“ OR „physical medicine“ OR „physical endurance“ OR „physical strength“ OR „walking“ OR „exercise“ OR „exercises“ OR „exercising“ OR „exercise tolerance“ OR „functional status“ OR „load bearing“ OR „loadbearing“ OR „weight bearing“ OR „weightbearing“ OR „locomotion“ OR „locomotor activity“ OR „locomotor activities“ OR „muscle strength“ OR „muscle strengthening“ OR „recovery of function“ OR „function recovery“ OR „functional recoveries“ OR „functional recovery“ OR „functional training“ OR „joint mobilization“ OR „joint mobilization“ OR „movement“ OR „physical stimulation“ OR „stimulation“ OR „cycle“ OR „cycling“ OR „leg-cycle“ OR „leg-cycling“ OR „bicycle“ OR „bicycling“ OR „in-bed cycling“ OR „ergometer“ OR „ergometry“ OR „electrostimulation“ OR „electric stimulation“ OR „electrical stimulation“ OR „electrotherapy“ OR „electrotherapies“ OR „electric stimulation therapy“ OR „electric stimulation therapies“ OR „electrical stimulation therapy“ OR „electrical stimulation therapies“ OR „neuromuscular stimulation“ OR „neuromuscular electric stimulation“ OR „neuromuscular electrical stimulation“ OR „transcutaneous electric stimulation“ OR „transcutaneous electrical stimulation“ OR „muscle stimulation“ OR „muscular stimulation“ OR „muscle excitation“ OR „electromyostimulation“ OR „functional electrical stimulation“ OR „TENS“ OR „NMES“ OR „EMS“ OR „FES“ OR „assistive technology devices“

Search #3 (Critical Care)	„critically ill“ OR „critical illness“ OR “catastrophic illness“ OR „critical care“ OR „critical care unit“ OR „critical care units“ OR „intensive care“ OR „intensive care unit“ OR „intensive care units“ OR „respiratory care unit“ OR „respiratory care units“ OR „intensive treatment unit“ OR „intensive therapy unit“ OR „special care unit“ OR „ICU“ OR „ITU“ OR „MICU“ OR „controlled ventilation“ OR „intensive care patient“ OR „invasive ventilation“ OR „invasive respiration“ OR „artificial respiration“ OR „mechanical ventilation“
Final Search (#1 OR #2) AND #3	

Table A2. Patient characteristics of studies with one intervention. Numbers are shown with percentages, means and standard deviations are shown in round brackets and interquartile range ranges with 25th and 75th percentile in squared brackets.

