

S3 Leitlinie Invasive Beatmung und Einsatz extrakorporaler Verfahren bei akuter respiratorischer Insuffizienz – Evidenzbericht Teil 1

Literaturrecherche, Literaturselektion, Bewertung Meta-Analysen (SIGN-Checklisten)

Erläuterung:

Der Evidenzbericht ist aufgrund seines Umfangs sowie aufgrund unterschiedlicher verwendeter Tabellenformate in der Evidenzbewertung in 3 Teile aufgeteilt.

1. Teil (fortlaufend):

- PICO Fragen Kapitelweise
- Dokumentation Leitlinien-Recherche
- Dokumentation Leitlinienselektion
- Literaturrecherche Filteralgorithmen
- Literaturselektion Übersicht
- Literaturanalyse/bewertung_Meta-Analysen_externe Bewertung nach SIGN Standard
-

2. Teil (fortlaufend):

Leitlinienbewertung, Evidenztabelle und – profile in der Abfolge der Unterkapitel der Langversion

3. Teil (fortlaufend):

Leitlinienbewertung, Evidenztabelle und – profile ausgewählter Unterkapitel:

- 3.5 Adaptive Beatmungsverfahren
- 4.5 Inspiration-Expiration-Verhältnis
- 5.1 Sedierung, Analgesie, Delirmanagement und neuromuskuläre Blockade
- 5.6.4 Transfusion von Erythrozytenkonzentraten
- 7.1 Definition von Weaning-Kategorien
- 7.2 Weaning-Protokolle
- 7.3 Prädiktion für die Entwöhnbarkeit vom Beatmungsgerät
- 8.x Spezifische Langzeitfolgen

140425 S3-LL "Invasive Beatmung und Einsatz extrakorporaler Verfahren bei akuter respir. Insuffizienz"

Fragestellungen für die Literaturrecherche

PICO - Struktur

Variable: Outcome

Kategorien:

1	Überleben	1.a) Sterblichkeit 1.b) Überleben 1.c) Langzeitüberleben
2	Lebensqualität	2. Lebensqualität (Health Related Quality of Life)
3	Neurologie	3.a) Neurol. Funktion (inkl. Fatigue, kogn. Dysfunktion) 3.b) Integration in Arbeitsalltag, Functional Independence
4	Intensivtherapiedauer	4.) Intensivstationsverweildauer (ICU- LOS)
5	Dauer Invas. Beatmung	5.a) Beatmungsdauer/Beatmungsfreie Tage 5.b) Weaningserfolg/Weaningversagen 5.c) Erforderliche Langzeitbeatmung
6	Krankenhausverweildauer	6. Krankenhausverweildauer (H-LOS)
7	Ausmaß pulm. Dysfunktion	7.a) Oxygenierung 7.b) Decarboxylierung 7.c) Korrektur Azidose 7.d) Lungenfunktion (Compliance/Resistance) 7.e) Reduktion ECMO Inzidenz 7.f) Pneumonie 7.g) bleibende Lungenschäden 7.h) bei PAH Reduktion PAP
8	Organdysfunktion akut/chron.	8. (Multi-) Organdysfunktion (-versagen)/Morbidity
9	Stress	9.a) Sedierungs/Katecholaminbedarf 9.b) Patientenkomfort am Beatmungsgerät
10	Komplikationen	10.) Häufigkeit und Schwere von Komplikationen
11	Ökonomie	11.) Ökonom. Bewertung

A	B	C	D	E	F
1 Thema	Population/Patient	Intervention	Comparison	Outcome/Ziele	Bemerkung
2 1. Hypoxämisch akutes respir. Versagen	akutes hypoxäm. Respir. Versagen	1. invasive Beatmung	1. NIV 2. Sauerstoff	1. a Sterblichkeit 1.b Langzeitüberleben 2. Lebensqualität 3.a neurol. Funktion 4. ICU-LOS 6. KH-LOS 5.b) weaning-Versagen 7.a) Gasaustausch 7.f) Pneumonie 8. Organversagen	
3		2. Intubation	1. NIV 2. Sauerstoff 3. Nicht Intubation	s. o.	
4	Untergruppen für jede Hauptfrage				
5	~ + Pneumonie				
6	~ + Schock				
7	~ + kardiogener Schock				
8	~ + Akute Herzinsuffizienz				
9	~ + kardiogenes Lungenödem				
10	~ + Trauma				
11	~ + SHT				
12	~ + Adipositas				
13	~ + Kinder				
14	~ + Säugling				
15	~ + Neugeborene				
16	akut auf chron. Hypoxämie				
17					
18 2. Hyperkapnisch akutes respir. Versagen	akute Hyperkapnie	1. invasive Beatmung	1. NIV 2. CPAP 3. Kürossbeatmung	1. a Sterblichkeit 1.b Langzeitüberleben 2. Lebensqualität 3.a neurol. Funktion 4. ICU-LOS 6. KH-LOS 5.b) weaning-Versagen 7.a) Gasaustausch 7.f) Pneumonie 8. Organversagen	
19	Untergruppen für jede Hauptfrage				
20	akute Hyperkapnie + COPD				
21	akute Hyperkapnie + neuromuskuläre Erkrankungen				
22	akute Hyperkapnie + Adipositas				
23	akute Hyperkapnie + Kinder				
24	akute Hyperkapnie + Säuglinge				
25		2. Intubation	1. NIV 2. CPAP 3. Kürossbeatmung 4. Nicht Intubation	s.o.	
26					
27					
28 3. Andere Indikationen	Vigilanzminderung/Koma	1. Invasive Beatmung 2. Intubation	1. NIV 2. Nicht Intubation 3. Sauerstoff	1. Sterblichkeit 2. Lebensqualität 3.a) Neurolog. Funktion 7.f) Pneumonie	
29	Vigilanzminderung/Koma + Kinder	s.1./2.	s.1.-3.	s.o. 1./2./3.a)/7.f)	
30	Trauma/Polytrauma	s.1./2.	s.1.-3.	s.o. 1/2/3/7f	
31	Trauma/Polytrauma + Kinder	s.1./2.	s.1.-3.	s.o. 1/2/3/7f	
32					
33 4. Zielkriterien in der BGA /SaO2	ARDS	SaO2 < 90% oder paO2 < 60 mmHg	SaO2 > 90 oder > 60 mmHg	1.a) Sterblichkeit, 4. ICU-LOS, 5.a) VFD	
34	ARDS mit PaO2/FiO2 < 100	SaO2 < 90% oder paO2 < 60 mmHg	SaO2 > 90 oder > 60 mmHg	1.a) Sterblichkeit, 4. ICU-LOS, 5.a) VFD	
35	ARDS	pH < 7,30 oder pCO2 > 60 mmHg	pH > 7,30 oder pCO2 < 60 mmHg	1.a) Sterblichkeit, 4. ICU-LOS, 5.a) VFD	
36	ARDS mit PaO2/FiO2 < 100	pH < 7,30 oder pCO2 > 60 mmHg	pH > 7,30 oder pCO2 < 60 mmHg	1.a) Sterblichkeit, 4. ICU-LOS, 5.a) VFD	
37					
38				Initial gefasste freie Fragen, welche die Grundaussagen des Kapitels beantworten sollten.	
39					1. Welche Ziele verfolgt die invasive Beatmung?
40					2. Welche Gefahren der Beeinflussung der Indikationsstellung zur invasiven Beatmung gibt es?
41					3. Welche Patienten benötigen unmittelbare Intubation und invas. Beatmung zur Sicherung des Überlebens und Vermeidung von Komplikation?
42					4. Welche Patientin können initial mit nicht-invasiven Verfahren versorgt werden?
43					5. Wann sollte ein initial mit nicht-invasivem Verfahren behandelter Patient invasiv beatmet werden?
44					6. Bei welchen Patienten sollte eine IN und invasive Beatmung vermieden werden?
45					7. Wann und wie sollte eine invasive Beatmungstherapie beendet werden?

Thema	Population/Patient	Intervention	Comparison	Outcome/Ziele	Bemerkung
1) Kontrollierte Beatmungsmodi	1. Hypoxämisches Lungenversagen 2. Hyperkapnisches Lungenversagen 3. kombin. Gasaustauschstörung 4. Trauma- Patienten	Kontrollierte Modi	alle Modi	1.a). Mortalität, eventuell: 28, 30, 90, 180 Tage Mortalität 2. Health related QoL 3.b) Integration in Arbeitsalltag oder functional independence 4. ICU LOS 5.a) Tage invasiver Beatmung oder Ventilator free days 7.a) Oxygenierung 7.b) Dekarboxygenierung 7.d) Lungenfunktion: Vitalkapazität und FEV1 9.a) Sedierung und Katecholamine Vergleich kontrolliert zu assistiert 9.b) Patientenkomfort am Beatmungsgerät	Jegliche Vergleiche der Beatmungsmodi zulassen!
2) Assistierte Beatmungsmodi	s. Thema 1 (1-4)	Assis. Modi	s. Thema 1	s.o.	
3) BIPAP APRV	s. Thema 1 (1-4)	APRV/BIPAP/BIlevel/Bivent	s. Thema 1	s.o.	
4)Adaptiv/Automatisiert	s. Thema 1 (1-4)	SmartCare/ASV/Intelligent/ PAV/NAVA/ ATC	s. Thema 1	s.o.	
5) HFOV	s. Thema 1 (1-4)	HFOV/HFO/Jet-Ventilation	s. Thema 1	s.o.	

Thema	Population/Patient	Intervention	Comparison	Outcome	Bemerkung
1. PEEP	Akutes respiratorisches Versagen	PEEP	PEEP Niveau?	1.a) Überleben	Evidenz optim. Niveau?
	Untergruppen für Hauptfrage ~ + Erwachsener+Hypoxämisch ~ + Erwachsener+Hyperkapnisch ~ + Kinder ab Neugeborenen+Hypoxämisch ~ + Kinder ab Neugeborenen+Hyperkapnisch ~ + erhöhter ICP ~ + angeborene Herzfehler ~ + Adipositas ~ + erhöhter IAP ~ + verminderte Thoraxcompliance	ggf. PEEP - Trial/Titration (Übernahme von AG VI)		2.) Lebensqualität 4.) ICU-LOS 5.a) Beatmungsdauer 7.g) bleibender pulm. Schaden	Beste Kriterien indiv. Dosisfindung
2. FiO2	s.1. Thema + Untergruppen s.1.	FiO2		s.o. 3.a) kognitive Schäden 7.g) pulmon. Hypertonie	Optim. Niveau ? Beste Kriterien?
3. Vt	s.1. Thema + Untergruppen s.1.	Tidalvolumen	Tidalvolumen	s.1. Thema	Optim. Volumen? Berechnungsgrundlage?
4. I:E inkl. IRV	s.1. Thema + Untergruppen s.1.	Atemzeitverhältnis (Inspirations- zu Expirationszeit)		s.1. Thema	s.1.
5. permiss. Hyperkapnie	s.1. Thema + Untergruppen s.1.	normokapnisch	hyperkapnisch	s.1. Thema	s.1.
6. permiss. Hypoxämie	s.1. Thema + Untergruppen s.1.			s.1. Thema	
7. PAW	s.1. Thema + Untergruppen s.1.	Höhe PAW		s.1. Thema	s.1.
8. Beatmungsfrequenz	s.1. Thema + Untergruppen s.1.	Frequenz		s.1. Thema	s.1. Kinder altersabhängig
9. Gewichtung von Beatmungskriterien	s.1. Thema + Untergruppen s.1.	Kriterien: PEEP, FiO2, Vt, PAW, RR, pH		s.1. Thema	
10. Monitoring	Akutes respiratorisches Versagen	BGA während SpO2 und etCO2	BGA Häufigkeit	1.a Mortalität 8.) Morbidität	Optimale Häufigkeit BGA?
	Untergruppen für Hauptfrage: ~ + Erwachsener ~ + Kind				
11. Welche Messparameter sind entscheidend?	s.1. Thema + Untergruppen s.1.	pH, Cardiac Output, SpO2, pO2, pCO2, nicht suchen: "good clinical practice"		s.1. Thema	

Thema	Population/Patient	Intervention	Comparison	Outcome	Bemerkung		
Sedierung invas. Beatmeter Patienten	ALI / ARDS	Analgesiedierung		1.a) Sterblichkeit	hohe Relevanz aus Sicht der Patientenvertreter		
				2.) Qual. of life			
				5.b) Weaningserfolg			
				6.) KH Entlassung			
				9.b) Patientenkomfort – Symptomkontrolle			
ARDS spez. AS	ALI / ARDS	Spezifische Analgesiedierung	Vergleichsgruppe	s.o.			
Muskelrelaxantien	ALI / ARDS	Relaxierung	Keine Relaxierung	s.o.			
Muskelrelaxantien	ALI / ARDS P/F <150	Muskelrelaxantien	Keine Relaxierung	s.o.			
Delirrate	ALI / ARDS	Delirmonitoring CAM-ICU	kein Monitoring	s.o.			
Delirrate	ALI / ARDS	Spezifische Delirtherapie	kein Therapie	s.o.			
			keine				
Ernährung	ALI / ARDS	spezifische hochkalorische Ernährung	Standardtherapie	s.o.			
Ernährung	ALI / ARDS	parenterale Ernährung	enterale Ernährung	s.o.			
Ernährung	ALI / ARDS	Immunonutrition	Standardtherapie	s.o.			
Mobilisation	ALI / ARDS	Wann beginnen	keine	s.o.	hohe Relevanz aus Sicht der Patientenvertreter		
				Wie lange		keine	
				Wie oft		keine	s.o.
				Welche Techniken		keine	s.o.
VAP Prophylaxe	ALI / ARDS	SOD	keine SOD	Sterblichkeit, VAP-rate,			
		SDD	Keine SDD	s.o.			
	ALI / ARDS	Geschlossenes Absaugen,	Standardvorgehen	s.o.			
	ALI/ARDS	Oberkörperhochlagerung	Standardtherapie	s.o.			
	ALI/ARDS	Ulcusprophylaxe	Standardtherapie	Komplikation Blutung			
		Subglott. Absaugung					
		Bündeltherapie					
		Intubationsweg orotrach	nasotracheal				
		aktive Befeuchtung	passiv				
		Cufftypen	standard				
Tracheotomie	ALI / ARDS	ja	nein	s.o.	hohe Relevanz aus Sicht der Patientenvertreter		
subgruppenanalyse							
Zeitpunkt		Früh	Spät	s.o.			
Technik		Dilatativ	Chirurgisch	s.o.			
Medikamentöse Adj.	ALI / ARDS	ja	nein	s.o.			
Antioxidantien	ALI / ARDS	ja	nein	s.o.			
Beta2Mimienika	ALI / ARDS	ja	nein	s.o.			
Surfactant	ALI / ARDS	ja	nein	s.o.			
Statine	ALI / ARDS	ja	nein	s.o.			
volumenmanagement	ALI / ARDS	restriktive	liberal	s.o.			
Kolloide	ALI / ARDS	ja	nein	s.o.			
HAS	ALI / ARDS	ja	nein	s.o.			
Diuretika							
Albumine	ALI / ARDS	ja	nein	s.o.			

Thema	Population/Patient	Intervention	Comparison	Outcome	Bemerkung
1. Recruitment	1. Pat mit schwerem ARDS 2. Pat mit mildem/moderaten ARDS und akuter Hypoxämie 3. Pat mit akuter respiratorischer Insuffizienz und akuter Hypoxämie *+ Untergruppen: Erwachsene Kinder	Kurzzeitige akute Erhöhung des Atemwegdrucks; "Lachmann-Manöver"	Keine Recruitmentmanöver	1.a). Letalität 2.) . Lebensqualität 4.) ICU-LOS 5.a) beatmungsfreie Tage 6) . KH-LOS 7.a) akute Verbesserung der Oxygenierung /.a). nachhaltige Verbesserung der Oxygenierung 7.d) Verbesserung der Atemmechanik 10.) Komplikationen (Pneu)	voraussichtlich Bearbeitung PEEP-Trial/PEEP-Titration in AGIV systematische Erfassung der Nebenwirkungen/Komplikationen Art der Lungenschädigung kann für Effektivität / Komplikationen der RM ausschlaggebend sein
2. Bauchlage	1. Pat mit moderatem/schwerem ARDS 2. Pat mit Risiko f. ARDS	1. Bauchlage (180/135) 2. für eine bestimmte Zeitdauer	Rückenlage / konventionelle re-li-Lagerung	s. 1. Thema 10.) Lagerungsschäden 10.) andere Lagerungskomplikationen	Weitere Lagerungsmassnahmen (Rotorest, OK-Hochlagerung) ggf für Überarbeitung der LL betrachten Outcome Nr. 8/9 nicht Gegenstand des Thema Rescue-Verfahren
3. iNO/iProstaglandine	1. Neugeborene (34.-44. GW) mit neonatalem ARDS 2. Kind/Erwachsener ARDS 3. PAH, Rechtsherzdekompensation	1. iNO 2. iPG	1. kein iNO 2. kein iPG 3 PDE3/5 Inhibitoren 4. ECMO	s.1. Thema 7.e) Reduktion ECMO Inzidenz 7.g) bei Neugeborenen: Reduktion strukturelle Lungenerkrankungen 7.h). bei PAH: Reduktion PA Druck	Grundsätzlich auch Vergleich iNO/iPG 10. mutmasslich kein Gegenstand der 1. Auflage der Leitlinie
4. Extrakorporale Verfahren	1. Schweres ARDS (Kinder/Erwachsene) 2. Schwere Hyperkapnie (Kinder/Erwachsene) 3. Neugeborene mit PHT 4. Rechtsherzversagen 5. bridge to Lu-Transplant 6. Ermöglichung lungenprotektiver Beatmung 7. Pat mit ECMO Therapie aufgrund pulmonaler Erkrankung	1. vvECMO 2. vaECMO 3.. pECLA 4. vvaECMO 1. Komplikationen 2. Erfassung Management technischer Aspekte, e.g. Antikoagulation, Kanülenart und -platzierungsort, Platzierungsart, Flüsse, Drücke, Transfusionshäufigkeit etc... 3. Erfassung spezifischer Indikationen/Erkrankungen	1. kein extrakorporales Verfahren 2. vs. andere Rescueverfahren 3. Surfactant (bei Neugeborenen) 4. Beatmungseinstellungen unter ECMO keine ECMO	s.1. Thema 7.b/c.). bei Hyperkapnie: Korrektur pCO2, pH s.1 Thema 10.) Komplikationsart 10.) Komplikationsart	1. allgemeines Ziel: bei mutmasslich fehlenden RCT Bildung einer Datengrundlage für Expertenmeinung zu ECMO-Therapie bei pulmonalen und Rechtsherzkrankungen daher: weite Suchstrategie ohne vorherige Einschränkung (z.B keine spezifische Suche nach H1N1), nach Literatursichtung ggf Bildung einer Empfehlung auf Expertenniveau mutmasslich keine Studien zu Vergleich Komplikationen/Komplikationsmanagement nach KH-Typ-Stratifizierung vorhanden Daher: durch Erfassung der Komplikationen Rückschluss auf notwendigerweise zu ECMO-Therapie vorzuhaltender med Einrichtungen geplant Ziel: bei mutmasslich fehlenden RCT Bildung einer Datengrundlage für Expertenmeinung zu ECMO-Therapie bei pulmonalen und Rechtsherzkrankungen
5. Surfactant 6. ggf. PLV	Patient mit ARDS Patient mit ARDS	Surfactant PLV	keine Gabe keine Gabe	s.1. Thema s.1. Thema	voraussichtlich Verzicht auf Bearbeitung wg. Fehlender Zulassung
zusätzlich für Thema 1. - 6.:	Patienten mit schwerer Hyperkapnie	Anwendung von Rescue-Verfahren	keine Rescue-Verfahren	s.1. Thema	

Thema	Population/Patient	Intervention	Comparison	Outcome	Bemerkung
Abgrenzung zur S2k-LL „Prolongiertes Weaning“ (Als „Elaborierte Einführung in unser Kapitel)	Weaningkategorie 1+2 ggf. Untergruppen für Hauptfrage ~ + Erwachsene ~ + Kinder (' ~ + ECMO)			1.a) Sterblichkeit 1.c) 1, 5, 10 Jahresüberleben 2. Lebensqualität 4. ICU LOS 5.a) Beatmungszeit 10.) Komplikationen	
Benötigen wir Weaningprotokolle	s.1. Thema + Untergruppen s.1.	Protokolle ja/nein automatisiertes Weaning ja/nein		s.1. Thema	Kooperation mit AG VIII. Folgeversorgung und
Diagnostische Verfahren (Prädiktoren des erfolgreichen Weaning) z.B. SBT, SAT	s.1. Thema + Untergruppen s.1.				
Beatmungsverfahren	s.1. Thema + Untergruppen s.1.	Unterschiedliche Beatmungsverfahren		s.1. Thema	Kooperation mit AG III. Wahl des Beatmungsmodus
Beatmungszugang	s.1. Thema + Untergruppen	1. Tubus 2. Tracheostoma 3. Nichtinvasiver Zugang		s.1. Thema	Kooperation mit AG III. Wahl des Beatmungsmodus
Adjunktive Maßnahme	s.1. Thema + Untergruppen	1. Ernährung 2. Mobilisation/Sekret- management 3. Delirmanagement 4. Transfusionstrigger		s.1. Thema	Kooperation mit AG V. Supportive Maßnahmen
Überleitung bei fortbestehender Indikation für Beatmung aus der Sicht der Klinik		Außerklinische Beatmung			Kooperation mit AG VIII: Folgeversorgung und Langzeitfolgen
Terminales Weaning		Techniken der Deeskalation		in Anlehnung an S3 Palliativmedizin UK Symptomkontrolle	

