Supplemental Digital Content 1. Search Strategy

Database: Ovid MEDLINE(R) ALL <1946 to February 17, 2022>

Search Strategy:

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1 ((acute$ or hypoxemic$ or severe$ or hypoxic$ or hypercapn$ or hypercarb$) and (respirat$ adj5 (failure$ or insufficien$ or paralysis$ or deficienc$ or disturbanc$ or depression))).mp. (36886)

2 ((acute or hypox$ or respirat$ or failure$) and (ARF or AHRF)).mp. (5540)

3 or/1-2 [concept 1 - acute respiratory/ hypoxemic failure] (41221)

4 Anoxia/ or exp Dyspnea/ or (anoxemia$ or anoxia$ or dyspnea$ or (deficien$ adj3 oxygen$) or hypoxemia$ or hypoxia$ or hypoxemic$ or hypoxic$ or hypercapn$ or hypercarb$).ti. or (anoxemia$ or anoxia$ or dyspnea$ or (deficien$ adj3 oxygen$) or hypoxemia$ or hypoxia$ or hypoxemic$ or hypoxic$ or hypercapn$ or hypercarb$).ab. /freq=2 (165492)

5 Acute Lung Injury/ or (acute$ and (lung$ adj2 injur$)).tw. or ((lung$ or pulmonary$) adj3 (failure$ or insufficien$)).tw. (31347)

6 Respiratory Distress Syndrome, Adult/ or ((respirator$ adj2 distress$ adj2 syndrom$) or ARDS).tw. or ((acute$ or adult$) adj3 (respirator$ adj3 distress$)).mp. (46421)

7 exp Respiratory Insufficiency/ or (respirat$ adj3 (failure$ or insufficien$ or paralysis$ or deficienc$ or disturbanc$ or depression)).tw. (105857)

8 (lung$ adj2 shock$).tw. (621)

9 ((post traumatic$ or posttraumatic$) adj3 pulmonar$ adj3 insufficienc$).tw. (69)

10 (((post traumatic$ or posttraumatic$) adj3 (respirator$ or lung$)) and failure$).tw. (70)

11 (2019-nCoV$ or nCoV or COVID-19 or covid19 or COVID or CoV-2 or (("2019$" or "19" or novel$ or new or newly or SARS-like or unknown$) adj5 (coronavir$ or corona-vir$ or CoV or CoVs or betacoronavir$ or betacorona-vir$ or beta-coronavir$ or beta-corona-vir$))).mp. (230629)

12 (Severe Acute Respiratory Syndrome Coronavirus 2 or Severe Acute Respiratory Syndrome Corona virus 2 or Severe Acute Respiratory Syndrome Coronavirus 19 or Severe Acute Respiratory Syndrome Corona virus 19).mp. (22599)

13 (SARS Coronavirus 2 or SARS-Cov-2).mp. (146715)

14 ((Wuhan or China or Chinese) and (coronavir$ or COVID or nCoV or corona-vir$ or CoV or CoVs or betacoronavir$ or betacorona-vir$ or beta-coronavir$ or beta-corona-vir$)).mp. (19091)

15 (pneumon$ adj3 ((unknown$ or unusual$ or atypical$ or abnormal$) and (etiolog$ or aetiology$ or Wuhan or China or Chinese))).mp. (1414)

16 or/4-15 [concept 1 Expanded - acute respiratory failure] (542774)

17 3 or 16 (547983)

18 exp Respiration, Artificial/ or exp Ventilators, Mechanical/ or Pneumonia, Ventilator-Associated/ (93853)

19 ((ventilat$ or respirat$) adj2 (artificial$ or mechanical$ or pneumon$ or controlled)).tw,kf. (79695)

20 (respirat$ adj2 assisted$).tw,kf. (303)

21 (ventilat$ adj3 patient$).mp. or (ventilat$ and patient$).ti. or (ventilat$ and patient$).ab. /freq=3 (43200)

22 (PPV and (pressure or ventilat$)).tw,kf. or (IPPB or IPPV).mp. or (CPAP or NCPAP or APVR).mp. (12904)

23 (positive adj3 pressure adj5 (ventilat$ or respir$ or intermittent$)).tw,kf. (11472)

24 (respirator or (ventilat$ adj3 pulmonary$) or interactive$ ventilat$ support$ or airway pressure release ventilati$).mp. (22581)

25 ((pressure$ or ventilat$) and (bilevel or bi-level or biphasic or bi-phasic or BIPAP)).tw,kf. (4489)

26 (((high$ flow$ or highflow$) adj5 therap$) and (nasal$ or can?ul$ or prong$)).tw,kf. (901)

27 (((high$ flow$ or highflow$) adj5 can?ul$) or (nasal$ adj5 (high$ flow$ or highflow$ or prong$))).tw,kf. (2871)