Author	Year	Patients intervention group 1 (n)	Age intervention group 1 (years)	Sex intervention group 1 (male, n, %)	APACHE II score intervention 1	SOFA score intervention 1	Main admission disease intervention 1	Patients control group (n)	Age control group (years)	Sex control group (male, n, %)	APACHE II score control	SOFA score control group	Main admission disease control group
Abu-Khaber [1]	2013	50	59.1 (5.3)	24 (60%)	24.5 (6.8)	na	Respiratory	40	57.6 (6.8)	27 (68%)	26.1 (5.3)	na	Respiratory
Baron [2]	2022	76	82.6 (17.4)	38 (50%)	na	2.0 [0.0-4.0]	Stroke	73	63.7 (18.2)	42 (58%)	na	2.0 [0.0-4.0]	Stroke
Berney [3]	2021	80	61.0 [51.0-69.0]	53 (66%)	22.0 [16.0-27.0]	11.0 [7.0-13.0]	Respiratory	82	59.0 [48.0-67.0]	54 (66%)	23.0 [17.0-27.0]	10.0 [7.0-14.0]	Respiratory
Campos [4]	2022	34	42.5 (14.9)	24 (70%)	na	8.8 (3.0)	Surgical	40	46.7 (17.9)	26 (65%)	na	9.4 (2.7)	Surgical
Cerqueira [5]	2018	26	41.8 (13.2)	18 (69%)	na	na	Surgical	33	42.2 (14.4)	23 (70%)	na	na	Surgical
Dall'Acqua [6]	2017	11	56.0 (13.0)	7 (64%)	26.0 (5.0)	na	Sepsis	14	61.0 (15.0)	9 (64%)	29.0 (7.0)	na	Sepsis
Dirks [7]	2015	6	63.3 (6.0)	3 (50%)	29.3 (2.0)	na	Cerebral						
Falavigna [8]	2013	11	34.0 (17.3)	na	15.7 (4.5)	na	Sepsis						
Figueiredo [9]	2023	29	65.0 [54.5–78.5]	9 (31%)	na	na	Resuscitation	20	64.5 [51.0–69.8]	9 (45%)	na	na	None
Figueiredo [10]	2024	20	61.0 (20.0)	13 (65%)	na	na	Arrhythmia						
Fischer [11]	2016	27	63.0 (15.5)	18 (67%)	na	9.0 [1.0-15.0]	Surgical	27	69.7 (13.1)	20 (74%)	na	7.0 [1.0-11.0]	Surgical
Fossat [12]	2018	158	63.0 (13.0)	103 (65%)	na	9.0 [6.0-12.0]	Respiratory	154	66.0 (15.0)	98 (64%)	na	8.5 [6.0-12.0]	Respiratory
Gerovasili [13]	2009	24	59.0 (23.0)	6 (46%)	19.0 (3.0)	10.0 (3.0)	Sepsis	25	56.0 (19.0)	8 (62%)	18.0 (6.0)	8.0 (3.0)	Sepsis
Gruther [14]	2010	8	52.0 (10.0)	7 (88%)	na	na	Trauma	9	48.0 (12.0)	8 (89%)	na	na	Trauma
Hirose [15]	2013	9	49.9 (16.5)	8 (89%)	na	na	Cerebral	6	59.8 (17.2)	3 (50%)	na	na	Cerebral
Karatzanos [16]	2012	24	55.0 (20.0)	19 (79%)	16.0 (4.0)	8.0 (3.0)	Cerebral	28	59.0 (21.0)	22 (79%)	19.0 (5.0)	8.0 (3.0)	Sepsis
Kho [17]	2015	16	54.0 (16.0)	7 (44%)	25.0 (8.0)	6.2 (4.7)	Sepsis	18	56.0 (18.0)	10 (56%)	25.0 (6.0)	5.6 (1.6)	Sepsis