Thema	Population/Patient	Intervention	Comparison	Outcome
1. Bedeutung von Risikofaktoren für Langzeitfolgen?	<p>Akutes respiratorisches Versagen >= 72 h Beatmung</p> <p>Untergruppen für Hauptfrage:</p> <p>~ + Erwachsene</p> <p>~ + Erwachsene >70 Jahre</p> <p>~ + Kinder</p> <p>~ + ECMO</p>		<p>Risikofaktoren für jede Untergruppe:</p> <p>~ + <u>chron. Vorerkrankung</u> (COPD/ILDs/Brain trauma (incl. Stroke)/neuromusk. Erkrankungen chron./Insuffizienz Herz-Leber-Niere/Tumor/hämolog. Erkrankungen/Vaskulitis/Immunsuppression/psychiatr. Erkrankung/geistige Behinderung</p> <p>~ + <u>akute Erkrankung vor Beatmung/ akut erworben während Beatmung</u> (Delir/Brain Trauma/CIM/Depression/ARDS/Lungenembolie/Schock/SIRS/Sepsis/Polytrauma/akute Herzinsuffizienz/ akutes Leberversagen/AKI</p>	<p>1.b) Überleben/Überlebensprognose</p> <p>2.) QoL</p> <p>3.a) Fatigue/zerebrale Dysfunktion/kognitive Dysfunktion/Depression/chron. Schmerzen</p> <p>3.b) Dauerhafte Heimversorgung/Pflegebedürftigkeit/funktional Inedpendence</p> <p>5.c) Überleitung zur Langzeitbeatmung</p> <p>8.) Häufigkeit spezif. Langzeitfolgen: CIM/Schluckstörung/respirat. Insuffizienz/Herzinsuffizienz/Niereninsuffizienz/Leberinsuffizienz/chron. Cholangitis/Hirnfarkt/Hirnblutung</p>
2. Wie sind Langzeitfolgen charakterisiert?	s.1. Thema + Untergruppen s.1.			<p>1.a) Erhöhte Sterblichkeit</p> <p>2.) QoL</p> <p>3.a) Fatigue/zerebrale Dysfunktion/kognitive Dysfunktion/Depression/chron. Schmerzen</p> <p>3.b) Dauerhafte Heimversorgung/Pflegebedürftigkeit/funktional Inedpendence</p> <p>5.c) Abhängigkeit Langzeitbeatmung</p> <p>8.) Weitere spezif. Langzeitfolgen: CIM/Schluckstörung/respirat. Insuffizienz/Herzinsuffizienz/Niereninsuffizienz/Leberinsuffizienz/chron. Cholangitis/Hirnfarkt/Hirnblutung</p> <p>11.) Ökonomie/Kostenanalyse</p>
3. Welche allgemeinen Einflussfaktoren/Zustände auf der ICU bestimmen LZ-Folgen?	s.1. Thema + Untergruppen s.1.	<p>1. akute Hypoxämie/hochinvasive Beatmung (Pimax>40mbar)/Hypotonie</p> <p>2. Beatmungsdauer/ICU-LOS/H-LOS</p> <p>3. Soziale Kontakte (Angehörige)</p> <p>4. Aufklärung/Angehörige, Patient</p> <p>5. Immobilisation</p> <p>6. Umfeld: Lärm, Tag-Nacht, Licht, Orientierungspunkte</p>		<p>s. Frage 2</p>
4. Prävention/Therapeut.Intervention während ICU mit Einfluß auf LZ-Folgen?	s.1. Thema + Untergruppen s.1.	<p>1. Delir/Sedierungsprotokoll</p> <p>2. Tagebücher/ Patient, Angehöriger</p> <p>3. Beatmungsprotokoll</p> <p>4. Lungenprotektive Beatmung</p> <p>5. Physiotherapie</p> <p>6. Frühmobilisation</p> <p>7. Pharmakotherapie-Untergruppen</p> <p>Sedative/Opiate/NichtopioidAnalg etika/Clonidin/Dexmedetomidin Antipsychotika/Antidepressiva Glukokortikoide/Insulin Immunsuppressiva/Chemotherap. Immunglobuline Melatonin Diuretika Antibiotika/Antimykotika Katecholamintherapie</p>		s. Frage 2
5. Folgeversorgung, Versorgungsstrukturen?	s.1. Thema + Untergruppen s.1.	<p>stationäre Rehabilitation</p> <p>ambulante Rehabilitation Hausarzt ambulante Betreuung durch Berufsgruppen: Physiotherapie/Atemtherapie/Ergotherapie/Psychotherapie Selbsthilfegruppen</p>		s. Frage 2

Leitlinien-Recherche

1. Quellen

- AWMF
<http://www.awmf.org/leitlinien/leitlinien-suche.html>
- Leitlinie.de
<http://www.leitlinien.de/leitlinien-finden/leitlinien-finden>
- Arztbibliothek
<http://www.arztbibliothek.de/>
- G-I-N
<http://g-i-n.net/>
- National Guideline Clearinghouse
<http://www.guideline.gov/>
- Arzneimittelkommission der dt. Ärzteschaft
<http://www.akdae.de/>
- SIGN Scottish Intercollegiate Guidelines Network (SIGN)
<http://www.sign.ac.uk/guidelines/published/index.html>
- National Institute for Health and Care Excellence (NICE)
<http://guidance.nice.org.uk/CG/Published>

2. Leitliniensuche

AWMF:

Suchbegriff: Beatmung → 102 Treffer → 21 ausgewählt

(Recherche Mai 2015: Beatmung → 114 Treffer)

Ergebnis: AWMF website fehler 23.06.2015 Fichtner

Suchbegriff: respiratorisches Versagen → 1 zusätzlicher Treffer

Nach Titel Ausgewählt als inhaltlich relevant: 55

GIN:

mechanical ventilation → 6 Treffer → 5 ausgewählt

(Recherche Mai 2015: 6 Treffer) → keine neuen

ventilation → 10 Treffer → 1 zusätzlich ausgewählt

(Recherche Mai 2015: 10 Treffer) → keine neuen

respiratory failure → 6 Treffer → 1 zusätzlich ausgewählt

(Recherche Mai 2015: 6 Treffer) → keine neuen

Ausgewählt als inhaltlich relevant: 7 Treffer

- 3 Treffer als NGC Guideline aufgenommen

1. Capnography/capnometry during mechanical ventilation: 2011. American Association for Respiratory Care. NGC:008739 → als NGC Guideline mit aufgenommen
2. Evidence-based clinical practice guideline: inhaled nitric oxide for neonates with acute hypoxic respiratory failure. American Association for Respiratory Care. NGC:008740 → als NGC Guideline mit aufgenommen
3. Humidification during invasive and noninvasive mechanical ventilation: 2012. American Association for Respiratory Care. NGC:009100 → als NGC Guideline mit aufgenommen

- 1 Treffer nicht aufgenommen:

1. Guidelines for the prehospital management of severe traumatic brain injury, second edition: Treatment: airway, ventilation, and oxygenation. Brain Trauma Foundation. NGC:006386 → nicht auffindbar, daher gelöscht. Aber von Brain Trauma Foundation folgende Publikation → ich würde die aber zum jetzigen Zeitpunkt außen vor lassen, die finden wir sicherlich bei der Recherche wieder. Siehst du das auch so? (Falls du Interesse hast: <https://www.braintrauma.org/coma-guidelines/searchable-guidelines/>)

- 3 Treffer sind als Zeitschriftenartikel nachgewiesen

Guideline.gov:

Mechanical ventilation → 76 Treffer

Dupletten zu vorherigen Suchen: II

ventilation OR mechanical ventilation OR respiratory failure → 317 Treffer

Davon nach Titel inhaltlich ausgewählt: 84 Treffer

10, 11, 12, 13, 15, 16, 17, 19, 20, 22, 23, 24, 26, 29, 32, 34, 35, 37, 38, 40, 41, 45, 46, 50, 53, 56, 58, 67, 68, 72, 73, 75, 79, 80, 83, 84, 90, 100, 102, 103, 104, 110, 113, 116, 117, 119, 120, 125, 139, 141, 145, 146, 147, 152, 154, 155, 158, 160, 161, 163, 179, 180, 191, 194, 195, 201, 202, 205, 224, 235, 239, 259, 265, 269, 277, 286, 300, 307, 308, 309, 314,

Recherche Mai 2015:

Advanced Search: ventilation OR respiratory failure , Jahre 2014 und 2015

<http://www.guideline.gov/search/results.aspx?99=2015,2014,&term=ventilation%20OR%20respiratory%20failure>

Davon nach Titel Inhaltliche Selektion des Ergebnisses aus dem Link (23.06.2015, Fichtner): 10 Treffer

1,5,7,8,13,23,33,40,42,95

NICE

Alle angesehen

A (ersetzt durch CG48), CG4 (ersetzt durch CG56), CG5 (ersetzt durch CG108), CG12 (ersetzt durch CG101), CG50, CG56, CG68, CG69, CG94, CG95, CG101, CG105, CG108, CG112, CG163, CG167

Recherche Mai 2015:

<http://www.nice.org.uk/guidance/published?type=guidelines>

Inhaltliche Selektion des Ergebnisses aus dem Link (23.06.2015):

NG9, CG 131, CG191 (Pneumonia), CG37 (Postnatal Care), CG187 (acute heart failure), CG176 (head injury), CG174 (fluid)

Insgesamt nach Titel inhaltlich ausgewählt: 19

SIGN

“Mechanical Ventilation”

“Ventilation OR mechanical ventilation OR respiratory failure”

Insgesamt nach Titel inhaltlich ausgewählt: 6

Recherche Mai 2015: <http://www.sign.ac.uk/guidelines/published/index.html>

Ergebnis: keine neuen Leitlinien (23.06.2015 Fichtner)

Leitlinien.de → durch internationale Leitlinienrecherche und bei arztbibliothek.de abgedeckt → keine Suche

Arztbibliothek.de

→ Keine neuen Treffer gefunden

Österreichische Gesellschaft für Anästhesiologie, Reanimation und Intensivmedizin

<http://www.oegari.at/arbeitsgruppe.asp?id=473>

→ 1 Leitlinie gefunden

Nach individueller Recherche nachgereicht:

National Guideline Clearinghouse	2011	The management of community-acquired pneumonia in infants and children older than 3 months of age: clinical	Internetdokument	0	nicht thema
National Guideline Clearinghouse	2012	AARC clinical practice guideline: transcutaneous monitoring of carbon dioxide and oxygen: 2012	Internetdokument	0	nicht thema
National Guideline Clearinghouse	2012	British Thoracic Society guideline for respiratory management of children with neuromuscular weakness	Internetdokument	0	nicht thema
National Guideline Clearinghouse	2012	Global strategy for asthma management and prevention	Internetdokument	0	nicht inhalt
National Guideline Clearinghouse	2012	Infection: Prevention and control of healthcare-associated infections in primary and community care	Internetdokument	0	nicht inhalt
National Guideline Clearinghouse	2012	Management of pulmonary contusion and flail chest: an Eastern Association for the Surgeon of Trauma practice	Internetdokument	0	vor 2010
National Guideline Clearinghouse	2012	Traumatic brain injury medical treatment guidelines	Internetdokument	0	nicht inhalt
National Guideline Clearinghouse	2008	Comprehensive assessment and management of the critically ill. In: Evidence-based geriatric nursing protocols	Internetdokument	0	nicht thema
National Guideline Clearinghouse		Management of lung cancer. A national clinical guideline	Zeitschriftenaufsatz	0	nicht thema
National Guideline Clearinghouse		Special populations. In: Prevention and treatment of pressure ulcers: clinical practice guideline	Zeitschriftenaufsatz	0	nicht thema
National Guideline Clearinghouse		Treatment of pressure ulcers. In: Prevention and treatment of pressure ulcers: clinical practice guideline	Zeitschriftenaufsatz	0	nicht thema
National Guideline Clearinghouse	2008	American Association of Clinical Endocrinologists, The Obesity Society, and American Society for Metabolic & B	Internetdokument	0	vor 2010
National Guideline Clearinghouse		Bi-level positive airway pressure (BPAP) devices	Zeitschriftenaufsatz	0	nicht thema
National Guideline Clearinghouse	2013	Practice guidelines for conscious sedation: an updated report by the American Society of Anesthesiologists Task	Internetdokument	0	nicht thema
National Institute of Health and Clinical Excellence	1990	Pneumonia: Diagnosis and management of community- and hospital-acquired pneumonia in adults	Musikwerk / Musikalbum	0	nicht thema
National Institute of Health and Clinical Excellence	1993	Colorectal cancer: The diagnosis and management of colorectal cancer	Buch (Monografie)	0	nicht thema
National Institute of Health and Clinical Excellence	1993	Postnatal care	Buch (Monografie)	0	nicht thema
National Institute of Health and Clinical Excellence	2013	Myocardial infarction with ST-segment elevation	Internetdokument	0	nicht thema
National Institute of Health and Clinical Excellence	2007	Acute ill patients in hospital	Internetdokument	0	vor 2010
National Institute of Health and Clinical Excellence	2010	Chronic heart failure	Internetdokument	0	nicht thema
National Institute of Health and Clinical Excellence	2010	Unstable angina and NSTEMI	Internetdokument	0	nicht thema
Paul Ehrlich-Gesellschaft für Chemotherapie: Deutscher Gesellschaft	2009	Epidemiologie, Diagnostik, antimikrobielle Therapie und Management von erwachsenen Patienten mit ambulant	Internetdokument	0	nicht thema
Rima, Johannes; Bever, Kirsten; Biedermann, Tilo; Bircher, Andreas; Di	2014	Leitlinie zu Akuttherapie und Management der Anaschylie	Zeitschriftenaufsatz	0	nicht thema
Scottish Intercollegiate Guidelines Network (SIGN)	2003	Management of Obstructive Sleep Apnoea/Hypopnoea Syndrome in Adults. (SIGN Guideline No 73)	Internetdokument	0	nicht them
Scottish Intercollegiate Guidelines Network (SIGN)	2004	Postoperative management in adults. (SIGN Guideline No 77)	Internetdokument	0	nicht thema
Scottish Intercollegiate Guidelines Network (SIGN)	2009	Early management of patients with a head injury. (SIGN Guideline No 110)	Internetdokument	0	nicht thema
Scottish Intercollegiate Guidelines Network (SIGN)	2013	Acute coronary syndromes	Internetdokument	0	nicht thema
Vicente Plaza, A.; Myriam Calle, b; Jesus Molina; c; Santiago Quirced Jor		Brazilian Guideline Inhalation	Zeitschriftenaufsatz	0	nicht thema
National Guideline Clearinghouse	2010	Sedation in children and young people. Sedation for diagnostic and therapeutic procedures in children and you	Internetdokument	0	nicht inhalt

S3Leitlinie Invasive Beatmung und Einsatz extrakorporaler Verfahren bei akuter respiratorischer Insuffizienz

Systematische Literaturrecherche Oktober-Dezember 2014

Verwendete Filteralgorithmen

Systematic Reviews Filter von PubMed¹ für Metaanalysen und Systematic Reviews

```
(systematic review [ti] OR meta-analysis [pt] OR meta-analysis [ti] OR
systematic literature review [ti] OR
this systematic review [tw] OR pooling project [tw] OR (systematic review
[tiab] AND review [pt]) OR
meta synthesis [ti] OR meta-analy*[ti] OR integrative review [tw] OR
integrative research review [tw] OR
rapid review [tw] OR umbrella review [tw] OR consensus development
conference [pt] OR practice guideline [pt] OR
drug class reviews [ti] OR cochrane database syst rev [ta] OR acp journal
club [ta] OR health technol assess [ta] OR
evid rep technol assess summ [ta] OR jbi database system rev implement rep
[ta]) OR
(clinical guideline [tw] AND management [tw]) OR ((evidence based[ti] OR
evidence-based medicine [mh] OR
best practice* [ti] OR evidence synthesis [tiab])
AND (review [pt] OR diseases category[mh] OR behavior and behavior
mechanisms [mh] OR therapeutics [mh] OR
evaluation studies[pt] OR validation studies[pt] OR guideline [pt] OR
pmcbook))
OR
((systematic [tw] OR systematically [tw] OR critical [tiab] OR (study
selection [tw]) OR
(predetermined [tw] OR inclusion [tw] AND criteri* [tw]) OR exclusion
criteri* [tw] OR main outcome measures [tw] OR
standard of care [tw] OR standards of care [tw])
AND
(survey [tiab] OR surveys [tiab] OR overview* [tw] OR review [tiab] OR
reviews [tiab] OR search* [tw] OR
handsearch [tw] OR analysis [ti] OR critique [tiab] OR appraisal [tw] OR
(reduction [tw]AND (risk [mh] OR risk [tw]) AND (death OR recurrence)))
AND
(literature [tiab] OR articles [tiab] OR publications [tiab] OR publication
[tiab] OR
bibliography [tiab] OR bibliographies [tiab] OR published [tiab] OR pooled
data [tw] OR
unpublished [tw] OR citation [tw] OR citations [tw] OR database [tiab] OR
internet [tiab] OR textbooks [tiab] OR
references [tw] OR scales [tw] OR papers [tw] OR datasets [tw] OR trials
[tiab] OR meta-analy* [tw] OR
(clinical [tiab] AND studies [tiab]) OR treatment outcome [mh] OR treatment
outcome [tw] OR pmcbook))
NOT
```

¹ http://www.nlm.nih.gov/bsd/pubmed_subsets/sysreviews_strategy.html

(letter [pt] OR newspaper article [pt])

Cochrane Highly Sensitive Search Strategy for identifying randomized trials in MEDLINE: sensitivity- and precision-maximizing version² für randomisierte klinische Studien

#1	randomized controlled trial [pt]
#2	controlled clinical trial [pt]
#3	randomized [tiab]
#4	placebo [tiab]
#5	clinical trials as topic [mesh: noexp]
#6	randomly [tiab]
#7	trial [ti]
#8	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7
#9	animals [mh] NOT humans [mh]
#10	#8 NOT #9

University of Texas Library filter für Case-Control-Studies³

“Case-Control Studies”[Mesh:noexp] OR “retrospective studies”[mesh:noexp] OR “Control Groups”[Mesh:noexp]
OR (case[TIAB] AND control[TIAB]) OR (cases[TIAB] AND controls[TIAB]) OR (cases[TIAB] AND
controlled[TIAB]) OR (case[TIAB] AND comparison*[TIAB]) OR (cases[TIAB] AND comparison*[TIAB]) OR
“control group”[TIAB] OR “control groups”[TIAB]

² http://handbook.cochrane.org/chapter_6/box_6_4_b_cochrane_hsss_2008_sensprec_pubmed.htm

³ http://libguides.sph.uth.tmc.edu/pubmed_filters

Literaturselektion in 2stufiger Selektion: Titelselektion und Selektion nach hierarchischer Volltextsichtung									
Arbeitsgruppe/ Kapitel	Abschnitt	Treffer PubMed	Treffer Embase	Treffer Cochrane (HTA)	#Dubletten (gelöscht)	Gesamtzahl	Gesamtzahl nach Titelselektion und Ergänzungen individueller Handrecherche	Finale Kapitelnummer Anmerkungen/Änderungen	Gesamtzahl für LL-Empfehlung verwendeter, bewerteter Quellen (LL, SR/MA, RCT, etc.) nach hierarchischer Volltextsichtung, -selektion und Bewertung
IV Beatmungsparameter	: PEEP [41neu]	288	267		105	450	116		23
	FiO2 [42]	255	146		47	354	24		3
	Vt [43neu]	213	226		87	352	103		6
	I/E [44neu]	34	8		4	38	23	Wechsel Reihenfolge 4.5 aus [44neu]	4
	: Permissive Hypoxämie/Hyperkapnie/Target Saturation/Zielparameter Gasaustausch [45neu]	186	232		65	353	27	Wechsel Reihenfolge 4.6 aus [45neu]	5
								Wechsel Reihenfolge 4.4 aus [46neu]	
	PAW [46neu]	142	144		103	183	36		8
	Frequenz [47]	27	22		11	38	28		2
	Gewichtung [48]	85	240		33	292	187	entfallen	
Monitoring: (49neu)	392	512		121	783	29	4.8 aus [49neu]	9	