28 (high$ flow$ or highflow$ or high pressure$ or highpressure$ or high tension$ or hyperbaric$).tw,kf. and ((oxygen or O2).tw,kf. or exp Oxygen Inhalation Therapy/) and (nasal$ or can?ul$ or prong$).tw,kf. (1973)

29 (Vapotherm or Airvo 2 or Optiflow).tw,kf. or (High$ adj2 FiO2).tw. or (HFNC or hfnp or HHFNox or HHFNC or HHHFNC or HHFO2).tw. (1420)

30 or/18-29 [concept 3 - ventilated patients MEDLINE] (172687)

31 8 and 17 (621)

32 exp clinical pathway/ or exp clinical protocol/ or exp consensus/ or exp consensus development conference/ or exp consensus development conferences as topic/ or critical pathways/ or exp guideline/ or guidelines as topic/ or exp practice guideline/ or practice guidelines as topic/ or health planning guidelines/ or exp treatment guidelines/ (415147)

33 (guideline or practice guideline or consensus development conference or consensus development conference, NIH).pt. (46623)

34 (position statement* or policy statement* or practice parameter* or best practice*).ti,ab,kf,kw. (40389)

35 (standards or guideline or guidelines).ti,kf,kw. (124518)

36 ((practice or treatment* or clinical) adj guideline*).ab. or clinical$ guide$.ti,ab,tw,kf. (49788)

37 (CPG or CPGs).ti. (6141)

38 consensus*.ti,kf,kw. (30933)

39 consensus*.ab. /freq=2 (30036)

40 ((critical or clinical or practice) adj2 (path or paths or pathway or pathways or protocol*)).ti,ab,kf,kw. (23793)

41 recommendat*.ti,kf,kw. (48177)

42 (care adj2 (standard or path or paths or pathway or pathways or map or maps or plan or plans)).ti,ab,kf,kw. (72258)

43 (algorithm* adj2 (screening or examination or test or tested or testing or assessment* or diagnosis or diagnoses or diagnosed or diagnosing)).ti,ab,kf,kw. (9136)

44 (algorithm* adj2 (pharmacotherap* or chemotherap* or chemotreatment* or therap* or treatment* or intervention*)).ti,ab,kf,kw. (11608)

45 or/32-44 [concept 2 - CADTH database search filters Guidelines — OVID Medline, Embase, PsycINFO] (692979)

46 17 and 30 and 45 [Expanded] (2172)

47 (ventilat$ adj2 mechanical$).ti. or (ventilat$ adj2 mechanical$).ab. /freq=2 (24443)

48 (guideline or guidelines).ti,kf,kw. or ((practice or treatment* or clinical) adj guideline*).ab. or clinical$ guide$.ti,ab,tw,kf. (132717)

49 47 and 48 (251)

50 46 or 49 (2328)

51 limit 50 to yr="2010 -Current" (1652)

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Database: Embase Classic+Embase <1947 to 2022 February 17>

Search Strategy:

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1 ((acute$ or hypoxemic$ or severe$ or hypoxic$ or hypercapn$ or hypercarb$) and (respirat$ adj5 (failure$ or insufficien$ or paralysis$ or deficienc$ or disturbanc$ or depression))).mp. (79959)

2 ((acute or hypox$ or respirat$ or failure$) and (ARF or AHRF)).tw,kw. (8369)

3 or/1-2 [concept 1 - acute respiratory/ hypoxemic failure] (86101)

4 *Anoxia/ or exp *Dyspnea/ or (anoxemia$ or anoxia$ or dyspnea$ or (deficien$ adj3 oxygen$) or hypoxemia$ or hypoxia$ or hypoxemic$ or hypoxic$ or hypercapn$ or hypercarb$).ti. or (anoxemia$ or anoxia$ or dyspnea$ or (deficien$ adj3 oxygen$) or hypoxemia$ or hypoxia$ or hypoxemic$ or hypoxic$ or hypercapn$ or hypercarb$).ab. /freq=2 (192282)

5 *acute lung injury/ or (acute$ and (lung$ adj2 injur$)).tw,kw. or ((lung$ or pulmonary$) adj3 (failure$ or insufficien$)).tw,kw. (46636)

6 *respiratory distress syndrome/ or ((respirator$ adj2 distress$ adj2 syndrom$) or ARDS).tw. or ((acute$ or adult$) adj3 (respirator$ adj3 distress$)).tw,kw. (56914)

7 exp *respiratory failure/ or (respirat$ adj3 (failure$ or insufficien$ or paralysis$ or deficienc$ or disturbanc$ or depression)).tw,kw. (110295)

8 (lung$ adj2 shock$).tw. (969)