Kourek [18]	2024	16	46.6 (13.7)	6 (37%)	na	na	Cardiac						
Koutsoumpa [19]	2018	38	64.0 (12.4)	26 (68%)	17.0 (7.6)	8.0 (4.2)	Respiratory	42	66.0 (13.1)	34 (81%)	21.0 (7.9)	7.0 (4.1)	Respiratory
Leite [20]	2018	24	48.8 (19.7)	18 (75%)	18.7 (4.0)	na	Cerebral	26	42.4 (12.7)	20 (77%)	18.9 (1.9)	na	Cerebral
Liu [21]	2023	40	58.1 (15.5)	25 (63%)	20.6 (6.4)	na	Sepsis	40	59.1 (16.0)	23 (58%)	19.8 (6.4)	na	Sepsis
Mahran [22]	2023	60	31.0 (10.0)	46 (77%)	12.3 (4.2)	na	Cerebral	58	32.0 (9.0)	50 (86%)	15.4 (7.3)	na	Cerebral
Medrinal [23]	2018	19	65.3 (9.7)	13 (68%)	na	na	Sepsis						
Meesen [24]	2010	7	65.3 (16.5)	3 (43%)	na	na	Surgical	12	67.2 (13.2)	9 (75%)	na	na	Surgical
Nakamura [25]	2019	21	76.6 (11.0)	14 (67%)	22.8 (6.2)	8.6 (3.7)	Sepsis	16	74.6 (13.1)	11 (69%)	22.9 (3.9)	8.7 (2.8)	Sepsis
Nakanishi [26]	2020	17	73.0 (3.0)	12 (71%)	25.0 [20.0–31.0]	9.0 [6.0–12.0]	Respiratory	19	66.0 (3.0)	12 (63%)	22.0 [19.0–30.0]	7.0 [5.0–10.0]	Respiratory
Poulsen [27]	2011	8	67.0 [64.0–72.0]	8 (100%)	25.0 [20.0–29.0]	13.0 [11.0–15.0]	Sepsis						
Rodriguez [28]	2012	14	72.0 [63.0–80.0]	7 (50%)	20.0 [18.0–27.0]	10.0 [9.0–12.0]	Respiratory						
Routsi [29]	2010	68	61.0 (19.0)	46 (68%)	18.0 (4.0)	9.0 (3.0)	Cerebral	72	58.0 (18.0)	49 (68%)	18.0 (5.0)	9.0 (3.0)	Cerebral
Segers [30]	2021	47	60.0 (15.0)	25 (53%)	26.0 (8.0)	na	Respiratory						
Silva [31]	2017	11	39.0 (16.0)	11 (100%)	15.1 (0.9)	na	Trauma						
Silva [32]	2019	30	30.0 [27.0–33.0]	26 (87%)	11.0 [8.0–13.0]	5.0 [5.0–8.0]	Cerebral	30	33.0 [29.0–37.0]	26 (87%)	11.0 [9.0–14.0]	6.0 [4.0–9.0]	Cerebral
Stefanou [33]	2016	32	58.0 (14.0)	23 (72%)	21.0 (8.0)	7.0 (3.0)	Surgical						
Verceles [34]	2023	16	62.0 (9.3)	8 (50%)	17.8 (5.5)	na	Respiratory	23	62.0 (9.3)	10 (43%)	15.4 (7.4)	na	Respiratory
Vieira [35]	2023	20	34.7 (11.2)	16 (80%)	16.1 (4.6)	na	Cerebral	20	36.5 (13.5)	16 (80%)	16.7 (4.5)	na	Cerebral
Waldauf [36]	2021	75	59.0 (15.1)	53 (71%)	22.1 (5.2)	8.8 (2.6)	Respiratory	75	62,3 ± 15,4	57 (76%)	22.2 (7.7)	8.8 (3.2)	Respiratory
Wollersheim [37]	2019	33	54.0 [45.0–68.0]	24 (73%)	24.0 [20.0–28.0]	12.0 [11.0–14.0]	Respiratory	17	45 [39–61]	9 (53%)	26.0 [19.0–31.0]	14.0 [12.0–17.0]	Respiratory
Woo [38]	2018	10	63.5 [53.8–71.0]	7 (70%)	23.5 [21.2–29.0]	2.0 [2.0–4.0]	Surgical						
Zulbaran-Rojas [39]	2022	8	66.8 (9.8)	3 (38%)	na	na	Respiratory	8	62.9 (9.5)	6 (75%)	na	na	Respiratory

na not available

Table A3. Patient characteristics of studies with two or more interventions. Numbers are shown with percentages, means and standard deviations are shown in round brackets and interquartile range ranges with 25th and 75th percentile in squared brackets.

Author	Year	Patients intervention group 1 (n)	Age intervention group 1 (years)	Sex intervention group 1 (male, n, %)	APACHE II score intervention 1	SOFA score intervention 1	Main admission disease	Patients intervention group 2 (n)	Age intervention group 2 (years)	Sex intervention group 2 (male, n, %)	APACHE II score intervention 2	SOFA score intervention 2	Main admission disease	Patients intervention group 3 (n)	Age intervention group 3 (years)	Sex intervention group 3 (male, n, %)	APACHE II score intervention 3	SOFA score intervention 3	Main admission disease	Patients control group (n)	Age control group (years)	Sex control group (male, n, %)	APACHE II score control	SOFA score control group	Main admission disease
Akar [40]	2017	10	70.0 (12.3)	4 (40%)	na	na	Respiratory	10	62.8 (6.8)	6 (60%)	na	na	Respiratory							10	68.0 (17.8)	5 (50%)	na	na	Respiratory
Bao [41]	2022	20	52.8 (10.7)	14 (70%)	9.4 (4.5)	na	Trauma	20	51.1 (17.6)	18 (90%)	9.7 (5.2)	na	Trauma							20	52.5 (12.5)	19 (95%)	9.2 (3.0)	na	Trauma
Dos Santos [42]	2020	12	55.6 (10.8)	8 (67%)	15.5 (3.5)	na	Respiratory	13	55.3 (12.7)	9 (69%)	17.0 (3.8)	na	Respiratory	11	50.2 (12.8)	7 (67%)	6.1 (2.9)	na	Respiratory	15	51.8 (12.8)	11 (73%)	15.3 (3.7)	na	Sepsis
Guerra-Vega [43]	2025	18	62.0 (11.0)	12 (67%)	33.0 (3.0)	14.0 (1.0)	Sepsis	17	59.0 (16.0)	9 (53%)	31.0 (3.0)	15.0 (2.0)	Sepsis							17	53.0 (18.0)	8 (47%)	31.0 (2.0)	14.0 (1.0)	Sepsis
Othman [44]	2023	30	38.8 (11.0)	16 (53%)	29.9 (3.9)	na	Respiratory	30	40.3 (9.3)	15 (50%)	28.0 (4.4)	na	Respiratory	30	45.6 (8.9)	16 (53%)	29.8 (3.3)	na	Respiratory	30	42.4 (13.2)	14 (47%)	28.4 (4.0)	na	Respiratory