Literaturselektion in 2stufiger Selektion: Titelselektion und Selektion nach hierarchischer Volltextsichtung		Treffer PubMed	Treffer Embase	Treffer Cochrane (HTA)	#Dubletten (gelöscht)	Gesamtzahl	Gesamtzahl nach Titelselektion und Ergänzungen individueller Handrecherche	Finale Kapitelnummer Anmerkungen/Änderungen	Gesamtzahl für LL-Empfehlung verwendeter, bewerteter Quellen (LL, SR/MA, RCT, etc.) nach hierarchischer Volltextsichtung, -selektion und Bewertung
Arbeitsgruppe/ Kapitel	Abschnitt								
V Supportive Maßnahmen	Sedierung[51neu]	181	314		59	436	18	Zusammenfassung 5.1 aus [51neu], [52], [53]	1
	Muskelrelaxation [52]	61	37		11	87	13	s.o.	
	Delirmonitoring/therapie [53]	67	98		14	151	8	s.o.	
	Ernährung [54neu]	464	597		182	879	208	Änderung Reihenfolge 5.3 aus [54neu]	11
	Mobilisation [55]	236	205		33	408	74	Änderung Reihenfolge 5.2 aus [55]	6
	Prophyl. VAP [56]	586	757		272	1071	351	Änderung Reihenfolge 5.4 aus [56]	28
	Tracheotomie							Änderung Reihenfolge 5.5 aus [57_75_neu]	
	[57_75_neu [581neu] antioxidantien	474	570		202	842	110		13
	[581neu] beta mimetika	241	217		86	372	59	entfallen	
	[582] surfactant	502	298		34	766	70	Änderung Reihenfolge 5.6.1 aus [582]	5
	[583neu] statine	445	289		95	639	78	Änderung Reihenfolge 5.6.2 aus [583]	6
	[584] fluid therapy transfusion	97	88		19	166	entfällt	entfallen	
	[585neu]	694	312		82	924	201	Änderung Reihenfolge 5.6.3 aus [585neu] 5.6.4 aus [585neu]	5 10

Literaturselektion in 2stufiger Selektion: Titelselektion und Selektion nach hierarchischer Volltextsichtung		Treffer PubMed	Treffer Embase	Treffer Cochrane (HTA)	#Dubletten (gelöscht)	Gesamtzahl	Gesamtzahl nach Titelselektion und Ergänzungen individueller Handrecherche	Finale Kapitelnummer Anmerkungen/Änderungen	Gesamtzahl für LL-Empfehlung verwendeter, bewerteter Quellen (LL, SR/MA, RCT, etc.) nach hierarchischer Volltextsichtung, -selektion und Bewertung
Arbeitsgruppe/ Kapitel	Abschnitt								
VI Verfahren bei therapierefrakt. Gasaustauschstörung	Recruitment [61neu]				53	227	61		4
	Bauchlagerung [62]	134	146			407	116		10
	iNO, [631neu]	254	262		109	756	118		
	iPGs [632]	479	404		127	190	30	Zusammenfassung	
		80	141		31	2654	601	6.3 aus [631neu] und [632]	5
	Extrakorporal [641_644_neu]	1541	1538	16	441	225	22	6.4.1	16
	ECCO2 R [642neu]	133	134		42	117	26	6.4.2	4
	PE, PAH, bridgetransplant_vveCMO [643]	93	46		22			entfallen	
[65] PLV	107	123	0	21	209	28		3	

Literaturselektion in 2stufiger Selektion: Titelselektion und Selektion nach hierarchischer Volltextsichtung									
Arbeitsgruppe/ Kapitel	Abschnitt	Treffer PubMed	Treffer Embase	Treffer Cochrane (HTA)	#Dubletten (gelöscht)	Gesamtzahl	Gesamtzahl nach Titelselektion und Ergänzungen individueller Handrecherche	Finale Kapitelnummer Anmerkungen/Änderungen	Gesamtzahl für LL-Empfehlung verwendeter, bewerteter Quellen (LL, SR/MA, RCT, etc.) nach hierarchischer Volltextsichtung, -selektion und Bewertung
VII weaning	Abgrenzung akutes Weaning/Klassifikation [71neu]	185	66		30	221	21		5
	Weaningprotokolle [72]	103	108		49	162	70		6
	Diagnostik/Prädiktoren [73]	193	191		65	319	83		5
	Adjuvante Maßnahmen [761neu] Nutrition	64	63		43	84	22	entfallen	
	[762neu] Mobilisation	96	47		25	118	38	entfallen	
	[763neu] Delir	93	62		22	133	43	entfallen	
	[764neu] Transfusion	141	84		37	188	32	entfallen	
	Überleitung/Heimbeatmung [77neu]	106	218		26	298	51		-
	Terminales weaning/deeskalation [78neu]	211	150		62	299	81		-
	VIII Langzeitfolgen Folgeversorgung	Langzeitfolgen/Outcome: Überleben [811]	362	225		83	504	130	Neugliederung 8.1 aus [811], [812], [816]
Langzeitfolgen/Outcome: QoL [812]		101	118		23	196	61	Neugliederung 8.2 aus [811], [812], [816]	5
Langzeitfolgen/Outcome: fatigue [813]		432	217		25	624	32	Neugliederung 8.3 aus [811], [812], [813], [816]	6
Langzeitfolgen/Outcome: longterm-ventilation [814 815]		196	122		34	284	11		
Langzeitfolgen/Outcome: chronic complications [816]		543	309		136	716	107	Neugliederung 8.4 aus [816]	1
Folgeversorgung Socialsupport [83neu]		70	143		4	209	20	Neugliederung 8.5 Übernahme DAS-LL	1
Folgeversorgung [85]			167			167	48		
								Gesamtzahl aller eingesetzten, bewerteten Literaturstellen	362
							Gesamtzahl aller verwendeten Referenzen	297	



Methodology Checklist 1: Systematic Reviews and Meta-analyses

SIGN

SIGN gratefully acknowledges the permission received from the authors of the AMSTAR tool to base this checklist on their work: *Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C, et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Medical Research Methodology 2007, 7:10 doi:10.1186/1471-2288-7-10. Available from <http://www.biomedcentral.com/1471-2288/7/10> [cited 10 Sep 2012]*

Study identification (Include author, title, year of publication, journal title, pages)

< SokolJ_2003 >

Cochrane review 2010 (7)

Guideline topic: **AG VI**

Key Question No: **6.3.1 (V2(12.10.15ff))**

Before completing this checklist, consider:

1. Is the paper a systematic review or meta-analysis? IF NO reject. IF **YES** continue.
2. Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO reject. IF YES complete the checklist.

Checklist completed by: **AF, ZKSL**

Section 1: Internal validity

In a well conducted systematic review:

Does this study do it?

1.1	The study addresses a clearly defined research question. ⁱ	Yes <input type="checkbox"/>	No <input type="checkbox"/>	Can't say <input type="checkbox"/>	
1.2	At least two people should select studies and extract data. ⁱⁱ	Yes <input type="checkbox"/>	No <input type="checkbox"/>	Can't say <input type="checkbox"/>	
1.3	A comprehensive literature search is carried out. ⁱⁱⁱ	Yes <input type="checkbox"/>	No <input type="checkbox"/>	Can't say <input type="checkbox"/>	Does not apply <input type="checkbox"/>
1.4	The authors clearly state if or how they limited their review by publication type. ^{iv}	Yes <input type="checkbox"/>	No <input type="checkbox"/>		
1.5	The included and excluded studies are listed. ^v	Yes <input type="checkbox"/>	No <input type="checkbox"/>		
1.6	The characteristics of the included studies are provided. ^{vi}	Yes <input type="checkbox"/>	No <input type="checkbox"/>		
1.7	The scientific quality of the included studies is assessed and documented. ^{vii}	Yes <input type="checkbox"/>	No <input type="checkbox"/>		

1.8	The scientific quality of the included studies was assessed appropriately. ^{viii}	Yes <input type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.9	Appropriate methods are used to combine the individual study findings. ^{ix}	Yes <input type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.10	The likelihood of publication bias is assessed. ^x	Yes <input type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.11	Conflicts of interest are declared. ^{xi}	Yes <input type="checkbox"/> No <input type="checkbox"/>
SECTION 2: OVERALL ASSESSMENT OF THE STUDY		
2.1	What is your overall assessment of the methodological quality of this review? ^{xii}	High quality (++) <input type="checkbox"/> Acceptable (+) <input checked="" type="checkbox"/> Unacceptable – reject 0 <input type="checkbox"/>
2.2	Are the results of this study directly applicable to the patient group targeted by this guideline?	Yes <input type="checkbox"/> No <input type="checkbox"/>
2.3	Notes: ^{xiii} Acc. to convention Cochrane rev. are not to be reviewed in detail	

ⁱ The research question and inclusion criteria should be established before the review is conducted. To score a 'yes' for this factor there must be reference to a protocol, ethics approval, or pre-determined/a priori published research objectives.

ⁱⁱ At least two people should select papers and extract data. There should be a consensus procedure to resolve any differences.

ⁱⁱⁱ At least two major electronic databases should be searched. The report must include years and databases searched (e.g., Central, EMBASE, MEDLINE, OpenGrey, 1999-2009). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found. In rare cases this may not apply where authors have carried out a meta analysis focusing on a specified range of major trials in their field.

^{iv} The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status or language. If searching sources that contains both grey and non-grey literature, must specify that they were searching for both.

^v A list of included and excluded studies should be provided. Limiting the excluded studies to references is acceptable.

^{vi} In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analyzed e.g., age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported. (**Note** that a format other than a table is acceptable, as long as the information noted here is provided).

^{vii} This relates to the scientific quality of the studies included in the review. I can include use of a quality scoring tool or checklist, e.g., Jadad scale, risk of bias, sensitivity analysis, or a description of quality items, with some kind of result for EACH study (“low” or “high” is fine, as long as it is clear which studies scored “low” and which scored “high”; a summary score/range for all studies is not acceptable).

^{viii} The methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations. (**Note**: The review might say something like “the results should be interpreted with caution due to poor quality of included studies.” Cannot score “yes” for this question if scored “no” for question 7).

^{ix} For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e., Chi-squared test for homogeneity, *I*²). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e., is it sensible to combine?). Indicate “yes” where the authors mention or describe heterogeneity or variability between results and discuss the consequences (eg where authors declare they cannot pool results because of heterogeneity).

^x An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test, Hedges-Olken). (**Note**: Score “Can’t say” if there were fewer than 10 included studies).

^{xi} Potential sources of support should be clearly acknowledged in both the systematic review and the included studies.

^{xii} Rate the overall methodological quality of the study, using the following as a guide: **High quality** (++) : Majority of criteria met. Little or no risk of bias. Results unlikely to be changed by further research. **Acceptable** (+) : Most criteria met. Some flaws in the study with an associated risk of bias, Conclusions may change in the light of further studies. **Low quality** (0) : Either most criteria not met, or significant flaws relating to key aspects of study design. Conclusions likely to change in the light of further studies.

^{xiii} Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above. This is a very important part of the evaluation and will feature in the evidence table. PLEASE FILL IN.



Methodology Checklist 1: Systematic Reviews and Meta-analyses

SIGN

SIGN gratefully acknowledges the permission received from the authors of the AMSTAR tool to base this checklist on their work: *Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C, et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Medical Research Methodology 2007, 7:10 doi:10.1186/1471-2288-7-10. Available from <http://www.biomedcentral.com/1471-2288/7/10> [cited 10 Sep 2012]*

Study identification (Include author, title, year of publication, journal title, pages)

<AfshariA_2010_A> Cochrane review 2010 (8) on aerosolized prostacyclin

Guideline topic: **AG VI**

Key Question No: **6.3.2 (20.10.15ff)**

Before completing this checklist, consider:

1. Is the paper a systematic review or meta-analysis? IF NO reject. IF **YES** continue.
2. Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO reject. IF YES complete the checklist.

Checklist completed by: **AF, ZKSL**

Section 1: Internal validity

In a well conducted systematic review:

Does this study do it?

1.1	The study addresses a clearly defined research question. ⁱ	Yes <input type="checkbox"/>	No <input type="checkbox"/>	Can't say <input type="checkbox"/>	
1.2	At least two people should select studies and extract data. ⁱⁱ	Yes <input type="checkbox"/>	No <input type="checkbox"/>	Can't say <input type="checkbox"/>	
1.3	A comprehensive literature search is carried out. ⁱⁱⁱ	Yes <input type="checkbox"/>	No <input type="checkbox"/>	Can't say <input type="checkbox"/>	Does not apply <input type="checkbox"/>
1.4	The authors clearly state if or how they limited their review by publication type. ^{iv}	Yes <input type="checkbox"/>	No <input type="checkbox"/>		
1.5	The included and excluded studies are listed. ^v	Yes <input type="checkbox"/>	No <input type="checkbox"/>		
1.6	The characteristics of the included studies are provided. ^{vi}	Yes <input type="checkbox"/>	No <input type="checkbox"/>		
1.7	The scientific quality of the included studies is assessed and documented. ^{vii}	Yes <input type="checkbox"/>	No <input type="checkbox"/>		

1.8	The scientific quality of the included studies was assessed appropriately. ^{viii}	Yes <input type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.9	Appropriate methods are used to combine the individual study findings. ^{ix}	Yes <input type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.10	The likelihood of publication bias is assessed. ^x	Yes <input type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.11	Conflicts of interest are declared. ^{xi}	Yes <input type="checkbox"/> No <input type="checkbox"/>
SECTION 2: OVERALL ASSESSMENT OF THE STUDY		
2.1	What is your overall assessment of the methodological quality of this review? ^{xii}	High quality (++) <input type="checkbox"/> Acceptable (+) <input checked="" type="checkbox"/> (at least) Unacceptable – reject 0 <input type="checkbox"/>
2.2	Are the results of this study directly applicable to the patient group targeted by this guideline?	Yes <input type="checkbox"/> No <input type="checkbox"/>
2.3	Notes: ^{xiii} Acc. to convention Cochrane rev. are not to be methodologically reviewed in detail	

ⁱ The research question and inclusion criteria should be established before the review is conducted. To score a 'yes' for this factor there must be reference to a protocol, ethics approval, or pre-determined/a priori published research objectives.

ⁱⁱ At least two people should select papers and extract data. There should be a consensus procedure to resolve any differences.

ⁱⁱⁱ At least two major electronic databases should be searched. The report must include years and databases searched (e.g., Central, EMBASE, MEDLINE, OpenGrey, 1999-2009). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found. In rare cases this may not apply where authors have carried out a meta analysis focusing on a specified range of major trials in their field.

^{iv} The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status or language. If searching sources that contains both grey and non-grey literature, must specify that they were searching for both.

^v A list of included and excluded studies should be provided. Limiting the excluded studies to references is acceptable.

^{vi} In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analyzed e.g., age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported. (**Note** that a format other than a table is acceptable, as long as the information noted here is provided).

^{vii} This relates to the scientific quality of the studies included in the review. I can include use of a quality scoring tool or checklist, e.g., Jadad scale, risk of bias, sensitivity analysis, or a description of quality items, with some kind of result for EACH study (“low” or “high” is fine, as long as it is clear which studies scored “low” and which scored “high”; a summary score/range for all studies is not acceptable).

^{viii} The methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations. (**Note**: The review might say something like “the results should be interpreted with caution due to poor quality of included studies.” Cannot score “yes” for this question if scored “no” for question 7).

^{ix} For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e., Chi-squared test for homogeneity, *I*²). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e., is it sensible to combine?). Indicate “yes” where the authors mention or describe heterogeneity or variability between results and discuss the consequences (eg where authors declare they cannot pool results because of heterogeneity).

^x An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test, Hedges-Olken). (**Note**: Score “Can’t say” if there were fewer than 10 included studies).

^{xi} Potential sources of support should be clearly acknowledged in both the systematic review and the included studies.

^{xii} Rate the overall methodological quality of the study, using the following as a guide: **High quality** (++) : Majority of criteria met. Little or no risk of bias. Results unlikely to be changed by further research. **Acceptable** (+) : Most criteria met. Some flaws in the study with an associated risk of bias, Conclusions may change in the light of further studies. **Low quality** (0) : Either most criteria not met, or significant flaws relating to key aspects of study design. Conclusions likely to change in the light of further studies.

^{xiii} Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above. This is a very important part of the evaluation and will feature in the evidence table. PLEASE FILL IN.



Methodology Checklist 1: Systematic Reviews and Meta-analyses

SIGN

SIGN gratefully acknowledges the permission received from the authors of the AMSTAR tool to base this checklist on their work: *Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C, et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Medical Research Methodology 2007, 7:10 doi:10.1186/1471-2288-7-10. Available from <http://www.biomedcentral.com/1471-2288/7/10> [cited 10 Sep 2012]*

Study identification (Include author, title, year of publication, journal title, pages)

< AndrewsPL_2013> J Trauma Acute Care Surg 2013;75:635ff

Guideline topic: AGIII ventilation strategies

Key Question No: 3.3

Before completing this checklist, consider:

1. Is the paper a systematic review or meta-analysis? IF NO reject. IF YES continue.
2. Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO reject. IF YES complete the checklist.

Checklist completed by: AF, ZKLS

Section 1: Internal validity

In a well conducted systematic review:

Does this study do it?

1.1	The study addresses a clearly defined research question. ⁱ	Yes <input checked="" type="checkbox"/>	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	
1.2	At least two people should select studies and extract data. ⁱⁱ	Yes <input checked="" type="checkbox"/>	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	
1.3	A comprehensive literature search is carried out. ⁱⁱⁱ	Yes <input checked="" type="checkbox"/>	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	Does not apply <input type="checkbox"/>
1.4	The authors clearly state if or how they limited their review by publication type. ^{iv}	Yes <input checked="" type="checkbox"/>	No <input type="checkbox"/>
1.5	The included (and excluded) studies are listed. ^v K=16 resp. 15	Yes <input checked="" type="checkbox"/>	No <input type="checkbox"/>
1.6	The characteristics of the included studies are provided. ^{vi}	Yes <input type="checkbox"/>	No <input checked="" type="checkbox"/>
1.7	The scientific quality of the included studies is assessed and documented. ^{vii}	Yes <input type="checkbox"/>	No <input type="checkbox"/>

1.8	The scientific quality of the included studies was assessed appropriately. ^{viii}	Yes <input type="checkbox"/> No <input checked="" type="checkbox"/> Can't say <input type="checkbox"/>
1.9	Appropriate methods are used to combine the individual study findings. ^{ix}	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.10	The likelihood of publication bias is assessed. ^x But all publication acc. to i/E criteria used	Yes <input type="checkbox"/> No <input checked="" type="checkbox"/> Can't say <input type="checkbox"/>
1.11	Conflicts of interest are declared. ^{xi}	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/>
SECTION 2: OVERALL ASSESSMENT OF THE STUDY		
2.1	What is your overall assessment of the methodological quality of this review? ^{xii}	High quality (++) <input checked="" type="checkbox"/> Acceptable (+) <input type="checkbox"/> Unacceptable – reject <input type="checkbox"/>
2.2	Are the results of this study directly applicable to the patient group targeted by this guideline?	Yes <input type="checkbox"/> No <input type="checkbox"/>
2.3	Notes: ^{xiii} SR/MA of published observational data from a valid lit-search; comparison of conventional vs airways pressure release ventilation performed in trauma pt.; methods convincing and well reasoned although beyond „mainstream“ SR larger samples used to enhance generalizability; RCT exclusion well reasoned certain problem of differing retrospection times in conventional (1995 to 2012) vs APRV (2002-2005)	

ⁱ The research question and inclusion criteria should be established before the review is conducted. To score a 'yes' for this factor there must be reference to a protocol, ethics approval, or pre-determined/a priori published research objectives.

ⁱⁱ At least two people should select papers and extract data. There should be a consensus procedure to resolve any differences.

ⁱⁱⁱ At least two major electronic databases should be searched. The report must include years and databases searched (e.g., Central, EMBASE, MEDLINE, OpenGrey, 1999-2009). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found. In rare cases this may not apply where authors have carried out a meta analysis focusing on a specified range of major trials in their field.

^{iv} The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status or language. If searching sources that contains both grey and non-grey literature, must specify that they were searching for both.

^v A list of included and excluded studies should be provided. Limiting the excluded studies to references is acceptable.

^{vi} In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analyzed e.g., age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported. (**Note** that a format other than a table is acceptable, as long as the information noted here is provided).

^{vii} This relates to the scientific quality of the studies included in the review. I can include use of a quality scoring tool or checklist, e.g., Jadad scale, risk of bias, sensitivity analysis, or a description of quality items, with some kind of result for EACH study ("low" or "high" is fine, as long as it is clear which studies scored "low" and which scored "high"; a summary score/range for all studies is not acceptable).

^{viii} The methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations. (**Note:** The review might say something like "the results should be interpreted with caution due to poor quality of included studies." Cannot score "yes" for this question if scored "no" for question 7).

^{ix} For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e., Chi-squared test for homogeneity, /2). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e., is it sensible to combine?). Indicate "yes" where the authors mention or describe heterogeneity or variability between results and discuss the consequences (eg where authors declare they cannot pool results because of heterogeneity).

^x An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test, Hedges-Olken). (**Note:** Score "Can't say" if there were fewer than 10 included studies).

^{xi} Potential sources of support should be clearly acknowledged in both the systematic review and the included studies.

^{xii} Rate the overall methodological quality of the study, using the following as a guide: **High quality** (++) : Majority of criteria met. Little or no risk of bias. Results unlikely to be changed by further research. **Acceptable** (+) : Most criteria met. Some flaws in the study with an associated risk of bias, Conclusions may change in the light of further studies. **Low quality** (0) : Either most criteria not met, or significant flaws relating to key aspects of study design. Conclusions likely to change in the light of further studies.

^{xiii} Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above. This is a very important part of the evaluation and will feature in the evidence table. PLEASE FILL IN.