9 ((post traumatic$ or posttraumatic$) adj3 pulmonar$ adj3 insufficienc$).tw. (107)

10 (((post traumatic$ or posttraumatic$) adj3 (respirator$ or lung$)) and failure$).tw. (100)

11 (2019-nCoV$ or nCoV or COVID-19 or covid19 or COVID or CoV-2 or (("2019$" or "19" or novel$ or new or newly or SARS-like or unknown$) adj5 (coronavir$ or corona-vir$ or CoV or CoVs or betacoronavir$ or betacorona-vir$ or beta-coronavir$ or beta-corona-vir$))).tw,kw. (232148)

12 (Severe Acute Respiratory Syndrome Coronavirus 2 or Severe Acute Respiratory Syndrome Corona virus 2 or Severe Acute Respiratory Syndrome Coronavirus 19 or Severe Acute Respiratory Syndrome Corona virus 19).tw,kw. (21361)

13 (SARS Coronavirus 2 or SARS-Cov-2).tw,kw. (76388)

14 ((Wuhan or China or Chinese) and (coronavir$ or COVID or nCoV or corona-vir$ or CoV or CoVs or betacoronavir$ or betacorona-vir$ or beta-coronavir$ or beta-corona-vir$)).tw,kw. (16267)

15 (pneumon$ adj3 ((unknown$ or unusual$ or atypical$ or abnormal$) and (etiolog$ or aetiology$ or Wuhan or China or Chinese))).tw,kw. (2347)

16 or/4-15 [concept 1 Expanded - acute respiratory failure] (596194)

17 3 or 16 (619596)

18 exp *artificial ventilation/ or exp *assisted ventilation/ or (ventilat$ adj2 (artificial$ or mechanical$ or pneumon$)).tw. or *ventilator associated pneumonia/ (171905)

19 ((ventilat$ or respirat$) adj2 (artificial$ or mechanical$ or pneumon$ or controlled)).tw,kw. (125621)

20 (respirat$ adj2 assisted$).tw,kw. (741)

21 (ventilat$ adj3 patient$).tw,kw. or (ventilat$ and patient$).ti. or (ventilat$ and patient$).ab. /freq=3 (72030)

22 ((PPV and (pressure or ventilat$)) or (IPPB or IPPV) or (CPAP or NCPAP or APVR)).tw,kw. (23864)

23 (positive adj3 pressure adj5 (ventilat$ or respir$ or intermittent$)).tw,kw. (16355)

24 (respirator or (ventilat$ adj3 pulmonary$) or interactive$ ventilat$ support$ or airway pressure release ventilati$).tw,kw. (16633)

25 ((pressure$ or ventilat$) and (bilevel or bi-level or biphasic or bi-phasic or BIPAP)).tw,kw. (7128)

26 *hyperbaric oxygen/ and (exp *nasal cannula/ or (nasal$ or can?ul$ or prong$).tw. or ((nasal or nose) adj3 tube$1).tw. or (Filterline or Smart CapnoLine).tw.) (66)

27 (((high$ flow$ or highflow$) adj5 therap$) and (nasal$ or can?ul$ or prong$)).tw,kw. (1391)

28 (((high$ flow$ or highflow$) adj5 can?ul$) or (nasal$ adj5 (high$ flow$ or highflow$ or prong$))).tw,kw. (4942)

29 (high$ flow$ or highflow$ or high pressure or highpressure or high tension or hightension or hyperbaric$).tw. and ((oxygen or O2).tw. or exp *oxygen therapy/) and (exp *nasal cannula/ or ((nasal or nose) adj3 tube$1).tw. or (nasal$ or can?ul$ or prong$).tw.) (3192)

30 (Vapotherm or Airvo 2 or Optiflow or (High$ adj2 FiO2) or (HFNC or hfnp or HHFNox or HHFNC or HHHFNC or HHFO2)).tw. (2869)

31 (high$ flow$ or highflow$ or (High$ adj2 FiO2)).tw. and (exp *nasal cannula/ or (nasal$ or can?ul$ or prong$).tw. or ((nasal or nose) adj3 tube$1).tw. or (Filterline or Smart CapnoLine).tw.) (4963)

32 or/18-31 [concept 3 - ventilated patients EMBASE] (245785)

33 8 and 17 (969)

34 exp clinical pathway/ or exp clinical protocol/ or exp consensus/ or exp consensus development conference/ or exp consensus development conferences as topic/ or critical pathways/ or exp guideline/ or guidelines as topic/ or exp practice guideline/ or practice guidelines as topic/ or health planning guidelines/ or exp treatment guidelines/ (797750)

35 (guideline or practice guideline or consensus development conference or consensus development conference, NIH).pt. (0)

36 (position statement* or policy statement* or practice parameter* or best practice*).ti,ab,kw. (58004)