na not available

Table A4. Risk of Bias Assessment using the ROBINS-E Tool for Prospective Non-randomized Studies.

Author	Year	D1	D2	D3	D4	D5	D6	D7	Overall
Figueiredo	2023	High	Some concerns	Low	Some concerns	Low	Some concerns	Some concerns	High
Figueiredo	2024	High	High	Low	Low	Low	Low	Some concerns	High
Kourek	2024	Some concerns	High	Low	Low	Low	Some concerns	Some concerns	High
Silva	2017	High	High	Some concerns	Some concerns	Low	Some concerns	Low	High

D1 Confounding; D2 Selection of participants; D3 Classification of exposure; D4 Deviations from intended exposure; D5 Missing data; D6 Measurement of outcomes; D7 Selection of the reported result

Table A5. Risk of Bias Assessment using the RoB-2 Tool for Randomized Controlled Studies.

Author	D1	D2	D3	D4	D5	Overall
Abu-Khaber	⊖	⊖	!	⊖	!	⊖
Akar	!	+	+	+	+	!
Bao	+	+	+	!	+	!
Baron	+	!	!	+	!	!
Berney	+	+	+	!	+	!
Campos	+	+	!	!	+	!
Cerqueira	+	!	⊖	+	!	⊖
Dall'Acqua	+	+	+	+	!	!
Dirks	+	!	⊖	+	!	⊖
Dos Santos	+	⊖	⊖	+	!	⊖
Falavigna	!	+	+	+	!	!
Fischer	!	+	+	+	!	!
Fossat	+	+	+	+	+	+
Gerovasili	+	+	+	+	+	+
Gruther	+	+	!	+	!	!
Hirose	⊖	+	+	⊖	!	⊖
Karatzanos	+	+	!	!	+	!
Kho	+	+	!	+	⊖	⊖
Koutsioumpa	!	+	⊖	!	!	⊖
Leite	⊖	+	⊖	+	⊖	⊖
Liu	!	⊖	+	⊖	!	⊖
Mahran	!	⊖	+	+	⊖	⊖
Medrinal	+	+	+	!	!	!
Meesen	+	+	!	+	!	!
Nakamura	!	+	+	+	!	!
Nakanishi	+	+	+	!	!	!
Othman	+	!	⊖	!	⊖	⊖
Poulsen	+	+	+	+	!	!
Rodriguez	+	+	+	+	!	!
Routsi	+	+	+	+	+	+
Segers	+	+	+	!	!	!
Silva	+	!	+	!	+	!
Stefanou	!	!	+	!	!	!
Verceles	+	+	+	+	!	!
Vieira	+	!	!	!	!	!
Waldauf	+	+	+	!	+	!
Wollersheim	+	+	!	+	!	!
Woo	⊖	!	+	!	⊖	⊖
Zulbaran-Rojas	!	!	!	⊖	!	!

+

 Low risk

!

 Some concerns

⊖

 High risk

D1

 Randomisation process

D2

 Deviations from the intended interventions

D3

 Missing outcome data

D4

 Measurement of the outcome

D5

 Selection of the reported result

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