Methodology Checklist 1: Systematic Reviews and Meta-analyses

SIGN

SIGN gratefully acknowledges the permission received from the authors of the AMSTAR tool to base this checklist on their work: *Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C, et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Medical Research Methodology 2007, 7:10 doi:10.1186/1471-2288-7-10. Available from <http://www.biomedcentral.com/1471-2288/7/10> [cited 10 Sep 2012]*

Study identification (Include author, title, year of publication, journal title, pages)

< BlackwoodB_2011 >

BMJ 2011;342:c7237ff

Guideline topic: **AG VII**

Key Question No: **7.2**

Before completing this checklist, consider:

1. Is the paper a systematic review or meta-analysis? IF NO reject. IF **YES** continue.
2. Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO reject. IF **YES** complete the checklist.

Checklist completed by: **AF, ZKSL**

Section 1: Internal validity

In a well conducted systematic review:

Does this study do it?

1.1	The study addresses a clearly defined research question. ⁱ	Yes X	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	
1.2	At least two people should select studies and extract data. ⁱⁱ	Yes X	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	
1.3	A comprehensive literature search is carried out. ⁱⁱⁱ	Yes X	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	Does not apply <input type="checkbox"/>
1.4	The authors clearly state if or how they limited their review by publication type. ^{iv}	Yes X	No <input type="checkbox"/>
1.5	The included and excluded studies are listed. ^v	Yes X	No <input type="checkbox"/>
1.6	The characteristics of the included studies are provided. ^{vi}	Yes X	No <input type="checkbox"/>
1.7	The scientific quality of the included studies is assessed and documented. ^{vii}	Yes X	No <input type="checkbox"/>

1.8	The scientific quality of the included studies was assessed appropriately. ^{viii}	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.9	Appropriate methods are used to combine the individual study findings. ^{ix}	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.10	The likelihood of publication bias is assessed. ^x	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.11	Conflicts of interest are declared. ^{xi}	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/>
SECTION 2: OVERALL ASSESSMENT OF THE STUDY		
2.1	What is your overall assessment of the methodological quality of this review? ^{xii}	High quality (++) <input checked="" type="checkbox"/> Acceptable (+) <input type="checkbox"/> Unacceptable – reject <input type="checkbox"/>
2.2	Are the results of this study directly applicable to the patient group targeted by this guideline?	Yes <input type="checkbox"/> No <input type="checkbox"/>
2.3	Notes: ^{xiii}	

ⁱ The research question and inclusion criteria should be established before the review is conducted. To score a 'yes' for this factor there must be reference to a protocol, ethics approval, or pre-determined/a priori published research objectives.

ⁱⁱ At least two people should select papers and extract data. There should be a consensus procedure to resolve any differences.

ⁱⁱⁱ At least two major electronic databases should be searched. The report must include years and databases searched (e.g., Central, EMBASE, MEDLINE, OpenGrey, 1999-2009). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found. In rare cases this may not apply where authors have carried out a meta analysis focusing on a specified range of major trials in their field.

^{iv} The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status or language. If searching sources that contains both grey and non-grey literature, must specify that they were searching for both.

^v A list of included and excluded studies should be provided. Limiting the excluded studies to references is acceptable.

^{vi} In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analyzed e.g., age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported. (**Note** that a format other than a table is acceptable, as long as the information noted here is provided).

^{vii} This relates to the scientific quality of the studies included in the review. I can include use of a quality scoring tool or checklist, e.g., Jadad scale, risk of bias, sensitivity analysis, or a description of quality items, with some kind of result for EACH study (“low” or “high” is fine, as long as it is clear which studies scored “low” and which scored “high”; a summary score/range for all studies is not acceptable).

^{viii} The methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations. (**Note:** The review might say something like “the results should be interpreted with caution due to poor quality of included studies.” Cannot score “yes” for this question if scored “no” for question 7).

^{ix} For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e., Chi-squared test for homogeneity, I^2). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e., is it sensible to combine?). Indicate “yes” where the authors mention or describe heterogeneity or variability between results and discuss the consequences (eg where authors declare they cannot pool results because of heterogeneity).

^x An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test, Hedges-Olken). (**Note:** Score “Can’t say” if there were fewer than 10 included studies).

^{xi} Potential sources of support should be clearly acknowledged in both the systematic review and the included studies.

^{xii} Rate the overall methodological quality of the study, using the following as a guide: **High quality** (++) : Majority of criteria met. Little or no risk of bias. Results unlikely to be changed by further research. **Acceptable** (+) : Most criteria met. Some flaws in the study with an associated risk of bias, Conclusions may change in the light of further studies. **Low quality** (0) : Either most criteria not met, or significant flaws relating to key aspects of study design. Conclusions likely to change in the light of further studies.

^{xiii} Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above. This is a very important part of the evaluation and will feature in the evidence table. PLEASE FILL IN.



Methodology Checklist 1: Systematic Reviews and Meta-analyses

SIGN

SIGN gratefully acknowledges the permission received from the authors of the AMSTAR tool to base this checklist on their work: *Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C, et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Medical Research Methodology 2007, 7:10 doi:10.1186/1471-2288-7-10. Available from <http://www.biomedcentral.com/1471-2288/7/10> [cited 10 Sep 2012]*

Study identification (Include author, title, year of publication, journal title, pages)

<BlackwoodB_2014> Cochrane review 2010 (5)

Guideline topic: AG V

Key Question No: 7.2 (27.10.15ff)

Before completing this checklist, consider:

1. Is the paper a systematic review or meta-analysis? IF NO reject. IF **YES** continue.
2. Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO reject. IF YES complete the checklist.

Checklist completed by: AF, ZKSL

Section 1: Internal validity

In a well conducted systematic review:

Does this study do it?

1.1	The study addresses a clearly defined research question. ⁱ	Yes <input type="checkbox"/>	No <input type="checkbox"/>	Can't say <input type="checkbox"/>	
1.2	At least two people should select studies and extract data. ⁱⁱ	Yes <input type="checkbox"/>	No <input type="checkbox"/>	Can't say <input type="checkbox"/>	
1.3	A comprehensive literature search is carried out. ⁱⁱⁱ	Yes <input type="checkbox"/>	No <input type="checkbox"/>	Can't say <input type="checkbox"/>	Does not apply <input type="checkbox"/>
1.4	The authors clearly state if or how they limited their review by publication type. ^{iv}	Yes <input type="checkbox"/>	No <input type="checkbox"/>		
1.5	The included and excluded studies are listed. ^v	Yes <input type="checkbox"/>	No <input type="checkbox"/>		
1.6	The characteristics of the included studies are provided. ^{vi}	Yes <input type="checkbox"/>	No <input type="checkbox"/>		
1.7	The scientific quality of the included studies is assessed and documented. ^{vii}	Yes <input type="checkbox"/>	No <input type="checkbox"/>		

1.8	The scientific quality of the included studies was assessed appropriately. ^{viii}	Yes <input type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.9	Appropriate methods are used to combine the individual study findings. ^{ix}	Yes <input type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.10	The likelihood of publication bias is assessed. ^x	Yes <input type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.11	Conflicts of interest are declared. ^{xi}	Yes <input type="checkbox"/> No <input type="checkbox"/>
SECTION 2: OVERALL ASSESSMENT OF THE STUDY		
2.1	What is your overall assessment of the methodological quality of this review? ^{xii}	High quality (++) <input type="checkbox"/> Acceptable (+) <input checked="" type="checkbox"/> (at least) Unacceptable – reject 0 <input type="checkbox"/>
2.2	Are the results of this study directly applicable to the patient group targeted by this guideline?	Yes <input type="checkbox"/> No <input type="checkbox"/>
2.3	Notes: ^{xiii} Acc. to convention Cochrane rev. are not to be methodologically reviewed in detail	

ⁱ The research question and inclusion criteria should be established before the review is conducted. To score a 'yes' for this factor there must be reference to a protocol, ethics approval, or pre-determined/a priori published research objectives.

ⁱⁱ At least two people should select papers and extract data. There should be a consensus procedure to resolve any differences.

ⁱⁱⁱ At least two major electronic databases should be searched. The report must include years and databases searched (e.g., Central, EMBASE, MEDLINE, OpenGrey, 1999-2009). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found. In rare cases this may not apply where authors have carried out a meta analysis focusing on a specified range of major trials in their field.

^{iv} The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status or language. If searching sources that contains both grey and non-grey literature, must specify that they were searching for both.

^v A list of included and excluded studies should be provided. Limiting the excluded studies to references is acceptable.

^{vi} In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analyzed e.g., age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported. (**Note** that a format other than a table is acceptable, as long as the information noted here is provided).

^{vii} This relates to the scientific quality of the studies included in the review. I can include use of a quality scoring tool or checklist, e.g., Jadad scale, risk of bias, sensitivity analysis, or a description of quality items, with some kind of result for EACH study (“low” or “high” is fine, as long as it is clear which studies scored “low” and which scored “high”; a summary score/range for all studies is not acceptable).

^{viii} The methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations. (**Note**: The review might say something like “the results should be interpreted with caution due to poor quality of included studies.” Cannot score “yes” for this question if scored “no” for question 7).

^{ix} For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e., Chi-squared test for homogeneity, *I*²). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e., is it sensible to combine?). Indicate “yes” where the authors mention or describe heterogeneity or variability between results and discuss the consequences (eg where authors declare they cannot pool results because of heterogeneity).

^x An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test, Hedges-Olken). (**Note**: Score “Can’t say” if there were fewer than 10 included studies).

^{xi} Potential sources of support should be clearly acknowledged in both the systematic review and the included studies.

^{xii} Rate the overall methodological quality of the study, using the following as a guide: **High quality** (++) : Majority of criteria met. Little or no risk of bias. Results unlikely to be changed by further research. **Acceptable** (+) : Most criteria met. Some flaws in the study with an associated risk of bias, Conclusions may change in the light of further studies. **Low quality** (0) : Either most criteria not met, or significant flaws relating to key aspects of study design. Conclusions likely to change in the light of further studies.

^{xiii} Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above. This is a very important part of the evaluation and will feature in the evidence table. PLEASE FILL IN.



Methodology Checklist 1: Systematic Reviews and Meta-analyses

SIGN

SIGN gratefully acknowledges the permission received from the authors of the AMSTAR tool to base this checklist on their work: *Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C, et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Medical Research Methodology 2007, 7:10 doi:10.1186/1471-2288-7-10. Available from <http://www.biomedcentral.com/1471-2288/7/10> [cited 10 Sep 2012]*

Study identification (Include author, title, year of publication, journal title, pages)

< BrieIM_2010 > JAMA 2010;303(3):865ff

Guideline topic: AG IV

Key Question No: 4.1

Before completing this checklist, consider:

1. Is the paper a systematic review or meta-analysis? IF NO reject. IF **YES** continue.
2. Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO reject. IF **YES** complete the checklist.

Checklist completed by: **AF, ZKLS**

Section 1: Internal validity

In a well conducted systematic review:

Does this study do it?

1.1	The study addresses a clearly defined research question. ⁱ	Yes X	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	
1.2	At least two people should select studies and extract data. ⁱⁱ	Yes X	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	
1.3	A comprehensive literature search is carried out. ⁱⁱⁱ	Yes X	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	Does not apply <input type="checkbox"/>
1.4	The authors clearly state if or how they limited their review by publication type. ^{iv}	Yes X	No <input type="checkbox"/>
1.5	The included and excluded studies are listed. ^v	Yes <input type="checkbox"/>	No X
1.6	The characteristics of the included studies are provided. ^{vi}	Yes X	No <input type="checkbox"/>
1.7	The scientific quality of the included studies is assessed and documented. ^{vii}	Yes X	No <input type="checkbox"/>

1.8	The scientific quality of the included studies was assessed appropriately. ^{viii}	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.9	Appropriate methods are used to combine the individual study findings. ^{ix}	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.10	The likelihood of publication bias is assessed. ^x k=3 (4) → not necessary	Yes <input type="checkbox"/> No <input checked="" type="checkbox"/> Can't say <input type="checkbox"/>
1.11	Conflicts of interest are declared. ^{xi}	Yes <input type="checkbox"/> No <input type="checkbox"/>
SECTION 2: OVERALL ASSESSMENT OF THE STUDY		
2.1	What is your overall assessment of the methodological quality of this review? ^{xii}	High quality (++) <input checked="" type="checkbox"/> Acceptable (+) Unacceptable – reject
2.2	Are the results of this study directly applicable to the patient group targeted by this guideline?	Yes <input type="checkbox"/> No <input type="checkbox"/>
2.3	Notes: ^{xiii}	

ⁱ The research question and inclusion criteria should be established before the review is conducted. To score a 'yes' for this factor there must be reference to a protocol, ethics approval, or pre-determined/a priori published research objectives.

ⁱⁱ At least two people should select papers and extract data. There should be a consensus procedure to resolve any differences.

ⁱⁱⁱ At least two major electronic databases should be searched. The report must include years and databases searched (e.g., Central, EMBASE, MEDLINE, OpenGrey, 1999-2009). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found. In rare cases this may not apply where authors have carried out a meta analysis focusing on a specified range of major trials in their field.

^{iv} The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status or language. If searching sources that contains both grey and non-grey literature, must specify that they were searching for both.

^v A list of included and excluded studies should be provided. Limiting the excluded studies to references is acceptable.

^{vi} In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analyzed

e.g., age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported. (**Note** that a format other than a table is acceptable, as long as the information noted here is provided).

^{vii} This relates to the scientific quality of the studies included in the review. I can include use of a quality scoring tool or checklist, e.g., Jadad scale, risk of bias, sensitivity analysis, or a description of quality items, with some kind of result for EACH study (“low” or “high” is fine, as long as it is clear which studies scored “low” and which scored “high”; a summary score/range for all studies is not acceptable).

^{viii} The methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations. (**Note**: The review might say something like “the results should be interpreted with caution due to poor quality of included studies.” Cannot score “yes” for this question if scored “no” for question 7).

^{ix} For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e., Chi-squared test for homogeneity, *I*²). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e., is it sensible to combine?). Indicate “yes” where the authors mention or describe heterogeneity or variability between results and discuss the consequences (eg where authors declare they cannot pool results because of heterogeneity).

^x An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test, Hedges-Olken). (**Note**: Score “Can’t say” if there were fewer than 10 included studies).

^{xi} Potential sources of support should be clearly acknowledged in both the systematic review and the included studies.

^{xii} Rate the overall methodological quality of the study, using the following as a guide: **High quality** (++) : Majority of criteria met. Little or no risk of bias. Results unlikely to be changed by further research. **Acceptable** (+) : Most criteria met. Some flaws in the study with an associated risk of bias, Conclusions may change in the light of further studies. **Low quality** (0) : Either most criteria not met, or significant flaws relating to key aspects of study design. Conclusions likely to change in the light of further studies.

^{xiii} Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above. This is a very important part of the evaluation and will feature in the evidence table. PLEASE FILL IN.



Methodology Checklist 1: Systematic Reviews and Meta-analyses

SIGN

SIGN gratefully acknowledges the permission received from the authors of the AMSTAR tool to base this checklist on their work: *Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C, et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Medical Research Methodology 2007, 7:10 doi:10.1186/1471-2288-7-10. Available from <http://www.biomedcentral.com/1471-2288/7/10> [cited 10 Sep 2012]*

Study identification (Include author, title, year of publication, journal title, pages)

Briel M et al. Higher vs Lower Positive End-Expiratory Pressure in Patients With Acute Lung Injury and Acute Respiratory Distress Syndrome. *JAMA* 2010;303(9):865ff

Guideline topic: Chap. 4 (ID:02)

Key Question No:

Before completing this checklist, consider:

1. Is the paper a systematic review or meta-analysis? IF NO reject. IF YES continue.
2. Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO reject. IF YES complete the checklist.

Checklist completed by: **AF, ZKSL**

Section 1: Internal validity

<i>In a well conducted systematic review:</i>		<i>Does this study do it?</i>	
1.1	The study addresses a clearly defined research question. ⁱ	Yes <input checked="" type="checkbox"/>	No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.2	At least two people should select studies and extract data. ⁱⁱ	Yes <input checked="" type="checkbox"/>	No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.3	A comprehensive literature search is carried out. ⁱⁱⁱ	Yes <input checked="" type="checkbox"/>	No <input type="checkbox"/> Can't say <input type="checkbox"/> Does not apply <input type="checkbox"/>
1.4	The authors clearly state if or how they limited their review by publication type. ^{iv}	Yes <input checked="" type="checkbox"/>	No <input type="checkbox"/>
1.5	The included and excluded studies are listed. ^v	Yes in~ <input checked="" type="checkbox"/> k=3(4)	No ex~ <input checked="" type="checkbox"/> (l=5)
1.6	The characteristics of the included studies are provided. ^{vi}	Yes <input checked="" type="checkbox"/>	No <input type="checkbox"/>
1.7	The scientific quality of the included studies is assessed and documented. ^{vii}	Yes <input checked="" type="checkbox"/>	No <input type="checkbox"/>

1.8	The scientific quality of the included studies was assessed appropriately. ^{viii}	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.9	Appropriate methods are used to combine the individual study findings. ^{ix}	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.10	The likelihood of publication bias is assessed. ^x	Yes <input type="checkbox"/> No <input type="checkbox"/> Can't say <input checked="" type="checkbox"/> wg. k<10
1.11	Conflicts of interest are declared. ^{xi}	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/>
SECTION 2: OVERALL ASSESSMENT OF THE STUDY		
2.1	What is your overall assessment of the methodological quality of this review? ^{xii}	High quality (++) Acceptable (+) <input type="checkbox"/> Unacceptable – reject 0 <input type="checkbox"/>
2.2	Are the results of this study directly applicable to the patient group targeted by this guideline?	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/>
2.3	Notes: ^{xiii} although no overall significance when considering interaction → borderline significant benefits for lower PEEP in ALI; in ARDS higher PEEP significantly better	

ⁱ The research question and inclusion criteria should be established before the review is conducted. To score a 'yes' for this factor there must be reference to a protocol, ethics approval, or pre-determined/a priori published research objectives.

ⁱⁱ At least two people should select papers and extract data. There should be a consensus procedure to resolve any differences.

ⁱⁱⁱ At least two major electronic databases should be searched. The report must include years and databases searched (e.g., Central, EMBASE, MEDLINE, OpenGrey, 1999-2009). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found. In rare cases this may not apply where authors have carried out a meta analysis focusing on a specified range of major trials in their field.

^{iv} The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status or language. If searching sources that contains both grey and non-grey literature, must specify that they were searching for both.

^v A list of included and excluded studies should be provided. Limiting the excluded studies to references is acceptable.

^{vi} In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analyzed e.g., age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported. (**Note** that a format other than a table is acceptable, as long as the information noted here is provided).

^{vii} This relates to the scientific quality of the studies included in the review. I can include use of a quality scoring tool or checklist, e.g., Jadad scale, risk of bias, sensitivity analysis, or a description of quality items, with some kind of result for EACH study (“low” or “high” is fine, as long as it is clear which studies scored “low” and which scored “high”; a summary score/range for all studies is not acceptable).

^{viii} The methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations. (**Note**: The review might say something like “the results should be interpreted with caution due to poor quality of included studies.” Cannot score “yes” for this question if scored “no” for question 7).

^{ix} For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e., Chi-squared test for homogeneity, *I*²). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e., is it sensible to combine?). Indicate “yes” where the authors mention or describe heterogeneity or variability between results and discuss the consequences (eg where authors declare they cannot pool results because of heterogeneity).

^x An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test, Hedges-Olken). (**Note**: Score “Can’t say” if there were fewer than 10 included studies).

^{xi} Potential sources of support should be clearly acknowledged in both the systematic review and the included studies.

^{xii} Rate the overall methodological quality of the study, using the following as a guide: **High quality** (++) : Majority of criteria met. Little or no risk of bias. Results unlikely to be changed by further research. **Acceptable** (+) : Most criteria met. Some flaws in the study with an associated risk of bias, Conclusions may change in the light of further studies. **Low quality** (0) : Either most criteria not met, or significant flaws relating to key aspects of study design. Conclusions likely to change in the light of further studies.

^{xiii} Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above. This is a very important part of the evaluation and will feature in the evidence table. PLEASE FILL IN.



Methodology Checklist 1: Systematic Reviews and Meta-analyses

SIGN

SIGN gratefully acknowledges the permission received from the authors of the AMSTAR tool to base this checklist on their work: *Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C, et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Medical Research Methodology 2007, 7:10 doi:10.1186/1471-2288-7-10. Available from <http://www.biomedcentral.com/1471-2288/7/10> [cited 10 Sep 2012]*

Study identification (Include author, title, year of publication, journal title, pages)

<BurnsK_2014>

Cochrane review 2014 (9)

Guideline topic: **AG V**

Key Question No: **7.2 (27.10.15ff)**

Before completing this checklist, consider:

1. Is the paper a systematic review or meta-analysis? IF NO reject. IF **YES** continue.
2. Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO reject. IF YES complete the checklist.

Checklist completed by: **AF, ZKSL**

Section 1: Internal validity

In a well conducted systematic review:

Does this study do it?