37 (standards or guideline or guidelines).ti,kw. (155690)

38 ((practice or treatment* or clinical) adj guideline*).ab. or clinical$ guide$.ti,ab,tw. (74317)

39 (CPG or CPGs).ti. (7352)

40 consensus*.ti,kw. (37494)

41 consensus*.ab. /freq=2 (39675)

42 ((critical or clinical or practice) adj2 (path or paths or pathway or pathways or protocol*)).ti,ab,kw. (35414)

43 recommendat*.ti,kw. (59389)

44 (care adj2 (standard or path or paths or pathway or pathways or map or maps or plan or plans)).ti,ab,kw. (126879)

45 (algorithm* adj2 (screening or examination or test or tested or testing or assessment* or diagnosis or diagnoses or diagnosed or diagnosing)).ti,ab,kw. (12789)

46 (algorithm* adj2 (pharmacotherap* or chemotherap* or chemotreatment* or therap* or treatment* or intervention*)).ti,ab,kw. (17152)

47 or/34-46 [concept 2 - CADTH database search filters Guidelines — OVID Medline, Embase, PsycINFO] (1156687)

48 17 and 32 and 47 [Expanded] (3828)

49 (ventilat$ adj2 mechanical$).ti. or (ventilat$ adj2 mechanical$).ab. /freq=2 (38237)

50 (guideline or guidelines).ti,kw. or ((practice or treatment* or clinical) adj guideline*).ab. or clinical$ guide$.ti,ab,tw. (182031)

51 49 and 50 (399)

52 48 or 51 [ADD English language? AND last 10 or 5 years?] (4092)

53 limit 52 to yr="2010 -Current" [ADD mechanical ventilation and non-invasive ventilation (such as High-Flow Nasal Cannula, Face mask, and BiPAP] (3324)

54 limit 53 to embase [to remove conferences] (1783)

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Supplemental Digital Content 2. AGREE-II domain quality scores are presented. Green boxes are for scores >70%, yellow is 60-70%, and red are for scores <60%.

Study	Scope and Purpose	Stakeholder Involvement	Rigor of Development	Clarity and Presentation	Applicability	Editorial Independence
Fan 2017	97.2	80.6	92.7	94.4	83.3	100.0
Griffiths 2019	97.2	72.2	88.5	97.2	87.5	91.7
Rhodes 2016	100.0	75.0	91.7	88.9	81.3	100.0
Claesson 2014	91.7	77.8	70.8	63.9	62.5	87.5
Cho 2016	86.1	77.8	87.5	86.1	77.1	83.3
Alhazzani 2020	97.2	83.3	95.8	94.4	91.7	100.0
Quintard 2019	66.7	66.7	31.3	77.8	47.9	75.0
Fichtner 2018	83.3	80.6	85.4	80.6	81.3	91.7
Joannidis 2019	69.4	66.7	69.8	72.2	64.6	83.3
Hashmi 2015	91.7	77.8	64.6	69.4	75.0	95.8
Hashimoto 2017	91.7	86.1	95.8	97.2	95.8	95.8

Pappazian 2019	94.4	75.0	85.4	94.4	77.1	91.7
Neto 2021	91.4	83.1	88.7	92.9	89.1	96.6

Supplemental Digital Content 3. Characteristics and summary of included guidelines and their relevant recommendations.

Study	Recommendation	Country/ Region	Patient Population	Impact on Outcome		Level of Recommendation	Level of Evidence	Number of Studies (Patients) Included	Assessed Quality of Evidence?
				Morbidity	Mortality				
Fan 2017	Limit Tidal Volumes to 4-8mL/kg and maintain plateau pressure <30cm H2O	North America and Europe	ARDS patients in ICU	RR 0.96	RR 0.87	Strong	Moderate	7 (1481)	GRADE
	Patients with moderate or severe ARDS receive higher rather than lower levels of PEEP	North America and Europe	ARDS patients in ICU	-	RR 0.91	Conditional	Moderate	6 (2580)	GRADE
	Recommend High-Frequency Oscillatory Ventilation (HFOV) should not be routinely used in moderate to severe ARDS.	North America and Europe	ARDS patients in ICU	RR 1.15	RR 0.94	Strong	Moderate	6 (1715)	GRADE
	Suggest that adult patients with ARDS receive recruitment maneuvers (RMs)	North America and Europe	ARDS patients in ICU	-	RR 0.91	Conditional	Low-Moderate	6 (1423)	GRADE
Griffiths 2019	Lower tidal volume (less than or equal to 6 mL/kg predicted body weight) ventilation with a plateau pressure less than or equal to 30 cmH2O.	British	ARDS patients in ICU	RR 1.17	RR 0.83	Strong	Moderate	3 (1038)	GRADE

	Suggest the use of high PEEP strategies for patients with moderate or severe ARDS (P/F ratio <27 kPa)	British	ARDS patients in ICU	RR 0.97	RR 0.83	Weak	Moderate	3 (1921)	GRADE
	Do not recommend use of HFOV in ARDS patients.	British	ARDS patients in ICU	RR 1.21	RR 1.04	Strongly Against	Moderate	5 (1380)	GRADE
Claesson 2014	Suggest utilisation of small tidal volumes (5-8ml/kg) and plateau pressure <31 cm H2O	Scandanavia	ARDS patients in ICU	RR 0.92	RR 0.83	Strong	High	6 (1297)	GRADE
	In patients with moderate to severe ARDS we suggest increasing PEEP to improve oxyegnation efficiency	Scandanavia	ARDS patients in ICU	RR 1.19	RR 0.87	Weak	Moderate	6 (2299)	GRADE
	We suggest that partial modes of ventilatory support may be used if clinically feasible.	Scandanavia	ARDS patients in ICU	RR 1.23	RR 0.78	Weak	Very Low	3	GRADE

	We suggest that both pressure and volume-regulated ventilation may be used in mechanically ventilated patients with ARDS. We suggest that both modes of ventilation are equally beneficial or detrimental, and that both modes can be used at the discretion of the attending physician.	Scandanavia	ARDS patients in ICU	RR 1.23	RR 0.78	Weak	Low	3 (136)	GRADE
Alhazzani 2020	We recommend using low tidal volume ventilation (Vt 4-8mL/kg of predicted body weight), over higher tidal volumes (Vt > 8mL/kg)	North America and Europe	COVID-19 ARDS in ICU	-	RR 0.73	Strong	Moderate	5 (1181)	GRADE
	We recommend targeting plateau pressures (Pplat) of <30cm H2O	North America and Europe	COVID-19 ARDS in ICU	-	RR 0.80	Strong	Moderate	9 (1629)	GRADE
	We suggest using a higher PEEP strategy, over a lower PEEP strategy	North America and Europe	COVID-19 ARDS in ICU	-	RR 0.94	Weak	Low	3 (2299)	GRADE

Hashimoto 2017	We recommend the use of low tidal volume at 6-8 mL/kg (predicted body weight: PBW) in adult patients with ARDS	Japan	ARDS in ICU	RR 0.82	RR 0.84	Strong	Moderate	6 (1305)	GRADE
	We suggest setting the plateau pressure at 30cmH20 or less in adult patients with ARDS undergoing mechanical ventilation.	Japan	ARDS in ICU	RR 0.92	RR 0.84	Weak	Low	4 (1132)	GRADE
	We suggest using PEEP within the range of plateau pressures less than or equal to 30cmH2O, without compromising hemodynamics.	Japan	ARDS in ICU	RR 0.97	RR 0.83	Weak	Moderate	3	GRADE
	We suggest against the use of High Frequency Oscillation (HFO) in adult patients with ARDS	Japan	ARDS in ICU	RR 1.21	RR 1.05	Weak	Low	4	GRADE

Pappazian 2019	A tidal volume around 6 mL/kg of predicted body weight (PBW) should be used as a first approach in patients with recognized ARDS, in the absence of severe metabolic acidosis, including those with mild ARDS.	Germany	ARDS in ICU	-	RR 0.8	Strong	High	7 (1481)	GRADE
	Once tidal volume is set to around 6 mL/kg PBW, plateau pressure should be monitored continuously and should not exceed 30 cmH2O.	Germany	ARDS in ICU	-	-	Strong	High		GRADE
	High PEEP should probably be used in patients with moderate or severe ARDS, but not in patients with mild ARDS.	Germany	ARDS in ICU	-	-	Strong	High		GRADE
	High-frequency oscillation ventilation should not be used in ARDS patients.	Germany	ARDS in ICU	-	-	Strong	High		GRADE
	Recruitment maneuvers should probably not be used routinely in ARDS patients.	Germany	ARDS in ICU	-	-	Weak	Moderate	-	GRADE

Hashmi 2015	Lung protective strategies should be used i.e. a tidal volume of 6-8 ml/ kg of predicted body weight.	Pakistan	Sepsis/ARDS	-	-	Strong	High	-	GRADE
	Measuring and keeping plateau pressure < 30 mmHg.	Pakistan	Sepsis/ARDS	-	-	Strong	Moderate	-	GRADE
	Suggest adequate PEEP to avoid alveolar collapse.	Pakistan	Sepsis/ARDS	-	-	Strong	Moderate	-	GRADE
Rhodes 2016	Recommend using a target tidal volume of 6 mL/kg predicted body weight	British	ARDS patients in ICU	-	-	Strong	High	-	GRADE
	Recommend using an upper limit goal for plateau pressures of 30 cm H2O over higher plateau pressures in adult patients with sepsis-induced severe ARDS	British	ARDS patients in ICU	-	-	Strong	High	-	GRADE
	Suggest using higher PEEP over lower PEEP in adult patients with sepsis-induced moderate to severe ARDS	British	ARDS patients in ICU	-	-	Weak	Moderate	-	GRADE