1.1	The study addresses a clearly defined research question. ⁱ	Yes <input type="checkbox"/>	No <input type="checkbox"/>	Can't say <input type="checkbox"/>	
1.2	At least two people should select studies and extract data. ⁱⁱ	Yes <input type="checkbox"/>	No <input type="checkbox"/>	Can't say <input type="checkbox"/>	
1.3	A comprehensive literature search is carried out. ⁱⁱⁱ	Yes <input type="checkbox"/>	No <input type="checkbox"/>	Can't say <input type="checkbox"/>	Does not apply <input type="checkbox"/>
1.4	The authors clearly state if or how they limited their review by publication type. ^{iv}	Yes <input type="checkbox"/>	No <input type="checkbox"/>		
1.5	The included and excluded studies are listed. ^v	Yes <input type="checkbox"/>	No <input type="checkbox"/>		
1.6	The characteristics of the included studies are provided. ^{vi}	Yes <input type="checkbox"/>	No <input type="checkbox"/>		
1.7	The scientific quality of the included studies is assessed and documented. ^{vii}	Yes <input type="checkbox"/>	No <input type="checkbox"/>		

1.8	The scientific quality of the included studies was assessed appropriately. ^{viii}	Yes <input type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.9	Appropriate methods are used to combine the individual study findings. ^{ix}	Yes <input type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.10	The likelihood of publication bias is assessed. ^x	Yes <input type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.11	Conflicts of interest are declared. ^{xi}	Yes <input type="checkbox"/> No <input type="checkbox"/>
SECTION 2: OVERALL ASSESSMENT OF THE STUDY		
2.1	What is your overall assessment of the methodological quality of this review? ^{xii}	High quality (++) <input type="checkbox"/> Acceptable (+) <input checked="" type="checkbox"/> (at least) Unacceptable – reject 0 <input type="checkbox"/>
2.2	Are the results of this study directly applicable to the patient group targeted by this guideline?	Yes <input type="checkbox"/> No <input type="checkbox"/>
2.3	Notes: ^{xiii} Acc. to convention Cochrane rev. are not to be methodologically reviewed in detail	

ⁱ The research question and inclusion criteria should be established before the review is conducted. To score a 'yes' for this factor there must be reference to a protocol, ethics approval, or pre-determined/a priori published research objectives.

ⁱⁱ At least two people should select papers and extract data. There should be a consensus procedure to resolve any differences.

ⁱⁱⁱ At least two major electronic databases should be searched. The report must include years and databases searched (e.g., Central, EMBASE, MEDLINE, OpenGrey, 1999-2009). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found. In rare cases this may not apply where authors have carried out a meta analysis focusing on a specified range of major trials in their field.

^{iv} The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status or language. If searching sources that contains both grey and non-grey literature, must specify that they were searching for both.

^v A list of included and excluded studies should be provided. Limiting the excluded studies to references is acceptable.

^{vi} In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analyzed e.g., age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported. (**Note** that a format other than a table is acceptable, as long as the information noted here is provided).

^{vii} This relates to the scientific quality of the studies included in the review. I can include use of a quality scoring tool or checklist, e.g., Jadad scale, risk of bias, sensitivity analysis, or a description of quality items, with some kind of result for EACH study (“low” or “high” is fine, as long as it is clear which studies scored “low” and which scored “high”; a summary score/range for all studies is not acceptable).

^{viii} The methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations. (**Note**: The review might say something like “the results should be interpreted with caution due to poor quality of included studies.” Cannot score “yes” for this question if scored “no” for question 7).

^{ix} For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e., Chi-squared test for homogeneity, *I*²). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e., is it sensible to combine?). Indicate “yes” where the authors mention or describe heterogeneity or variability between results and discuss the consequences (eg where authors declare they cannot pool results because of heterogeneity).

^x An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test, Hedges-Olken). (**Note**: Score “Can’t say” if there were fewer than 10 included studies).

^{xi} Potential sources of support should be clearly acknowledged in both the systematic review and the included studies.

^{xii} Rate the overall methodological quality of the study, using the following as a guide: **High quality** (++) : Majority of criteria met. Little or no risk of bias. Results unlikely to be changed by further research. **Acceptable** (+) : Most criteria met. Some flaws in the study with an associated risk of bias, Conclusions may change in the light of further studies. **Low quality** (0) : Either most criteria not met, or significant flaws relating to key aspects of study design. Conclusions likely to change in the light of further studies.

^{xiii} Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above. This is a very important part of the evaluation and will feature in the evidence table. PLEASE FILL IN.



Methodology Checklist 1: Systematic Reviews and Meta-analyses

SIGN

SIGN gratefully acknowledges the permission received from the authors of the AMSTAR tool to base this checklist on their work: *Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C, et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Medical Research Methodology 2007, 7:10 doi:10.1186/1471-2288-7-10. Available from <http://www.biomedcentral.com/1471-2288/7/10> [cited 10 Sep 2012]*

Study identification (Include author, title, year of publication, journal title, pages)

< DavidsonWJ_2006 >

Crit Care 2006;10:R41ff

Guideline topic: AG V

Key Question No: 5.8.3 (25.05.16ff)

Before completing this checklist, consider:

1. Is the paper a systematic review or meta-analysis? IF NO reject. IF **YES** continue.
2. Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO reject. IF YES complete the checklist.

Checklist completed by: AF, ZKSL

Section 1: Internal validity

In a well conducted systematic review:

Does this study do it?

1.1	The study addresses a clearly defined research question. ⁱ	Yes <input type="checkbox"/>	No <input type="checkbox"/>	Can't say <input type="checkbox"/>
1.2	At least two people should select studies and extract data. ⁱⁱ	Yes <input type="checkbox"/>	No <input type="checkbox"/>	Can't say <input type="checkbox"/>
1.3	A comprehensive literature search is carried out. ⁱⁱⁱ	Yes <input type="checkbox"/>	No <input type="checkbox"/>	Can't say <input type="checkbox"/> Does not apply <input type="checkbox"/>
1.4	The authors clearly state if or how they limited their review by publication type. ^{iv}	Yes <input type="checkbox"/>	No <input type="checkbox"/>	
1.5	The included and excluded studies are listed. ^v	Yes <input type="checkbox"/>	No <input type="checkbox"/>	
1.6	The characteristics of the included studies are provided. ^{vi}	Yes <input type="checkbox"/>	No <input type="checkbox"/>	
1.7	The scientific quality of the included studies is assessed and documented. ^{vii}	Yes <input type="checkbox"/>	No <input type="checkbox"/>	

1.8	The scientific quality of the included studies was assessed appropriately. ^{viii}	Yes <input type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.9	Appropriate methods are used to combine the individual study findings. ^{ix}	Yes <input type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.10	The likelihood of publication bias is assessed. ^x	Yes <input type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.11	Conflicts of interest are declared. ^{xi}	Yes <input type="checkbox"/> No <input type="checkbox"/>
SECTION 2: OVERALL ASSESSMENT OF THE STUDY		
2.1	What is your overall assessment of the methodological quality of this review? ^{xii}	High quality (++) <input type="checkbox"/> Acceptable (+) <input type="checkbox"/> Unacceptable – reject <input type="checkbox"/>
2.2	Are the results of this study directly applicable to the patient group targeted by this guideline?	Yes <input type="checkbox"/> No <input type="checkbox"/>
2.3	Notes: ^{xiii} Already updated evidence available from <ZhangN 2013>/ <MengH 2012>, only abstract reviewed due to timely restrictions→ w/O difference to newer publications	

ⁱ The research question and inclusion criteria should be established before the review is conducted. To score a 'yes' for this factor there must be reference to a protocol, ethics approval, or pre-determined/a priori published research objectives.

ⁱⁱ At least two people should select papers and extract data. There should be a consensus procedure to resolve any differences.

ⁱⁱⁱ At least two major electronic databases should be searched. The report must include years and databases searched (e.g., Central, EMBASE, MEDLINE, OpenGrey, 1999-2009). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found. In rare cases this may not apply where authors have carried out a meta analysis focusing on a specified range of major trials in their field.

^{iv} The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status or language. If searching sources that contains both grey and non-grey literature, must specify that they were searching for both.

^v A list of included and excluded studies should be provided. Limiting the excluded studies to references is acceptable.

^{vi} In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analyzed e.g., age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported. (**Note** that a format other than a table is acceptable, as long as the information noted here is provided).

^{vii} This relates to the scientific quality of the studies included in the review. I can include use of a quality scoring tool or checklist, e.g., Jadad scale, risk of bias, sensitivity analysis, or a description of quality items, with some kind of result for EACH study ("low" or "high" is fine, as long as it is clear which studies scored "low" and which scored "high"; a summary score/range for all studies is not acceptable).

^{viii} The methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations. (**Note:** The review might say something like "the results should be interpreted with caution due to poor quality of included studies." Cannot score "yes" for this question if scored "no" for question 7).

^{ix} For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e., Chi-squared test for homogeneity, /2). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e., is it sensible to combine?). Indicate "yes" where the authors mention or describe heterogeneity or variability between results and discuss the consequences (eg where authors declare they cannot pool results because of heterogeneity).

^x An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test, Hedges-Olken). (**Note:** Score "Can't say" if there were fewer than 10 included studies).

^{xi} Potential sources of support should be clearly acknowledged in both the systematic review and the included studies.

^{xii} Rate the overall methodological quality of the study, using the following as a guide: **High quality** (++) : Majority of criteria met. Little or no risk of bias. Results unlikely to be changed by further research. **Acceptable** (+) : Most criteria met. Some flaws in the study with an associated risk of bias, Conclusions may change in the light of further studies. **Low quality** (0) : Either most criteria not met, or significant flaws relating to key aspects of study design. Conclusions likely to change in the light of further studies.

^{xiii} Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above. This is a very important part of the evaluation and will feature in the evidence table. PLEASE FILL IN.



Methodology Checklist 1: Systematic Reviews and Meta-analyses

SIGN

SIGN gratefully acknowledges the permission received from the authors of the AMSTAR tool to base this checklist on their work: *Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C, et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Medical Research Methodology 2007, 7:10 doi:10.1186/1471-2288-7-10. Available from <http://www.biomedcentral.com/1471-2288/7/10> [cited 10 Sep 2012]*

Study identification (Include author, title, year of publication, journal title, pages)

< Davydow_2008 > Psychosomat Med 2008;70:512ff

Guideline topic: **AG VIII**

Key Question No: **8.1.3 (& 8.1.2 QoL)**

Before completing this checklist, consider:

1. Is the paper a systematic review or meta-analysis? IF NO reject. IF **YES** continue.
2. Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO reject. IF **YES** complete the checklist.

Checklist completed by: **AF, ZKSL**

Section 1: Internal validity

<i>In a well conducted systematic review:</i>		<i>Does this study do it?</i>	
1.1	The study addresses a clearly defined research question. ⁱ EBM based clinical guidance	Yes X	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	
1.2	At least two people should select studies and extract data. ⁱⁱ	Yes X	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	
1.3	A comprehensive literature search is carried out. ⁱⁱⁱ	Yes X	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	Does not apply <input type="checkbox"/>
1.4	The authors clearly state if or how they limited their review by publication type. ^{iv} English only, adults	Yes X	No <input type="checkbox"/>
1.5	The included and excluded studies are listed. ^v K=10 ref. with n=321 pts. (2 excl. duplicates from 6 cohorts); 6 retrospect., 2 prospective, 2 cross-sectional); DO given	Yes X	No <input type="checkbox"/>
1.6	The characteristics of the included studies are provided. ^{vi} Tab.1	Yes X	No <input type="checkbox"/>
1.7	The scientific quality of the included studies is assessed and documented. ^{vii} → n.a.	Yes <input type="checkbox"/>	No <input type="checkbox"/>

1.8	The scientific quality of the included studies was assessed appropriately. ^{viii} → n.a.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	
1.9	Appropriate methods are used to combine the individual study findings. ^{ix} → Rather difficult to combine due to various length of FU	Yes <input type="checkbox"/>	No <input type="checkbox"/>
		Can't say X	
1.10	The likelihood of publication bias is assessed. ^x → But non-survivor anyway not regarded	Yes <input type="checkbox"/>	No X
		Can't say <input type="checkbox"/>	
1.11	Conflicts of interest are declared. ^{xi}	Yes <input type="checkbox"/>	No X
SECTION 2: OVERALL ASSESSMENT OF THE STUDY			
2.1	What is your overall assessment of the methodological quality of this review? ^{xii}	High quality (++) <input type="checkbox"/>	Acceptable (+) X
		Unacceptable – reject <input type="checkbox"/>	
2.2	Are the results of this study directly applicable to the patient group targeted by this guideline?	Yes <input type="checkbox"/>	No <input type="checkbox"/>
2.3	Notes: ^{xiii} SR of FU data regarding depression/ anxiety/ PTSD; interesting although marked heterogeneity seen and data from observational cohorts only QoL although presented		

ⁱ The research question and inclusion criteria should be established before the review is conducted. To score a 'yes' for this factor there must be reference to a protocol, ethics approval, or pre-determined/a priori published research objectives.

ⁱⁱ At least two people should select papers and extract data. There should be a consensus procedure to resolve any differences.

ⁱⁱⁱ At least two major electronic databases should be searched. The report must include years and databases searched (e.g., Central, EMBASE, MEDLINE, OpenGrey, 1999-2009). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found. In rare cases this may not apply where authors have carried out a meta analysis focusing on a specified range of major trials in their field.

^{iv} The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status or language. If searching sources that contains both grey and non-grey literature, must specify that they were searching for both.

^v A list of included and excluded studies should be provided. Limiting the excluded studies to references is acceptable.

^{vi} In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analyzed e.g., age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported. (**Note** that a format other than a table is acceptable, as long as the information noted here is provided).

^{vii} This relates to the scientific quality of the studies included in the review. I can include use of a quality scoring tool or checklist, e.g., Jadad scale, risk of bias, sensitivity analysis, or a description of quality items, with some kind of result for EACH study (“low” or “high” is fine, as long as it is clear which studies scored “low” and which scored “high”; a summary score/range for all studies is not acceptable).

^{viii} The methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations. (**Note**: The review might say something like “the results should be interpreted with caution due to poor quality of included studies.” Cannot score “yes” for this question if scored “no” for question 7).

^{ix} For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e., Chi-squared test for homogeneity, *I*²). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e., is it sensible to combine?). Indicate “yes” where the authors mention or describe heterogeneity or variability between results and discuss the consequences (eg where authors declare they cannot pool results because of heterogeneity).

^x An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test, Hedges-Olken). (**Note**: Score “Can’t say” if there were fewer than 10 included studies).

^{xi} Potential sources of support should be clearly acknowledged in both the systematic review and the included studies.

^{xii} Rate the overall methodological quality of the study, using the following as a guide: **High quality** (++) : Majority of criteria met. Little or no risk of bias. Results unlikely to be changed by further research. **Acceptable** (+) : Most criteria met. Some flaws in the study with an associated risk of bias, Conclusions may change in the light of further studies. **Low quality** (0) : Either most criteria not met, or significant flaws relating to key aspects of study design. Conclusions likely to change in the light of further studies.

^{xiii} Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above. This is a very important part of the evaluation and will feature in the evidence table. PLEASE FILL IN.



Methodology Checklist 1: Systematic Reviews and Meta-analyses

SIGN

SIGN gratefully acknowledges the permission received from the authors of the AMSTAR tool to base this checklist on their work: *Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C., et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Medical Research Methodology 2007, 7:10 doi:10.1186/1471-2288-7-10. Available from <http://www.biomedcentral.com/1471-2288/7/10> [cited 10 Sep 2012]*

Study identification (Include author, title, year of publication, journal title, pages)

< DuffettM_2007 > Crit Care 2007;11:R66ff

Guideline topic: AG V

Key Question No: 5.8.3 (25.05.16ff)

Before completing this checklist, consider:

1. Is the paper a systematic review or meta-analysis? IF NO reject. IF **YES** continue.
2. Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO reject. IF YES complete the checklist.

Checklist completed by: AF, ZKSL

Section 1: Internal validity

<i>In a well conducted systematic review:</i>		<i>Does this study do it?</i>	
1.1	The study addresses a clearly defined research question. ⁱ	Yes X	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	
1.2	At least two people should select studies and extract data. ⁱⁱ	Yes X	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	
1.3	A comprehensive literature search is carried out. ⁱⁱⁱ	Yes X	No <input type="checkbox"/>
	Available on request	Can't say (X)	Does not apply <input type="checkbox"/>
1.4	The authors clearly state if or how they limited their review by publication type. ^{iv}	Yes X	No <input type="checkbox"/>
1.5	The included and excluded studies are listed. ^v	Yes <input type="checkbox"/>	No X incl. only
	K=6 with n=314 children		
1.6	The characteristics of the included studies are provided. ^{vi}	Yes X	No <input type="checkbox"/>
1.7	The scientific quality of the included studies is assessed and documented. ^{vii}	Yes X	No <input type="checkbox"/>

1.8	The scientific quality of the included studies was assessed appropriately. ^{viii}	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.9	Appropriate methods are used to combine the individual study findings. ^{ix}	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.10	The likelihood of publication bias is assessed. ^x	Yes <input type="checkbox"/> No <input type="checkbox"/> Can't say <input checked="" type="checkbox"/>
1.11	Conflicts of interest are declared. ^{xi}	Yes <input type="checkbox"/> No <input type="checkbox"/>
SECTION 2: OVERALL ASSESSMENT OF THE STUDY		
2.1	What is your overall assessment of the methodological quality of this review? ^{xii}	High quality (++) <input checked="" type="checkbox"/> Acceptable (+) <input type="checkbox"/> Unacceptable – reject <input type="checkbox"/>
2.2	Are the results of this study directly applicable to the patient group targeted by this guideline?	Yes <input type="checkbox"/> No <input type="checkbox"/>
2.3	Notes: ^{xiii} rather old evidence, but with differences between children & adults and mortality benefits at that state surfactant ther. in children max be supported; AE seem to be comparable and/or sufficiently to dealt with	

ⁱ The research question and inclusion criteria should be established before the review is conducted. To score a 'yes' for this factor there must be reference to a protocol, ethics approval, or pre-determined/a priori published research objectives.

ⁱⁱ At least two people should select papers and extract data. There should be a consensus procedure to resolve any differences.

ⁱⁱⁱ At least two major electronic databases should be searched. The report must include years and databases searched (e.g., Central, EMBASE, MEDLINE, OpenGrey, 1999-2009). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found. In rare cases this may not apply where authors have carried out a meta analysis focusing on a specified range of major trials in their field.

^{iv} The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status or language. If searching sources that contains both grey and non-grey literature, must specify that they were searching for both.

^v A list of included and excluded studies should be provided. Limiting the excluded studies to references is acceptable.

^{vi} In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analyzed e.g., age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported. (**Note** that a format other than a table is acceptable, as long as the information noted here is provided).

^{vii} This relates to the scientific quality of the studies included in the review. I can include use of a quality scoring tool or checklist, e.g., Jadad scale, risk of bias, sensitivity analysis, or a description of quality items, with some kind of result for EACH study (“low” or “high” is fine, as long as it is clear which studies scored “low” and which scored “high”; a summary score/range for all studies is not acceptable).

^{viii} The methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations. (**Note**: The review might say something like “the results should be interpreted with caution due to poor quality of included studies.” Cannot score “yes” for this question if scored “no” for question 7).

^{ix} For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e., Chi-squared test for homogeneity, *I*²). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e., is it sensible to combine?). Indicate “yes” where the authors mention or describe heterogeneity or variability between results and discuss the consequences (eg where authors declare they cannot pool results because of heterogeneity).

^x An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test, Hedges-Olken). (**Note**: Score “Can’t say” if there were fewer than 10 included studies).

^{xi} Potential sources of support should be clearly acknowledged in both the systematic review and the included studies.

^{xii} Rate the overall methodological quality of the study, using the following as a guide: **High quality** (++) : Majority of criteria met. Little or no risk of bias. Results unlikely to be changed by further research. **Acceptable** (+) : Most criteria met. Some flaws in the study with an associated risk of bias, Conclusions may change in the light of further studies. **Low quality** (0) : Either most criteria not met, or significant flaws relating to key aspects of study design. Conclusions likely to change in the light of further studies.

^{xiii} Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above. This is a very important part of the evaluation and will feature in the evidence table. PLEASE FILL IN.



Methodology Checklist 1: Systematic Reviews and Meta-analyses

SIGN

SIGN gratefully acknowledges the permission received from the authors of the AMSTAR tool to base this checklist on their work: *Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C., et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Medical Research Methodology 2007, 7:10 doi:10.1186/1471-2288-7-10. Available from <http://www.biomedcentral.com/1471-2288/7/10> [cited 10 Sep 2012]*

Study identification (Include author, title, year of publication, journal title, pages)

< Fitzgerald_2014 > Clin Toxicol 2013;51:385ff

Guideline topic: AG VI

Key Question No: 6.4.2 (22.10.15ff)

Before completing this checklist, consider:

1. Is the paper a systematic review or meta-analysis? IF NO reject. IF YES continue.
2. Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO reject. IF YES complete the checklist.

Checklist completed by: AF, ZKSL

Section 1: Internal validity

In a well conducted systematic review:

Does this study do it?