Cho 2016	We recommend low tidal volume ventilation can be applied to patients with ARDS.	Korean	ARDS patients in ICU	-	-	Strong	High		GRADE
	We suggest high PEEP can be applied to patients with ARDS, who have Pao2/FIO2<200 mmHg.	Korean	ARDS patients in ICU	-	-	Weak	Moderate		GRADE
	We suggest recruitment maneuver can be applied to patients with ARDS to reduce mortality	Korean	ARDS patients in ICU	-	-	Weak	Moderate		GRADE
	The use of HFOV should not be recommended as a standard treatment method in adult patients with ARDS	Korean	ARDS patients in ICU	-	-	Strong	Moderate		GRADE
Joannidis 2019	We recommend monitoring of tidal volumes and ventilation pressures and application of lung protective ventilation strategies (low-tidal volume) in patients receiving mechanical ventilation to reduce the risk of new or worsening AKI	International	Multi-organ dysfunction patients in ICU	-	-	Strong	Low	1 (861)	GRADE

Quintard 2019	A PEEP of at least 5 cmH2O should probably be applied after intubation of hypoxaemic patients.	French	ICU Patients	-	-	Strong	-	-	GRADE
Fichtner 2018	A post-intubation recruitment manoeuvre should probably be used in ICU in hypoxaemic patients, by integrating it into the respiratory component	French	ICU Patients	-	-	Strong	-	-	GRADE
	Ventilation with high PEEP is recommended	Germany	ARDS Patients in ICU	-	-	Strong	High	-	GRADE
	It is recommended that ARDS patients should be ventilated with a Vt not exceeding 6 mL/kg standard body weight (BW)	Germany	ARDS Patients in ICU	-	-	Strong	Moderate	-	GRADE

	It is recommended that mechanically ventilated patients should be treated with the lowest possible FiO2 with which a target arterial oxygen saturation (SaO2) of 90–94% or an arterial partial pressure of oxygen (PaO2) of 60–80 mmHg (8.0–10.7 kPa) can be attained	Germany	ARDS Patients in ICU	-	-	Weak	Expert Consensus	-	GRADE
	The peak inspiratory pressure for patients with ARDS should not exceed 30 cm H2O	Germany	ARDS Patients in ICU	-	-	Strong	Moderate	-	GRADE
	It is recommended that high frequency oscillation ventilation (HFOV) should not be used to treat adult patients with ARDS	Germany	ARDS Patients in ICU	-	-	Strong	High	-	GRADE
Neto 2021	We recommend using a low tidal volume (4–8 mL/kg of PBM), and whenever possible, a tidal volume ≤6 mL/kg of PBW should be pursued	LMICs	COVID-19	-	-	Strong	High	-	GRADE

	We recommend using a “low PEEP/high FiO2 table”	LMICs	COVID-19	-	-	Moderate	Low	-	GRADE
	We recommend against using routine recruitment maneuvers, unless as a rescue therapy in refractory hypoxemia	LMICs	COVID-19	-	-	Moderate	Low	-	GRADE

Supplemental Digital Content 4. All the guidelines that made a recommendation on PEEP are presented below with effect size and confidence intervals.

Study	Recommendations	Impact on Morbidity	Impact on Mortality	Level of Recommendation	Confidence in Effect Estimate	Source of Evidence	Studies Included No. (Participants)	Mortality Effect Size (Confidence Interval)	Type of Morbidity	Studies Included, No.	Morbidity Effect Size (Confidence Interval)
Fan 2017	Suggest that patients with moderate or severe ARDS receive higher rather than lower levels of PEEP	No difference in barotrauma, new organ failure, or ventilator-free days.	No difference in mortality in RCTs but IPDMA from 3 large RCTs showed improved mortality in patients with moderate to severe ARDS.	Conditional	Moderate	RCTs and IPDMA	6 (2580)	RR 0.91 (0.8-1.03)	A) Oxygenation B) Higher PEEP strategies were not associated with significant difference in barotrauma, new organ failure, or VFDs (moderate confidence)		a) 61 mmHg (46-77)

Griffiths 2019	Suggest the use of high PEEP strategies for patients with moderate or severe ARDS (P/F ratio <27 kPa)	No difference in barotrauma or ICU free days.	Three RCTs and a meta-analysis show improved ICU mortality with high PEEP strategy.	Weakly In Favor	Moderate	RCTs and MA	5 (1921)	RR 0.83 (0.67-1.01)	A) Barotrauma b) ICU free days	5 (2504)	A) RR 0.97 (0.66-1.42) B) 0.04 Mean difference higher (0.03-1.1)
Rhodes 2016	Suggest using higher PEEP over lower PEEP in adult patients with sepsis-induced moderate to severe ARDS	Three RCTs and one plot trial did not show benefit or harm.	A patient-level meta-analysis showed no benefit in all patients with ARDS; however, patients with moderate or severe ARDS (Pao2/Fio2 ≤ 200 mm Hg) had decreased mortality with the use of higher PEEP, whereas those with mild ARDS did not.	Weak	Moderate	RCTs	3 large multicentre trials and a pilot trial	NR	NR	NR	NR

Clasesson 2014	High PEEP (>5cm H2O). In patients with moderate to severe ARDS we suggest increasing PEEP to improve oxyegnation efficiency	Higher PEEP improves oxygenation efficiency without any significant increase in barotrauma, but may increase duration of mechanical ventilation and LOS-ICU	Has no demonstrable effect on mortality. Evidence in two recent systematic reviews suggest that any mortality benefit of higher PEEP is limited to patients with moderate to severe ARDS	Weak	Moderate	RCTs	3 (2299)	1) ALL hospital Mortality RR0.94 (0.86-1.04) 2) ALL ICU mortality RR 0.87 (0.78-0.97)	1) Baro trauma 2) Ventilator Free days 3) Use of Rescue Therapies 4) Death after rescue therapy	3 (2299)	1) RR 1.19 (0.89-1.6) 2) N/A 3) RR 0.64 (0.54-0.75) 4) RR 0.65 (0.52-0.8)
Cho 2016	We suggest high PEEP can be applied to patients with ARDS, who have Pao2/FIO2<200 mmHg to reduce mortality	The cochrane review did not a show signifcant differenc ein barotraume between the two groups	A cochrane review which meta-analyzed 7 RCTs showed that high PEEP did not contribute to a reduction of hospital mortality, but in a secondary group where PaO2/FIO2 <200mmHg high PEEP decreased mortality within the ICU	Grade 2	B level	Meta Analysis + Clinical Studies	NR	NR	NR	NR	NR

Alhazzani COVID 21	For mechanically ventilated adults with COVID-19 and moderate to severe ARDS, we suggest using a higher PEEP strategy, over a lower PEEP strategy	In patients ARDS, a higher PEEP strategy resulted in a reduction in the use of rescue therapies	Individual patient data meta-analysis of 3 large trials of high PEEP found no difference in in-hospital mortality in all patients. However in patients ARDS, a higher PEEP strategy resulted in lower ICU mortality, lower in-hospital mortality	Weak	Low	RCTs	3 (2299)	RR 0.94 (0.86-1.04)	Use of rescue therapies	NR	RR 0.63 (0.53-0.75)

Fichtner 2018	In patients with ARDS, ventilation with high PEEP is recommended	NR	Two meta-analyses, each of which was based on three multicenter RCTs, showed that ventilation with high PEEP lowers the mortality of ARDS patients, compared to ventilation with low PEEP or conventional ventilation	Strong	++++	RCT and Meta-analysis	NR	ICU: 37.6% vs. 56.3%; In-hospital: 34.1% vs. 39.1%	NR	NR	NR
Hashmi 2015	Adequate PEEP to avoid alveolar collapse	NR	NR	Strong	Moderate	NR	NR	NR	NR	NR	NR

Hashimoto 2017	We suggest using PEEP within the range of plateau pressures less than or equal to 30cmH2O, without compromising hemodynamics	NR	We conducted a systematic review and included seven randomized clinical trials, which show that there are no differences in hospital mortality, incidence of barotrauma or ventilator-free days (VFD) comparing patient groups receiving higher PEEP and lower PEEP levels	Weak	Moderate	RCTs	3	RR 0.93 (0.83-1.04)	1) Barotrauma 2) Ventilator-Free Days	7	1) 0.97 2) mean 1.89 days more
Pappazian 2019	High PEEP should probably be used in patients with moderate or severe ARDS, but not in patients with mild ARDS.	NR	NR	Strong	High	NR	NR	NR	NR	NR	NR

Neto 2021	We recommend using a “low PEEP/high FiO2 table”	NR	NR	Moderate	Low	NR	NR	NR	NR	NR	NR

Supplemental Digital Content 5. A suggested framework for the design and development of a basic open-source ventilator that is evidence-based is shown below, divided into main categories of “Ventilation”, “Gas and Electricity”, and Monitoring and Alarms”.