1.1	The study addresses a clearly defined research question. ⁱ	Yes X	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	
1.2	At least two people should select studies and extract data. ⁱⁱ	Yes X	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	
1.3	A comprehensive literature search is carried out. ⁱⁱⁱ	Yes X	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	Does not apply <input type="checkbox"/>
1.4	The authors clearly state if or how they limited their review by publication type. ^{iv}	Yes X	No <input type="checkbox"/>
1.5	The included and excluded studies are listed. ^v 2 RCTs and 12 further CCs/ case series; n _{total} =495	Yes <input type="checkbox"/>	No X
1.6	The characteristics of the included studies are provided. ^{vi}	Yes X	No <input type="checkbox"/>
1.7	The scientific quality of the included studies is assessed and documented. ^{vii}	Yes X	No <input type="checkbox"/>

1.8	The scientific quality of the included studies was assessed appropriately. ^{viii}	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.9	Appropriate methods are used to combine the individual study findings. ^{ix} Not applicable	Yes <input type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.10	The likelihood of publication bias is assessed. ^x	Yes <input type="checkbox"/> No <input checked="" type="checkbox"/> Can't say <input type="checkbox"/>
1.11	Conflicts of interest are declared. ^{xi}	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/>
SECTION 2: OVERALL ASSESSMENT OF THE STUDY		
2.1	What is your overall assessment of the methodological quality of this review? ^{xii}	High quality (++) <input checked="" type="checkbox"/> Acceptable (+) <input type="checkbox"/> Unacceptable – reject <input type="checkbox"/>
2.2	Are the results of this study directly applicable to the patient group targeted by this guideline?	Yes <input type="checkbox"/> No <input type="checkbox"/>
2.3	Notes: ^{xiii} no statistical pooling but description of overall results due to heterogeneity of trials/studies; although methodologically satisfying only little evidence provided apparently an error in table 1 occurred p=0.000 unlikely with mortality rates of 7/40 ve. 6/39; see also par.1 in p.5	

ⁱ The research question and inclusion criteria should be established before the review is conducted. To score a 'yes' for this factor there must be reference to a protocol, ethics approval, or pre-determined/a priori published research objectives.

ⁱⁱ At least two people should select papers and extract data. There should be a consensus procedure to resolve any differences.

ⁱⁱⁱ At least two major electronic databases should be searched. The report must include years and databases searched (e.g., Central, EMBASE, MEDLINE, OpenGrey, 1999-2009). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found. In rare cases this may not apply where authors have carried out a meta analysis focusing on a specified range of major trials in their field.

^{iv} The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status or language. If searching sources that contains both grey and non-grey literature, must specify that they were searching for both.

^v A list of included and excluded studies should be provided. Limiting the excluded studies to references is acceptable.

^{vi} In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analyzed e.g., age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported. (**Note** that a format other than a table is acceptable, as long as the information noted here is provided).

^{vii} This relates to the scientific quality of the studies included in the review. I can include use of a quality scoring tool or checklist, e.g., Jadad scale, risk of bias, sensitivity analysis, or a description of quality items, with some kind of result for EACH study (“low” or “high” is fine, as long as it is clear which studies scored “low” and which scored “high”; a summary score/range for all studies is not acceptable).

^{viii} The methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations. (**Note**: The review might say something like “the results should be interpreted with caution due to poor quality of included studies.” Cannot score “yes” for this question if scored “no” for question 7).

^{ix} For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e., Chi-squared test for homogeneity, I^2). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e., is it sensible to combine?). Indicate “yes” where the authors mention or describe heterogeneity or variability between results and discuss the consequences (eg where authors declare they cannot pool results because of heterogeneity).

^x An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test, Hedges-Olken). (**Note**: Score “Can’t say” if there were fewer than 10 included studies).

^{xi} Potential sources of support should be clearly acknowledged in both the systematic review and the included studies.

^{xii} Rate the overall methodological quality of the study, using the following as a guide: **High quality** (++) : Majority of criteria met. Little or no risk of bias. Results unlikely to be changed by further research. **Acceptable** (+) : Most criteria met. Some flaws in the study with an associated risk of bias, Conclusions may change in the light of further studies. **Low quality** (0) : Either most criteria not met, or significant flaws relating to key aspects of study design. Conclusions likely to change in the light of further studies.

^{xiii} Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above. This is a very important part of the evaluation and will feature in the evidence table. PLEASE FILL IN.



Methodology Checklist 1: Systematic Reviews and Meta-analyses

SIGN

SIGN gratefully acknowledges the permission received from the authors of the AMSTAR tool to base this checklist on their work: *Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C, et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Medical Research Methodology 2007, 7:10 doi:10.1186/1471-2288-7-10. Available from <http://www.biomedcentral.com/1471-2288/7/10> [cited 10 Sep 2012]*

Study identification (Include author, title, year of publication, journal title, pages)

< GalvinIM_2013 > Cochrane review 2013 (7)

Guideline topic: **AG VI**

Key Question No: **6.4.4 (20.10.15ff)**

Before completing this checklist, consider:

1. Is the paper a systematic review or meta-analysis? IF NO reject. IF **YES** continue.
2. Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO reject. IF YES complete the checklist.

Checklist completed by: **AF, ZKSL**

Section 1: Internal validity

In a well conducted systematic review:

Does this study do it?

1.1	The study addresses a clearly defined research question. ⁱ	Yes <input type="checkbox"/>	No <input type="checkbox"/>	Can't say <input type="checkbox"/>	
1.2	At least two people should select studies and extract data. ⁱⁱ	Yes <input type="checkbox"/>	No <input type="checkbox"/>	Can't say <input type="checkbox"/>	
1.3	A comprehensive literature search is carried out. ⁱⁱⁱ	Yes <input type="checkbox"/>	No <input type="checkbox"/>	Can't say <input type="checkbox"/>	Does not apply <input type="checkbox"/>
1.4	The authors clearly state if or how they limited their review by publication type. ^{iv}	Yes <input type="checkbox"/>	No <input type="checkbox"/>		
1.5	The included and excluded studies are listed. ^v	Yes <input type="checkbox"/>	No <input type="checkbox"/>		
1.6	The characteristics of the included studies are provided. ^{vi}	Yes <input type="checkbox"/>	No <input type="checkbox"/>		
1.7	The scientific quality of the included studies is assessed and documented. ^{vii}	Yes <input type="checkbox"/>	No <input type="checkbox"/>		

1.8	The scientific quality of the included studies was assessed appropriately. ^{viii}	Yes <input type="checkbox"/>	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	
1.9	Appropriate methods are used to combine the individual study findings. ^{ix}	Yes <input type="checkbox"/>	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	
1.10	The likelihood of publication bias is assessed. ^x	Yes <input type="checkbox"/>	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	
1.11	Conflicts of interest are declared. ^{xi}	Yes <input type="checkbox"/>	No <input type="checkbox"/>
SECTION 2: OVERALL ASSESSMENT OF THE STUDY			
2.1	What is your overall assessment of the methodological quality of this review? ^{xii}	High quality (++) <input type="checkbox"/> Acceptable (+) <input checked="" type="checkbox"/> (at least) Unacceptable – reject 0 <input type="checkbox"/>	
2.2	Are the results of this study directly applicable to the patient group targeted by this guideline?	Yes <input type="checkbox"/>	No <input type="checkbox"/>
2.3	Notes: ^{xiii} Acc. to convention Cochrane rev. are not to be methodologically reviewed in detail;		

ⁱ The research question and inclusion criteria should be established before the review is conducted. To score a 'yes' for this factor there must be reference to a protocol, ethics approval, or pre-determined/a priori published research objectives.

ⁱⁱ At least two people should select papers and extract data. There should be a consensus procedure to resolve any differences.

ⁱⁱⁱ At least two major electronic databases should be searched. The report must include years and databases searched (e.g., Central, EMBASE, MEDLINE, OpenGrey, 1999-2009). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found. In rare cases this may not apply where authors have carried out a meta analysis focusing on a specified range of major trials in their field.

^{iv} The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status or language. If searching sources that contains both grey and non-grey literature, must specify that they were searching for both.

^v A list of included and excluded studies should be provided. Limiting the excluded studies to references is acceptable.

^{vi} In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analyzed e.g., age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported. (**Note** that a format other than a table is acceptable, as long as the information noted here is provided).

^{vii} This relates to the scientific quality of the studies included in the review. I can include use of a quality scoring tool or checklist, e.g., Jadad scale, risk of bias, sensitivity analysis, or a description of quality items, with some kind of result for EACH study (“low” or “high” is fine, as long as it is clear which studies scored “low” and which scored “high”; a summary score/range for all studies is not acceptable).

^{viii} The methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations. (**Note**: The review might say something like “the results should be interpreted with caution due to poor quality of included studies.” Cannot score “yes” for this question if scored “no” for question 7).

^{ix} For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e., Chi-squared test for homogeneity, I^2). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e., is it sensible to combine?). Indicate “yes” where the authors mention or describe heterogeneity or variability between results and discuss the consequences (eg where authors declare they cannot pool results because of heterogeneity).

^x An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test, Hedges-Olken). (**Note**: Score “Can’t say” if there were fewer than 10 included studies).

^{xi} Potential sources of support should be clearly acknowledged in both the systematic review and the included studies.

^{xii} Rate the overall methodological quality of the study, using the following as a guide: **High quality** (++) : Majority of criteria met. Little or no risk of bias. Results unlikely to be changed by further research. **Acceptable** (+) : Most criteria met. Some flaws in the study with an associated risk of bias, Conclusions may change in the light of further studies. **Low quality** (0) : Either most criteria not met, or significant flaws relating to key aspects of study design. Conclusions likely to change in the light of further studies.

^{xiii} Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above. This is a very important part of the evaluation and will feature in the evidence table. PLEASE FILL IN.



Methodology Checklist 1: Systematic Reviews and Meta-analyses

SIGN

SIGN gratefully acknowledges the permission received from the authors of the AMSTAR tool to base this checklist on their work: *Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C., et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Medical Research Methodology 2007, 7:10 doi:10.1186/1471-2288-7-10. Available from <http://www.biomedcentral.com/1471-2288/7/10> [cited 10 Sep 2012]*

Study identification (Include author, title, year of publication, journal title, pages)

<GonzalesM_2010> Int Care Med 2010; 36:817-27

Guideline topic: AGIII ventilation strategies

Key Question No: 3.1

Before completing this checklist, consider:

1. Is the paper a systematic review or meta-analysis? IF NO reject. IF YES continue.
→ No, secondary analysis of selected observational cohort data but no systematic review/ meta-analysis
2. Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO reject. IF YES complete the checklist.

Checklist completed by: AF, ZKLS

Section 1: Internal validity

<i>In a well conducted systematic review:</i>		<i>Does this study do it?</i>	
1.1	The study addresses a clearly defined research question. ⁱ	Yes	No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.2	At least two people should select studies and extract data. ⁱⁱ	Yes	No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.3	A comprehensive literature search is carried out. ⁱⁱⁱ	Yes	No <input type="checkbox"/> Can't say <input type="checkbox"/> Does not apply <input type="checkbox"/>
1.4	The authors clearly state if or how they limited their review by publication type. ^{iv}	Yes	No <input type="checkbox"/>
1.5	The included and excluded studies are listed. ^v	Yes	No <input type="checkbox"/>
1.6	The characteristics of the included studies are provided. ^{vi}	Yes	No <input type="checkbox"/>
1.7	The scientific quality of the included studies is	Yes	No <input type="checkbox"/>

	assessed and documented. ^{vii}	
1.8	The scientific quality of the included studies was assessed appropriately. ^{viii}	Yes <input type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.9	Appropriate methods are used to combine the individual study findings. ^{ix}	Yes <input type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.10	The likelihood of publication bias is assessed. ^x	Yes <input type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.11	Conflicts of interest are declared. ^{xi}	Yes <input type="checkbox"/> No <input type="checkbox"/>
SECTION 2: OVERALL ASSESSMENT OF THE STUDY		
2.1	What is your overall assessment of the methodological quality of this review? ^{xii}	High quality (++) Acceptable (+) <input type="checkbox"/> Unacceptable – reject X
2.2	Are the results of this study directly applicable to the patient group targeted by this guideline?	Yes <input type="checkbox"/> No <input type="checkbox"/>
2.3	Notes: ^{xiii} Secondary analysis of observational cohort data; no RCT, no systematic review; Propensity score method used to adjust for structural dysbalances between groups	

ⁱ The research question and inclusion criteria should be established before the review is conducted. To score a 'yes' for this factor there must be reference to a protocol, ethics approval, or pre-determined/a priori published research objectives.

ⁱⁱ At least two people should select papers and extract data. There should be a consensus procedure to resolve any differences.

ⁱⁱⁱ At least two major electronic databases should be searched. The report must include years and databases searched (e.g., Central, EMBASE, MEDLINE, OpenGrey, 1999-2009). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found. In rare cases this may not apply where authors have carried out a meta analysis focusing on a specified range of major trials in their field.

^{iv} The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status or language. If searching sources that contains both grey and non-grey literature, must specify that they were searching for both.

^v A list of included and excluded studies should be provided. Limiting the excluded studies to references is acceptable.

^{vi} In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analyzed e.g., age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported. (**Note** that a format other than a table is acceptable, as long as the information noted here is provided).

^{vii} This relates to the scientific quality of the studies included in the review. I can include use of a quality scoring tool or checklist, e.g., Jadad scale, risk of bias, sensitivity analysis, or a description of quality items, with some kind of result for EACH study (“low” or “high” is fine, as long as it is clear which studies scored “low” and which scored “high”; a summary score/range for all studies is not acceptable).

^{viii} The methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations. (**Note**: The review might say something like “the results should be interpreted with caution due to poor quality of included studies.” Cannot score “yes” for this question if scored “no” for question 7).

^{ix} For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e., Chi-squared test for homogeneity, *I*²). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e., is it sensible to combine?). Indicate “yes” where the authors mention or describe heterogeneity or variability between results and discuss the consequences (eg where authors declare they cannot pool results because of heterogeneity).

^x An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test, Hedges-Olken). (**Note**: Score “Can’t say” if there were fewer than 10 included studies).

^{xi} Potential sources of support should be clearly acknowledged in both the systematic review and the included studies.

^{xii} Rate the overall methodological quality of the study, using the following as a guide: **High quality** (++) : Majority of criteria met. Little or no risk of bias. Results unlikely to be changed by further research. **Acceptable** (+) : Most criteria met. Some flaws in the study with an associated risk of bias, Conclusions may change in the light of further studies. **Low quality** (0) : Either most criteria not met, or significant flaws relating to key aspects of study design. Conclusions likely to change in the light of further studies.

^{xiii} Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above. This is a very important part of the evaluation and will feature in the evidence table. PLEASE FILL IN.



Methodology Checklist 1: Systematic Reviews and Meta-analyses

SIGN

SIGN gratefully acknowledges the permission received from the authors of the AMSTAR tool to base this checklist on their work: *Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C, et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Medical Research Methodology 2007, 7:10 doi:10.1186/1471-2288-7-10. Available from <http://www.biomedcentral.com/1471-2288/7/10> [cited 10 Sep 2012]*

Study identification (Include author, title, year of publication, journal title, pages)

< HermansG_2014> Cochrane review 2014;1

Guideline topic: **AG VIII**

Key Question No: **5.6. (05.04.16)**

Before completing this checklist, consider:

1. Is the paper a systematic review or meta-analysis? IF NO reject. IF **YES** continue.
2. Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO reject. IF YES complete the checklist.

Checklist completed by: **AF, ZKSL**

Section 1: Internal validity

In a well conducted systematic review:

Does this study do it?

1.1	The study addresses a clearly defined research question. ⁱ	Yes <input type="checkbox"/>	No <input type="checkbox"/>	Can't say <input type="checkbox"/>	
1.2	At least two people should select studies and extract data. ⁱⁱ	Yes <input type="checkbox"/>	No <input type="checkbox"/>	Can't say <input type="checkbox"/>	
1.3	A comprehensive literature search is carried out. ⁱⁱⁱ	Yes <input type="checkbox"/>	No <input type="checkbox"/>	Can't say <input type="checkbox"/>	Does not apply <input type="checkbox"/>
1.4	The authors clearly state if or how they limited their review by publication type. ^{iv}	Yes <input type="checkbox"/>	No <input type="checkbox"/>		
1.5	The included and excluded studies are listed. ^v	Yes <input type="checkbox"/>	No <input type="checkbox"/>		
1.6	The characteristics of the included studies are provided. ^{vi}	Yes <input type="checkbox"/>	No <input type="checkbox"/>		
1.7	The scientific quality of the included studies is assessed and documented. ^{vii}	Yes <input type="checkbox"/>	No <input type="checkbox"/>		

1.8	The scientific quality of the included studies was assessed appropriately. ^{viii}	Yes <input type="checkbox"/>	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	
1.9	Appropriate methods are used to combine the individual study findings. ^{ix}	Yes <input type="checkbox"/>	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	
1.10	The likelihood of publication bias is assessed. ^x	Yes <input type="checkbox"/>	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	
1.11	Conflicts of interest are declared. ^{xi}	Yes <input type="checkbox"/>	No <input type="checkbox"/>
SECTION 2: OVERALL ASSESSMENT OF THE STUDY			
2.1	What is your overall assessment of the methodological quality of this review? ^{xii}	High quality (++) <input type="checkbox"/> Acceptable (+) <input checked="" type="checkbox"/> (at least) Unacceptable – reject 0 <input type="checkbox"/>	
2.2	Are the results of this study directly applicable to the patient group targeted by this guideline?	Yes <input type="checkbox"/>	No <input type="checkbox"/>
2.3	Notes: ^{xiii} Acc. to convention Cochrane rev. are not to be methodologically reviewed in detail;		

ⁱ The research question and inclusion criteria should be established before the review is conducted. To score a 'yes' for this factor there must be reference to a protocol, ethics approval, or pre-determined/a priori published research objectives.

ⁱⁱ At least two people should select papers and extract data. There should be a consensus procedure to resolve any differences.

ⁱⁱⁱ At least two major electronic databases should be searched. The report must include years and databases searched (e.g., Central, EMBASE, MEDLINE, OpenGrey, 1999-2009). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found. In rare cases this may not apply where authors have carried out a meta analysis focusing on a specified range of major trials in their field.

^{iv} The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status or language. If searching sources that contains both grey and non-grey literature, must specify that they were searching for both.

^v A list of included and excluded studies should be provided. Limiting the excluded studies to references is acceptable.

^{vi} In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analyzed e.g., age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported. (**Note** that a format other than a table is acceptable, as long as the information noted here is provided).

^{vii} This relates to the scientific quality of the studies included in the review. I can include use of a quality scoring tool or checklist, e.g., Jadad scale, risk of bias, sensitivity analysis, or a description of quality items, with some kind of result for EACH study (“low” or “high” is fine, as long as it is clear which studies scored “low” and which scored “high”; a summary score/range for all studies is not acceptable).

^{viii} The methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations. (**Note:** The review might say something like “the results should be interpreted with caution due to poor quality of included studies.” Cannot score “yes” for this question if scored “no” for question 7).

^{ix} For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e., Chi-squared test for homogeneity, I^2). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e., is it sensible to combine?). Indicate “yes” where the authors mention or describe heterogeneity or variability between results and discuss the consequences (eg where authors declare they cannot pool results because of heterogeneity).

^x An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test, Hedges-Olken). (**Note:** Score “Can’t say” if there were fewer than 10 included studies).

^{xi} Potential sources of support should be clearly acknowledged in both the systematic review and the included studies.

^{xii} Rate the overall methodological quality of the study, using the following as a guide: **High quality** (++) : Majority of criteria met. Little or no risk of bias. Results unlikely to be changed by further research. **Acceptable** (+) : Most criteria met. Some flaws in the study with an associated risk of bias, Conclusions may change in the light of further studies. **Low quality** (0) : Either most criteria not met, or significant flaws relating to key aspects of study design. Conclusions likely to change in the light of further studies.

^{xiii} Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above. This is a very important part of the evaluation and will feature in the evidence table. PLEASE FILL IN.



Methodology Checklist 1: Systematic Reviews and Meta-analyses

SIGN

SIGN gratefully acknowledges the permission received from the authors of the AMSTAR tool to base this checklist on their work: *Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C., et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Medical Research Methodology 2007, 7:10 doi:10.1186/1471-2288-7-10. Available from <http://www.biomedcentral.com/1471-2288/7/10> [cited 10 Sep 2012]*

Study identification (Include author, title, year of publication, journal title, pages)

< HosokawaK_2015> Crit Care 2015;19:424ff

Guideline topic: AG V

Key Question No: 5.7. (14.04.16)

Before completing this checklist, consider:

1. Is the paper a systematic review or meta-analysis? IF NO reject. IF **YES** continue.
2. Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO reject. IF YES complete the checklist.

Checklist completed by: AF, ZKSL

Section 1: Internal validity

In a well conducted systematic review:

Does this study do it?

1.1	The study addresses a clearly defined research question. ⁱ However def. of ET vs LT problematical due to overlapping times	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.2	At least two people should select studies and extract data. ⁱⁱ	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.3	A comprehensive literature search is carried out. ⁱⁱⁱ Only 2 (major) DB searched, compared to <HuangH_2014> xx diff. trials	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/> Does not apply <input type="checkbox"/>
1.4	The authors clearly state if or how they limited their review by publication type. ^{iv} Engl only, abs not	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/>
1.5	The included and excluded studies are listed. ^v K=12 RCT with n=2689; thereof ET: 7x (4d)/ 12x (10d) / LT: 10x (>10d)/ 2x (>5d)	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/>
1.6	The characteristics of the included studies are provided. ^{vi}	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/>

1.7	The scientific quality of the included studies is assessed and documented. ^{vii}	Yes <input checked="" type="checkbox"/>	No <input type="checkbox"/>
1.8	The scientific quality of the included studies was assessed appropriately. ^{viii} SD estimate=IQR/1,35 → questionable in my opinion; SD should be rather broader → more conservative estimates seem to be more reliable	Yes <input checked="" type="checkbox"/> Can't say <input type="checkbox"/>	No <input type="checkbox"/>
1.9	Appropriate methods are used to combine the individual study findings. ^{ix}	Yes <input checked="" type="checkbox"/> Can't say <input type="checkbox"/>	No <input type="checkbox"/>
1.10	The likelihood of publication bias is assessed. ^x	Yes <input type="checkbox"/> Can't say <input type="checkbox"/>	No <input checked="" type="checkbox"/>
1.11	Conflicts of interest are declared. ^{xi}	Yes <input type="checkbox"/>	No <input checked="" type="checkbox"/>

SECTION 2: OVERALL ASSESSMENT OF THE STUDY

2.1	What is your overall assessment of the methodological quality of this review? ^{xii}	High quality (++) <input type="checkbox"/> Acceptable (+) <input checked="" type="checkbox"/> Unacceptable – reject <input type="checkbox"/>
2.2	Are the results of this study directly applicable to the patient group targeted by this guideline?	Yes <input type="checkbox"/> No <input type="checkbox"/>
2.3	<p>Notes:^{xiii}</p> <p>Compared to <HuangH_2014> 1 RCT missing (Bouderk 2004 -> why?) and inclusion of <Koch 2012> of questionable use to me, since both arms with ET; overlapping timing definitions ET/LT should be evaluated by clinician regarding usefulness; Higher rates of trachotomy in ET groups when using 1:1 rando ratio may indicate a bias in RCTs although discussed in SR;</p> <p>Results of <HuangH_2014> also indicate a trend in favour of ET (see shifted confidence limits in aggregated short-/long.term mortality & incidence of VAP → therefore results not essentially contradicting those stated here. A trial sequential analysis would have been helpful to determine whether sufficient evidence is available by now (I doubt it).</p> <p>Possibly it would be useful to exclude most early trials because of changed regimens then and today</p>	

ⁱ The research question and inclusion criteria should be established before the review is conducted. To score a 'yes' for this factor there must be reference to a protocol, ethics approval, or pre-determined/a priori published research objectives.

ⁱⁱ At least two people should select papers and extract data. There should be a consensus procedure to resolve any differences.

ⁱⁱⁱ At least two major electronic databases should be searched. The report must include years and databases searched (e.g., Central, EMBASE, MEDLINE, OpenGrey, 1999-2009). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found. In rare cases this may not apply where authors have carried out a meta analysis focusing on a specified range of major trials in their field.

^{iv} The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status or language. If searching sources that contains both grey and non-grey literature, must specify that they were searching for both.

^v A list of included and excluded studies should be provided. Limiting the excluded studies to references is acceptable.

^{vi} In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analyzed e.g., age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported. (**Note** that a format other than a table is acceptable, as long as the information noted here is provided).

^{vii} This relates to the scientific quality of the studies included in the review. I can include use of a quality scoring tool or checklist, e.g., Jadad scale, risk of bias, sensitivity analysis, or a description of quality items, with some kind of result for EACH study ("low" or "high" is fine, as long as it is clear which studies scored "low" and which scored "high"; a summary score/range for all studies is not acceptable).

^{viii} The methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations. (**Note:** The review might say something like "the results should be interpreted with caution due to poor quality of included studies." Cannot score "yes" for this question if scored "no" for question 7).

^{ix} For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e., Chi-squared test for homogeneity, *I*²). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e., is it sensible to combine?). Indicate "yes" where the authors mention or describe heterogeneity or variability between results and discuss the consequences (eg where authors declare they cannot pool results because of heterogeneity).

^x An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test, Hedges-Olken). (**Note:** Score "Can't say" if there were fewer than 10 included studies).

^{xi} Potential sources of support should be clearly acknowledged in both the systematic review and the included studies.

^{xii} Rate the overall methodological quality of the study, using the following as a guide: **High quality** (++) : Majority of criteria met. Little or no risk of bias. Results unlikely to be changed by further research. **Acceptable** (+) : Most criteria met. Some flaws in the study with an associated risk of bias, Conclusions may change in the light of further studies. **Low quality** (0) : Either most criteria not met, or significant flaws relating to key aspects of study design. Conclusions likely to change in the light of further studies.

^{xiii} Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above. This is a very important part of the evaluation and will feature in the evidence table. PLEASE FILL IN.



Methodology Checklist 1: Systematic Reviews and Meta-analyses

SIGN

SIGN gratefully acknowledges the permission received from the authors of the AMSTAR tool to base this checklist on their work: *Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C, et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Medical Research Methodology 2007, 7:10 doi:10.1186/1471-2288-7-10. Available from <http://www.biomedcentral.com/1471-2288/7/10> [cited 10 Sep 2012]*

Study identification (Include author, title, year of publication, journal title, pages)

< KaushalKA_2013 > Cochrane review 2013 (2)

Guideline topic: **AG VIII**

Key Question No: **8.1.1 (20.10.15ff)**

Before completing this checklist, consider:

1. Is the paper a systematic review or meta-analysis? IF NO reject. IF **YES** continue.
2. Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO reject. IF YES complete the checklist.

Checklist completed by: **AF, ZKSL**

Section 1: Internal validity

In a well conducted systematic review:

Does this study do it?

1.1	The study addresses a clearly defined research question. ⁱ	Yes <input type="checkbox"/>	No <input type="checkbox"/>	Can't say <input type="checkbox"/>	
1.2	At least two people should select studies and extract data. ⁱⁱ	Yes <input type="checkbox"/>	No <input type="checkbox"/>	Can't say <input type="checkbox"/>	
1.3	A comprehensive literature search is carried out. ⁱⁱⁱ	Yes <input type="checkbox"/>	No <input type="checkbox"/>	Can't say <input type="checkbox"/>	Does not apply <input type="checkbox"/>
1.4	The authors clearly state if or how they limited their review by publication type. ^{iv}	Yes <input type="checkbox"/>	No <input type="checkbox"/>		
1.5	The included and excluded studies are listed. ^v	Yes <input type="checkbox"/>	No <input type="checkbox"/>		
1.6	The characteristics of the included studies are provided. ^{vi}	Yes <input type="checkbox"/>	No <input type="checkbox"/>		
1.7	The scientific quality of the included studies is assessed and documented. ^{vii}	Yes <input type="checkbox"/>	No <input type="checkbox"/>		

1.8	The scientific quality of the included studies was assessed appropriately. ^{viii}	Yes <input type="checkbox"/>	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	
1.9	Appropriate methods are used to combine the individual study findings. ^{ix}	Yes <input type="checkbox"/>	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	
1.10	The likelihood of publication bias is assessed. ^x	Yes <input type="checkbox"/>	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	
1.11	Conflicts of interest are declared. ^{xi}	Yes <input type="checkbox"/>	No <input type="checkbox"/>
SECTION 2: OVERALL ASSESSMENT OF THE STUDY			
2.1	What is your overall assessment of the methodological quality of this review? ^{xii}	High quality (++) <input type="checkbox"/> Acceptable (+) <input checked="" type="checkbox"/> (at least) Unacceptable – reject 0 <input type="checkbox"/>	
2.2	Are the results of this study directly applicable to the patient group targeted by this guideline?	Yes <input type="checkbox"/>	No <input type="checkbox"/>
2.3	Notes: ^{xiii} Acc. to convention Cochrane rev. are not to be methodologically reviewed in detail;		

ⁱ The research question and inclusion criteria should be established before the review is conducted. To score a 'yes' for this factor there must be reference to a protocol, ethics approval, or pre-determined/a priori published research objectives.

ⁱⁱ At least two people should select papers and extract data. There should be a consensus procedure to resolve any differences.

ⁱⁱⁱ At least two major electronic databases should be searched. The report must include years and databases searched (e.g., Central, EMBASE, MEDLINE, OpenGrey, 1999-2009). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found. In rare cases this may not apply where authors have carried out a meta analysis focusing on a specified range of major trials in their field.

^{iv} The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status or language. If searching sources that contains both grey and non-grey literature, must specify that they were searching for both.

^v A list of included and excluded studies should be provided. Limiting the excluded studies to references is acceptable.

^{vi} In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analyzed e.g., age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported. (**Note** that a format other than a table is acceptable, as long as the information noted here is provided).

^{vii} This relates to the scientific quality of the studies included in the review. I can include use of a quality scoring tool or checklist, e.g., Jadad scale, risk of bias, sensitivity analysis, or a description of quality items, with some kind of result for EACH study (“low” or “high” is fine, as long as it is clear which studies scored “low” and which scored “high”; a summary score/range for all studies is not acceptable).

^{viii} The methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations. (**Note:** The review might say something like “the results should be interpreted with caution due to poor quality of included studies.” Cannot score “yes” for this question if scored “no” for question 7).

^{ix} For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e., Chi-squared test for homogeneity, I^2). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e., is it sensible to combine?). Indicate “yes” where the authors mention or describe heterogeneity or variability between results and discuss the consequences (eg where authors declare they cannot pool results because of heterogeneity).

^x An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test, Hedges-Olken). (**Note:** Score “Can’t say” if there were fewer than 10 included studies).

^{xi} Potential sources of support should be clearly acknowledged in both the systematic review and the included studies.

^{xii} Rate the overall methodological quality of the study, using the following as a guide: **High quality** (++) : Majority of criteria met. Little or no risk of bias. Results unlikely to be changed by further research. **Acceptable** (+) : Most criteria met. Some flaws in the study with an associated risk of bias, Conclusions may change in the light of further studies. **Low quality** (0) : Either most criteria not met, or significant flaws relating to key aspects of study design. Conclusions likely to change in the light of further studies.

^{xiii} Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above. This is a very important part of the evaluation and will feature in the evidence table. PLEASE FILL IN.



Methodology Checklist 1: Systematic Reviews and Meta-analyses

SIGN

SIGN gratefully acknowledges the permission received from the authors of the AMSTAR tool to base this checklist on their work: *Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C., et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Medical Research Methodology 2007, 7:10 doi:10.1186/1471-2288-7-10. Available from <http://www.biomedcentral.com/1471-2288/7/10> [cited 10 Sep 2012]*

Study identification (Include author, title, year of publication, journal title, pages)

< KuriyamaA_2015 > Intens Care Med 2015;41:402ff

Guideline topic: AG V

Key Question No: 5.6. (11.04.16)

Before completing this checklist, consider:

1. Is the paper a systematic review or meta-analysis? IF NO reject. IF **YES** continue.
2. Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO reject. IF YES complete the checklist.

Checklist completed by: AF, ZKSL

Section 1: Internal validity

In a well conducted systematic review:

Does this study do it?

1.1	The study addresses a clearly defined research question. ⁱ	Yes X	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	
1.2	At least two people should select studies and extract data. ⁱⁱ	Yes X	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	
1.3	A comprehensive literature search is carried out. ⁱⁱⁱ	Yes X	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	Does not apply <input type="checkbox"/>
1.4	The authors clearly state if or how they limited their review by publication type. ^{iv} None (incl. inform. Abs)	Yes X	No <input type="checkbox"/>
1.5	The included and excluded studies are listed. ^v K=16 RCTs	Yes <input type="checkbox"/>	No X incl. only
1.6	The characteristics of the included studies are provided. ^{vi}	Yes X	No <input type="checkbox"/>
1.7	The scientific quality of the included studies is assessed and documented. ^{vii}	Yes X	No <input type="checkbox"/>

1.8	The scientific quality of the included studies was assessed appropriately. ^{viii}	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.9	Appropriate methods are used to combine the individual study findings. ^{ix}	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.10	The likelihood of publication bias is assessed. ^x	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.11	Conflicts of interest are declared. ^{xi}	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/>
SECTION 2: OVERALL ASSESSMENT OF THE STUDY		
2.1	What is your overall assessment of the methodological quality of this review? ^{xii}	High quality (++) <input checked="" type="checkbox"/> Acceptable (+) <input type="checkbox"/> Unacceptable – reject <input type="checkbox"/>
2.2	Are the results of this study directly applicable to the patient group targeted by this guideline?	Yes <input type="checkbox"/> No <input type="checkbox"/>
2.3	Notes: ^{xiii} CAVE: Superiority of CSS (not Non-Inferiority → s. Abs = Äquivalence) is question of interest –incorrect in Abs; Herterogeneity definition of trial is weaker than in Jongerden (2007)	

ⁱ The research question and inclusion criteria should be established before the review is conducted. To score a 'yes' for this factor there must be reference to a protocol, ethics approval, or pre-determined/a priori published research objectives.

ⁱⁱ At least two people should select papers and extract data. There should be a consensus procedure to resolve any differences.

ⁱⁱⁱ At least two major electronic databases should be searched. The report must include years and databases searched (e.g., Central, EMBASE, MEDLINE, OpenGrey, 1999-2009). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found. In rare cases this may not apply where authors have carried out a meta analysis focusing on a specified range of major trials in their field.

^{iv} The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status or language. If searching sources that contains both grey and non-grey literature, must specify that they were searching for both.

^v A list of included and excluded studies should be provided. Limiting the excluded studies to references is acceptable.

^{vi} In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analyzed e.g., age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported. (**Note** that a format other than a table is acceptable, as long as the information noted here is provided).

^{vii} This relates to the scientific quality of the studies included in the review. I can include use of a quality scoring tool or checklist, e.g., Jadad scale, risk of bias, sensitivity analysis, or a description of quality items, with some kind of result for EACH study (“low” or “high” is fine, as long as it is clear which studies scored “low” and which scored “high”; a summary score/range for all studies is not acceptable).

^{viii} The methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations. (**Note**: The review might say something like “the results should be interpreted with caution due to poor quality of included studies.” Cannot score “yes” for this question if scored “no” for question 7).

^{ix} For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e., Chi-squared test for homogeneity, I^2). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e., is it sensible to combine?). Indicate “yes” where the authors mention or describe heterogeneity or variability between results and discuss the consequences (eg where authors declare they cannot pool results because of heterogeneity).

^x An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test, Hedges-Olken). (**Note**: Score “Can’t say” if there were fewer than 10 included studies).

^{xi} Potential sources of support should be clearly acknowledged in both the systematic review and the included studies.

^{xii} Rate the overall methodological quality of the study, using the following as a guide: **High quality** (++) : Majority of criteria met. Little or no risk of bias. Results unlikely to be changed by further research. **Acceptable** (+) : Most criteria met. Some flaws in the study with an associated risk of bias, Conclusions may change in the light of further studies. **Low quality** (0) : Either most criteria not met, or significant flaws relating to key aspects of study design. Conclusions likely to change in the light of further studies.

^{xiii} Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above. This is a very important part of the evaluation and will feature in the evidence table. PLEASE FILL IN.



Methodology Checklist 1: Systematic Reviews and Meta-analyses

SIGN

SIGN gratefully acknowledges the permission received from the authors of the AMSTAR tool to base this checklist on their work: *Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C, et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Medical Research Methodology 2007, 7:10 doi:10.1186/1471-2288-7-10. Available from <http://www.biomedcentral.com/1471-2288/7/10> [cited 10 Sep 2012]*

Study identification (Include author, title, year of publication, journal title, pages)

< MaitraS_2015 > Anesthesiol 2015;122:841ff

Guideline topic: AGIII ventilation strategies

Key Question No: 3.5

Before completing this checklist, consider:

1. Is the paper a systematic review or meta-analysis? IF NO reject. IF **YES** continue.
2. Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO reject. IF **YES** complete the checklist.

Checklist completed by: **AF, ZKLS**

Section 1: Internal validity

In a well conducted systematic review:

Does this study do it?

1.1	The study addresses a clearly defined research question. ⁱ	Yes X	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	
1.2	At least two people should select studies and extract data. ⁱⁱ	Yes X	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	
1.3	A comprehensive literature search is carried out. ⁱⁱⁱ	Yes X	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	Does not apply <input type="checkbox"/>
1.4	The authors clearly state if or how they limited their review by publication type. ^{iv}	Yes X	No <input type="checkbox"/>
1.5	The included and excluded studies are listed. ^v k=7 (n=1759)	Yes X	No <input type="checkbox"/>
1.6	The characteristics of the included studies are provided. ^{vi}	Yes <input type="checkbox"/>	No <input type="checkbox"/>
1.7	The scientific quality of the included studies is assessed and documented. ^{vii}	Yes X	No <input type="checkbox"/>

1.8	The scientific quality of the included studies was assessed appropriately. ^{viii}	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.9	Appropriate methods are used to combine the individual study findings. ^{ix}	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.10	The likelihood of publication bias is assessed. ^x	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.11	Conflicts of interest are declared. ^{xi}	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/>
SECTION 2: OVERALL ASSESSMENT OF THE STUDY		
2.1	What is your overall assessment of the methodological quality of this review? ^{xii}	High quality (++) <input checked="" type="checkbox"/> Acceptable (+) <input type="checkbox"/> Unacceptable – reject <input type="checkbox"/>
2.2	Are the results of this study directly applicable to the patient group targeted by this guideline?	Yes <input type="checkbox"/> No <input type="checkbox"/>
2.3	Notes: ^{xiii} Respiratory adjunct therapies allowed in RCTs; RCTs with children/ neonates excluded	

ⁱ The research question and inclusion criteria should be established before the review is conducted. To score a 'yes' for this factor there must be reference to a protocol, ethics approval, or pre-determined/a priori published research objectives.

ⁱⁱ At least two people should select papers and extract data. There should be a consensus procedure to resolve any differences.

ⁱⁱⁱ At least two major electronic databases should be searched. The report must include years and databases searched (e.g., Central, EMBASE, MEDLINE, OpenGrey, 1999-2009). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found. In rare cases this may not apply where authors have carried out a meta analysis focusing on a specified range of major trials in their field.

^{iv} The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status or language. If searching sources that contains both grey and non-grey literature, must specify that they were searching for both.

^v A list of included and excluded studies should be provided. Limiting the excluded studies to references is acceptable.

^{vi} In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analyzed e.g., age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported. (**Note** that a format other than a table is acceptable, as long as the information noted here is provided).

^{vii} This relates to the scientific quality of the studies included in the review. I can include use of a quality scoring tool or checklist, e.g., Jadad scale, risk of bias, sensitivity analysis, or a description of quality items, with some kind of result for EACH study (“low” or “high” is fine, as long as it is clear which studies scored “low” and which scored “high”; a summary score/range for all studies is not acceptable).

^{viii} The methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations. (**Note**: The review might say something like “the results should be interpreted with caution due to poor quality of included studies.” Cannot score “yes” for this question if scored “no” for question 7).

^{ix} For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e., Chi-squared test for homogeneity, *I*²). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e., is it sensible to combine?). Indicate “yes” where the authors mention or describe heterogeneity or variability between results and discuss the consequences (eg where authors declare they cannot pool results because of heterogeneity).

^x An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test, Hedges-Olken). (**Note**: Score “Can’t say” if there were fewer than 10 included studies).

^{xi} Potential sources of support should be clearly acknowledged in both the systematic review and the included studies.

^{xii} Rate the overall methodological quality of the study, using the following as a guide: **High quality** (++) : Majority of criteria met. Little or no risk of bias. Results unlikely to be changed by further research. **Acceptable** (+) : Most criteria met. Some flaws in the study with an associated risk of bias, Conclusions may change in the light of further studies. **Low quality** (0) : Either most criteria not met, or significant flaws relating to key aspects of study design. Conclusions likely to change in the light of further studies.

^{xiii} Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above. This is a very important part of the evaluation and will feature in the evidence table. PLEASE FILL IN.



Methodology Checklist 1: Systematic Reviews and Meta-analyses

SIGN

SIGN gratefully acknowledges the permission received from the authors of the AMSTAR tool to base this checklist on their work: *Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C, et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Medical Research Methodology 2007, 7:10 doi:10.1186/1471-2288-7-10. Available from <http://www.biomedcentral.com/1471-2288/7/10> [cited 10 Sep 2012]*

Study identification (Include author, title, year of publication, journal title, pages)

< MengH_2012 >

J Cardiothor Vasc Anaest 2012;26(5):849ff

Guideline topic: AG V

Key Question No: 5.8.3 (25.05.16ff)

Before completing this checklist, consider:

1. Is the paper a systematic review or meta-analysis? IF NO reject. IF **YES** continue.
2. Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO reject. IF YES complete the checklist.

Checklist completed by: AF, ZKSL

Section 1: Internal validity

In a well conducted systematic review:

Does this study do it?

1.1	The study addresses a clearly defined research question. ⁱ	Yes X	No <input type="checkbox"/>	Can't say <input type="checkbox"/>
1.2	At least two people should select studies and extract data. ⁱⁱ	Yes X	No <input type="checkbox"/>	Can't say <input type="checkbox"/>
1.3	A comprehensive literature search is carried out. ⁱⁱⁱ	Yes X	No <input type="checkbox"/>	Can't say <input type="checkbox"/> Does not apply <input type="checkbox"/>
1.4	The authors clearly state if or how they limited their review by publication type. ^{iv}	Yes <input type="checkbox"/>	No X	
1.5	The included and excluded studies are listed. ^v	Yes <input type="checkbox"/>	No X	included only
1.6	The characteristics of the included studies are provided. ^{vi}	Yes X	No <input type="checkbox"/>	
1.7	The scientific quality of the included studies is assessed and documented. ^{vii}	Yes X	No <input type="checkbox"/>	

1.8	The scientific quality of the included studies was assessed appropriately. ^{viii}	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.9	Appropriate methods are used to combine the individual study findings. ^{ix} FEM	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.10	The likelihood of publication bias is assessed. ^x	Yes <input type="checkbox"/> No <input type="checkbox"/> Can't say <input checked="" type="checkbox"/>
1.11	Conflicts of interest are declared. ^{xi}	Yes <input type="checkbox"/> No <input checked="" type="checkbox"/>
SECTION 2: OVERALL ASSESSMENT OF THE STUDY		
2.1	What is your overall assessment of the methodological quality of this review? ^{xii}	High quality (++) <input type="checkbox"/> Acceptable (+) <input checked="" type="checkbox"/> Unacceptable – reject <input type="checkbox"/>
2.2	Are the results of this study directly applicable to the patient group targeted by this guideline?	Yes <input type="checkbox"/> No <input type="checkbox"/>
2.3	Notes: ^{xiii} No hints on benefits in mortality	

ⁱ The research question and inclusion criteria should be established before the review is conducted. To score a 'yes' for this factor there must be reference to a protocol, ethics approval, or pre-determined/a priori published research objectives.