Ventilation

1. Must have at least 1 *mode of ventilation*

    a. Must have continuous mode ventilation (CMV).

    b. The CMV mode must be either

        i. (ideally) Pressure-controlled ventilation (PCV), or

        ii. Volume-controlled ventilation (VCV).

    c. Pressure Control Ventilation - a set pressure is delivered for the period of inspiration and the volume achieved is measured and displayed.

    d. Volume Control Ventilation– the user sets a tidal volume and respiratory rate. The tidal volume is delivered during the inspiratory period. Acceptable only if additional pressure limiting controls are available.

    e. Ideally should have a spontaneous breathing pressure support mode for those patients spontaneously breathing, e.g. BIPAP. The user sets an inspiratory pressure and an expiratory pressure, which is applied when the ventilator senses a patient starting to breathe in and when breathing out, respectively. The expiratory pressure is still positive pressure but lower than the inspiratory pressure.

2. If a ventilator has a pressure support mode, as a safety precaution, it must automatically default into a mandatory mode ventilation if the patient stops breathing in.

3. *Inspiratory airway pressure*, the higher pressure setting that is applied to make the patient breathe in:

a. Can range from 20-70cm H2O.

b. Must have the ability to conduct an inspiratory pause for the measurement and monitoring of plateau pressure.

c. If volume control ventilation is used, the user must be able to set airway pressure limit between 15 – 40 cmH2O.

4. *Positive End Expiratory Pressure (PEEP).* The pressure maintained in the breathing system during expiration.

a. Ideal range 5-20 cm H2O adjustable in 2 cmH2O increments.

b. PEEP must be maintained during expiration phase.

5. *Inspiratory:Expiratory ratio (I:E).* The proportion of each breathing cycle that is spent breathing in compared to breathing out.

a. Must provide 1:2 (i.e. expiration lasts twice as long as inspiration) as the default setting.

b. Can provide adjustable I:E in the range 1:1 – 1:3.

6. *Respiratory Rate*. The number of breathing cycles every minute.

a. Must provide a range 10 – 30 breaths per minute in increments of 2 (only in mandatory mode) that can be set by the user.

7. *Tidal Volume (Vt) setting*, if provided. The volume of gas flowing into the lungs during one cycle.

a. Must have at least one setting of 400ml +/- 10 ml.

c. Could have a range 250 – 1000 ml in steps of 50ml.

Gas and Electricity

1. Incoming Gas Supply.

a. Must connect to wall pipeline oxygen supply.

b. Oxygen supply from wall outlets outside of ICU and theatres is limited to approximately 6-10 lpm. As such, ventilators could provide for a gas reservoir to manage peak inspiratory flow rates of up to 100 lpm or an oxygen concentrator as the source of oxygen.

2. Electricity Supply.

a. If electricity is required for functioning, there must be a battery backup of in case of electricity failure.

3. Gas supply to patient.

a. User must be able to control inspired oxygen proportion (FiO2). The percentage of oxygen in the gas being breathed in by the patient. Room air is 21% oxygen.

b. Must provide range of FiO2 from 40% - 100% with 10% steps.

Monitoring and Alarms

1. *Must alarm at*:

a. Gas or electricity supply failure.

b. Machine switched off while in mandatory ventilation mode.

c. Inspiratory airway pressure exceeded.

d. Inspiratory and PEEP pressure not achieved (equivalent to disconnection alarm).

e. Tidal volume not achieved or exceeded.

2. *Monitoring displayed continuously so the user can verify*.

a. Must show the current settings of tidal volume, frequency, PEEP, FiO2, ventilation mode.

b. Must show the actual current airway pressure.

c. Should show the achieved tidal volume, breathing rate, PEEP, and FiO2.

d. If pressure support mode is provided there must be real time confirmation of each patient breath and an alarm if below acceptable range.

e. Could provide CO2 monitoring.

Supplemental Digital Content 6. PRISMA checklist.

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	2-3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	3-4
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	4
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	5
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	6
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	39-43
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	5-6
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	6-7
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	6-7
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	6-7
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	7
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	6-7
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	7
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	N/A
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	7
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	N/A
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	N/A
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	N/A
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	N/A
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	7

Section and Topic	Item #	Checklist item	Location where item is reported
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	7-8
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	7-8
Study characteristics	17	Cite each included study and present its characteristics.	8-9
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	9
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Tables 1-2
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Tables 1-2
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	9-13
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	N/A
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	N/A
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	N/A
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Tables 2-3
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	13-16
	23b	Discuss any limitations of the evidence included in the review.	13-16
	23c	Discuss any limitations of the review processes used.	13-16
	23d	Discuss implications of the results for practice, policy, and future research.	13-16
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	5
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	5
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	N/A
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	1
Competing interests	26	Declare any competing interests of review authors.	1
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	N/A

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

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