ⁱⁱ At least two people should select papers and extract data. There should be a consensus procedure to resolve any differences.

ⁱⁱⁱ At least two major electronic databases should be searched. The report must include years and databases searched (e.g., Central, EMBASE, MEDLINE, OpenGrey, 1999-2009). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found. In rare cases this may not apply where authors have carried out a meta analysis focusing on a specified range of major trials in their field.

^{iv} The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status or language. If searching sources that contains both grey and non-grey literature, must specify that they were searching for both.

^v A list of included and excluded studies should be provided. Limiting the excluded studies to references is acceptable.

^{vi} In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analyzed e.g., age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported. (**Note** that a format other than a table is acceptable, as long as the information noted here is provided).

^{vii} This relates to the scientific quality of the studies included in the review. I can include use of a quality scoring tool or checklist, e.g., Jadad scale, risk of bias, sensitivity analysis, or a description of quality items, with some kind of result for EACH study ("low" or "high" is fine, as long as it is clear which studies scored "low" and which scored "high"; a summary score/range for all studies is not acceptable).

^{viii} The methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations. (**Note:** The review might say something like "the results should be interpreted with caution due to poor quality of included studies." Cannot score "yes" for this question if scored "no" for question 7).

^{ix} For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e., Chi-squared test for homogeneity, /2). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e., is it sensible to combine?). Indicate "yes" where the authors mention or describe heterogeneity or variability between results and discuss the consequences (eg where authors declare they cannot pool results because of heterogeneity).

^x An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test, Hedges-Olken). (**Note:** Score "Can't say" if there were fewer than 10 included studies).

^{xi} Potential sources of support should be clearly acknowledged in both the systematic review and the included studies.

^{xii} Rate the overall methodological quality of the study, using the following as a guide: **High quality** (++) : Majority of criteria met. Little or no risk of bias. Results unlikely to be changed by further research. **Acceptable** (+) : Most criteria met. Some flaws in the study with an associated risk of bias, Conclusions may change in the light of further studies. **Low quality** (0) : Either most criteria not met, or significant flaws relating to key aspects of study design. Conclusions likely to change in the light of further studies.

^{xiii} Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above. This is a very important part of the evaluation and will feature in the evidence table. PLEASE FILL IN.



Methodology Checklist 2: Controlled Trials

Study identification (Include author, title, year of publication, journal title, pages)

Peek et al., "Efficacy and economic assessment...", 2009, Lancet

Guideline topic: 6, ECMO vs. conventional

Key Question No:

Reviewer: CP, IMISE

Before completing this checklist, consider:

1. Is the paper a **randomised controlled trial** or a **controlled clinical trial**? If in doubt, check the study design algorithm available from SIGN and make sure you have the correct checklist. If it is a **controlled clinical trial** questions 1.2, 1.3, and 1.4 are not relevant, and the study cannot be rated higher than 1+
2. Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO REJECT (give reason below). IF YES complete the checklist.

Reason for rejection: 1. Paper not relevant to key question 2. Other reason (please specify):

SECTION 1: INTERNAL VALIDITY

<i>In a well conducted RCT study...</i>		<i>Does this study do it?</i>	
1.1	The study addresses an appropriate and clearly focused question. ⁱ	Yes X	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	
1.2	The assignment of subjects to treatment groups is randomised. ⁱⁱ	Yes X	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	
1.3	An adequate concealment method is used. ⁱⁱⁱ	Yes X	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	
1.4	Subjects and investigators are kept 'blind' about treatment allocation. ^{iv} Nicht möglich, allerdings Bewertung nach 6 Monaten verblindet.	Yes <input type="checkbox"/>	No X
		Can't say <input type="checkbox"/>	
1.5	The treatment and control groups are similar at the start of the trial. ^v	Yes X	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	
1.6	The only difference between groups is the treatment under investigation. ^{vi} Behandlung unterschiedlich, s. Tabelle 2!	Yes <input type="checkbox"/>	No X
		Can't say <input type="checkbox"/>	
1.7	All relevant outcomes are measured in a standard, valid and reliable way. ^{vii}	Yes X	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	
1.8	What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed? ^{viii}	Bei 0 bzw. 3 pro Gruppe (je 90 Patienten) konnte primärer Endpunkt nicht erhoben werden	
1.9	All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention to treat analysis). ^{ix}	Yes X	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	Does not apply <input type="checkbox"/>

1.10	Where the study is carried out at more than one site, results are comparable for all sites. ^x Patienten wurden für ECMO-Behandlung in ein bestimmtes Zentrum transferiert.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	Does not apply X
SECTION 2: OVERALL ASSESSMENT OF THE STUDY			
2.1	How well was the study done to minimise bias? <i>Code as follows:^{xi}</i>	High quality (++) <input type="checkbox"/>	Acceptable (+) X
		Unacceptable – reject 0 <input type="checkbox"/>	
2.2	Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, are you certain that the overall effect is due to the study intervention?	Kann ich nicht beurteilen, da unterschiedliche Behandlung (s. Tabelle 2). Evtl. auch Bias, da nur ein Zentrum die ECMO-Behandlung durchführt.	
2.3	Are the results of this study directly applicable to the patient group targeted by this guideline?		
2.4	Notes. Summarise the authors' conclusions. Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above.		
	ECMO führt in der Studie zu erhöhter Überlebensrate ohne Behinderung nach 6 Monaten. Allerdings limitiert durch oben erwähnte Probleme.		

ⁱ Unless a clear and well defined question is specified, it will be difficult to assess how well the study has met its objectives or how relevant it is to the question you are trying to answer on the basis of its conclusions.

ⁱⁱ Random allocation of patients to receive one or other of the treatments under investigation, or to receive either treatment or placebo, is fundamental to this type of study.

ⁱⁱⁱ Allocation concealment refers to the process used to ensure that researchers are unaware which group patients are being allocated to at the time they enter the study. Research has shown that where allocation concealment is inadequate, investigators can overestimate the effect of interventions by up to 40%.

^{iv} Blinding refers to the process whereby people are kept unaware of which treatment an individual patient has been receiving when they are assessing the outcome for that patient. It can be carried out up to three levels. Single blinding is where patients are unaware of which treatment they are receiving. In double blind studies neither the clinician nor the patient knows which treatment is being given. In very rare cases studies may be triple blinded, where neither patients, clinicians, nor those conducting the analysis are aware of which patients received which treatment. The higher the level of blinding, the lower the risk of bias in the study.

^v Patients selected for inclusion in a trial must be as similar as possible. The study should report any significant differences in the composition of the study groups in relation to gender mix, age, stage of disease (if appropriate), social background, ethnic origin, or co-morbid conditions. These factors may be covered by inclusion and exclusion criteria, rather than being reported directly. Failure to address this question, or the use of inappropriate groups, should lead to the study being downgraded.

^{vi} If some patients received additional treatment, even if of a minor nature or consisting of advice and counselling rather than a physical intervention, this treatment is a potential confounding factor that may invalidate the results. **If groups were not treated equally, the study should be rejected unless no other evidence is available.** If the study is used as evidence it should be treated with caution.

File name : Checklist 2 – Controlled Trials	Version 2.0	28/05/2012
Produced by: Carolyn Sleith	Page 2 of 3	Review date: None

vii The primary outcome measures used should be clearly stated in the study. **If the outcome measures are not stated, or the study bases its main conclusions on secondary outcomes, the study should be rejected.** Where outcome measures require any degree of subjectivity, some evidence should be provided that the measures used are reliable and have been validated prior to their use in the study.

viii The number of patients that drop out of a study should give concern if the number is very high. Conventionally, a 20% drop out rate is regarded as acceptable, but this may vary. Some regard should be paid to why patients dropped out, as well as how many. It should be noted that the drop out rate may be expected to be higher in studies conducted over a long period of time. A higher drop out rate will normally lead to downgrading, rather than rejection of a study.

ix In practice, it is rarely the case that all patients allocated to the intervention group receive the intervention throughout the trial, or that all those in the comparison group do not. Patients may refuse treatment, or contra-indications arise that lead them to be switched to the other group. If the comparability of groups through randomisation is to be maintained, however, patient outcomes must be analysed according to the group to which they were originally allocated irrespective of the treatment they actually received. (This is known as intention to treat analysis.) If it is clear that analysis was not on an intention to treat basis, the study may be rejected. If there is little other evidence available, the study may be included but should be evaluated as if it were a non-randomised cohort study.

x In multi-site studies, confidence in the results should be increased if it can be shown that similar results were obtained at the different participating centres.

xi Rate the overall methodological quality of the study, using the following as a guide: **High quality** (++) : Majority of criteria met. Little or no risk of bias. Results unlikely to be changed by further research. **Acceptable** (+) : Most criteria met. Some flaws in the study with an associated risk of bias, Conclusions may change in the light of further studies. **Low quality** (0) : Either most criteria not met, or significant flaws relating to key aspects of study design. Conclusions likely to change in the light of further studies.

File name : Checklist 2 – Controlled Trials	Version 2.0	28/05/2012
Produced by: Carolyn Sleith	Page 3 of 3	Review date: None



Methodology Checklist 1: Systematic Reviews and Meta-analyses

SIGN

SIGN gratefully acknowledges the permission received from the authors of the AMSTAR tool to base this checklist on their work: *Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C, et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Medical Research Methodology 2007, 7:10 doi:10.1186/1471-2288-7-10. Available from <http://www.biomedcentral.com/1471-2288/7/10> [cited 10 Sep 2012]*

Study identification (Include author, title, year of publication, journal title, pages)

< PetrucciN_2013>

Cochrane DB syst rev 2013 (2)

Guideline topic: **AG IV**

Key Question No: **4.3 & 8.1.1**

Before completing this checklist, consider:

1. Is the paper a systematic review or meta-analysis? IF NO reject. IF **YES** continue.
2. Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO reject. IF **YES** complete the checklist.

Checklist completed by: **AF, ZKSL**

Section 1: Internal validity

In a well conducted systematic review:

Does this study do it?

1.1	The study addresses a clearly defined research question. ⁱ	Yes X	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	
1.2	At least two people should select studies and extract data. ⁱⁱ	Yes X	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	
1.3	A comprehensive literature search is carried out. ⁱⁱⁱ	Yes X	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	Does not apply <input type="checkbox"/>
1.4	The authors clearly state if or how they limited their review by publication type. ^{iv}	Yes X	No <input type="checkbox"/>
1.5	The included and excluded studies are listed. ^v	Yes X	No <input type="checkbox"/>
1.6	The characteristics of the included studies are provided. ^{vi}	Yes X	No <input type="checkbox"/>
1.7	The scientific quality of the included studies is assessed and documented. ^{vii}	Yes X	No <input type="checkbox"/>

1.8	The scientific quality of the included studies was assessed appropriately. ^{viii}	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.9	Appropriate methods are used to combine the individual study findings. ^{ix}	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.10	The likelihood of publication bias is assessed. ^x	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.11	Conflicts of interest are declared. ^{xi}	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/>
SECTION 2: OVERALL ASSESSMENT OF THE STUDY		
2.1	What is your overall assessment of the methodological quality of this review? ^{xii}	High quality (++) <input checked="" type="checkbox"/> Acceptable (+) <input type="checkbox"/> Unacceptable – reject <input type="checkbox"/>
2.2	Are the results of this study directly applicable to the patient group targeted by this guideline?	Yes <input type="checkbox"/> No <input type="checkbox"/>
2.3	Notes: ^{xiii} Most recent update of Cochrane SR/MA from 2003 & 2007 as well as publication from 2004 (the former ones not assessed in every methodological detail)	

ⁱ The research question and inclusion criteria should be established before the review is conducted. To score a 'yes' for this factor there must be reference to a protocol, ethics approval, or pre-determined/a priori published research objectives.

ⁱⁱ At least two people should select papers and extract data. There should be a consensus procedure to resolve any differences.

ⁱⁱⁱ At least two major electronic databases should be searched. The report must include years and databases searched (e.g., Central, EMBASE, MEDLINE, OpenGrey, 1999-2009). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found. In rare cases this may not apply where authors have carried out a meta analysis focusing on a specified range of major trials in their field.

^{iv} The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status or language. If searching sources that contains both grey and non-grey literature, must specify that they were searching for both.

^v A list of included and excluded studies should be provided. Limiting the excluded studies to references is acceptable.

^{vi} In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analyzed e.g., age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported. (**Note** that a format other than a table is acceptable, as long as the information noted here is provided).

^{vii} This relates to the scientific quality of the studies included in the review. I can include use of a quality scoring tool or checklist, e.g., Jadad scale, risk of bias, sensitivity analysis, or a description of quality items, with some kind of result for EACH study ("low" or "high" is fine, as long as it is clear which studies scored "low" and which scored "high"; a summary score/range for all studies is not acceptable).

^{viii} The methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations. (**Note:** The review might say something like "the results should be interpreted with caution due to poor quality of included studies." Cannot score "yes" for this question if scored "no" for question 7).

^{ix} For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e., Chi-squared test for homogeneity, /2). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e., is it sensible to combine?). Indicate "yes" where the authors mention or describe heterogeneity or variability between results and discuss the consequences (eg where authors declare they cannot pool results because of heterogeneity).

^x An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test, Hedges-Olken). (**Note:** Score "Can't say" if there were fewer than 10 included studies).

^{xi} Potential sources of support should be clearly acknowledged in both the systematic review and the included studies.

^{xii} Rate the overall methodological quality of the study, using the following as a guide: **High quality** (++) : Majority of criteria met. Little or no risk of bias. Results unlikely to be changed by further research. **Acceptable** (+) : Most criteria met. Some flaws in the study with an associated risk of bias, Conclusions may change in the light of further studies. **Low quality** (0) : Either most criteria not met, or significant flaws relating to key aspects of study design. Conclusions likely to change in the light of further studies.

^{xiii} Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above. This is a very important part of the evaluation and will feature in the evidence table. PLEASE FILL IN.



Methodology Checklist 1: Systematic Reviews and Meta-analyses

SIGN

SIGN gratefully acknowledges the permission received from the authors of the AMSTAR tool to base this checklist on their work: *Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C, et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Medical Research Methodology 2007, 7:10 doi:10.1186/1471-2288-7-10. Available from <http://www.biomedcentral.com/1471-2288/7/10> [cited 10 Sep 2012]*

Study identification (Include author, title, year of publication, journal title, pages)

< Putensen_2014 > Crit Care 2014;18:544ff

Guideline topic: AG V

Key Question No: 5.7. (14.04.16)

Before completing this checklist, consider:

1. Is the paper a systematic review or meta-analysis? IF NO reject. IF YES continue.
2. Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO reject. IF YES complete the checklist.

Checklist completed by: AF, ZKSL

Section 1: Internal validity

In a well conducted systematic review:

Does this study do it?

1.1	The study addresses a clearly defined research question. ⁱ	Yes <input checked="" type="checkbox"/>	No <input type="checkbox"/>	Can't say <input type="checkbox"/>
1.2	At least two people should select studies and extract data. ⁱⁱ	Yes <input checked="" type="checkbox"/>	No <input type="checkbox"/>	Can't say <input type="checkbox"/>
1.3	A comprehensive literature search is carried out. ⁱⁱⁱ	Yes <input checked="" type="checkbox"/>	No <input type="checkbox"/>	Can't say <input type="checkbox"/> Does not apply <input type="checkbox"/>
1.4	The authors clearly state if or how they limited their review by publication type. ^{iv}	Yes <input checked="" type="checkbox"/>	No <input type="checkbox"/>	
1.5	The included and excluded studies are listed. ^v K=22; 14x PT vs ST & 8x various (6) PT techniques	Yes <input checked="" type="checkbox"/>	No <input type="checkbox"/>	
1.6	The characteristics of the included studies are provided. ^{vi}	Yes <input checked="" type="checkbox"/>	No <input type="checkbox"/>	
1.7	The scientific quality of the included studies is assessed and documented. ^{vii}	Yes <input checked="" type="checkbox"/>	No <input type="checkbox"/>	

1.8	The scientific quality of the included studies was assessed appropriately. ^{viii}	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.9	Appropriate methods are used to combine the individual study findings. ^{ix} Pooled PT vs ST/ diff. PT techniques against each other compared	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.10	The likelihood of publication bias is assessed. ^x Macaskill's test (weighted lin regress.)	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.11	Conflicts of interest are declared. ^{xi}	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/>
SECTION 2: OVERALL ASSESSMENT OF THE STUDY		
2.1	What is your overall assessment of the methodological quality of this review? ^{xii}	High quality (++) <input checked="" type="checkbox"/> Acceptable (+) <input type="checkbox"/> Unacceptable – reject <input type="checkbox"/>
2.2	Are the results of this study directly applicable to the patient group targeted by this guideline?	Yes <input type="checkbox"/> No <input type="checkbox"/>
2.3	Notes: ^{xiii}	

ⁱ The research question and inclusion criteria should be established before the review is conducted. To score a 'yes' for this factor there must be reference to a protocol, ethics approval, or pre-determined/a priori published research objectives.

ⁱⁱ At least two people should select papers and extract data. There should be a consensus procedure to resolve any differences.

ⁱⁱⁱ At least two major electronic databases should be searched. The report must include years and databases searched (e.g., Central, EMBASE, MEDLINE, OpenGrey, 1999-2009). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found. In rare cases this may not apply where authors have carried out a meta analysis focusing on a specified range of major trials in their field.

^{iv} The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status or language. If searching sources that contains both grey and non-grey literature, must specify that they were searching for both.

^v A list of included and excluded studies should be provided. Limiting the excluded studies to references is acceptable.

^{vi} In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analyzed e.g., age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported. (**Note** that a format other than a table is acceptable, as long as the information noted here is provided).

^{vii} This relates to the scientific quality of the studies included in the review. I can include use of a quality scoring tool or checklist, e.g., Jadad scale, risk of bias, sensitivity analysis, or a description of quality items, with some kind of result for EACH study (“low” or “high” is fine, as long as it is clear which studies scored “low” and which scored “high”; a summary score/range for all studies is not acceptable).

^{viii} The methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations. (**Note**: The review might say something like “the results should be interpreted with caution due to poor quality of included studies.” Cannot score “yes” for this question if scored “no” for question 7).

^{ix} For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e., Chi-squared test for homogeneity, *I*²). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e., is it sensible to combine?). Indicate “yes” where the authors mention or describe heterogeneity or variability between results and discuss the consequences (eg where authors declare they cannot pool results because of heterogeneity).

^x An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test, Hedges-Olken). (**Note**: Score “Can’t say” if there were fewer than 10 included studies).

^{xi} Potential sources of support should be clearly acknowledged in both the systematic review and the included studies.

^{xii} Rate the overall methodological quality of the study, using the following as a guide: **High quality** (++) : Majority of criteria met. Little or no risk of bias. Results unlikely to be changed by further research. **Acceptable** (+) : Most criteria met. Some flaws in the study with an associated risk of bias, Conclusions may change in the light of further studies. **Low quality** (0) : Either most criteria not met, or significant flaws relating to key aspects of study design. Conclusions likely to change in the light of further studies.

^{xiii} Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above. This is a very important part of the evaluation and will feature in the evidence table. PLEASE FILL IN.



Methodology Checklist 1: Systematic Reviews and Meta-analyses

SIGN

SIGN gratefully acknowledges the permission received from the authors of the AMSTAR tool to base this checklist on their work: *Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C., et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Medical Research Methodology 2007, 7:10 doi:10.1186/1471-2288-7-10. Available from <http://www.biomedcentral.com/1471-2288/7/10> [cited 10 Sep 2012]*

Study identification (Include author, title, year of publication, journal title, pages)

< PutensenC_2009 > Ann Intern Med 2009;151:566ff

Guideline topic: AG VI

Key Question No: 6.4.1 (28.10.15.ff)
→ gehört m.E. eher in Kap. IV

Before completing this checklist, consider:

1. Is the paper a systematic review or meta-analysis? IF NO reject. IF YES continue.
2. Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO reject. IF YES complete the checklist.

Checklist completed by: AF, ZKSL

Section 1: Internal validity

<i>In a well conducted systematic review:</i>		<i>Does this study do it?</i>	
1.1	The study addresses a clearly defined research question. ⁱ	Yes <input checked="" type="checkbox"/>	No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.2	At least two people should select studies and extract data. ⁱⁱ	Yes <input checked="" type="checkbox"/>	No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.3	A comprehensive literature search is carried out. ⁱⁱⁱ	Yes <input checked="" type="checkbox"/>	No <input type="checkbox"/> Does not apply <input type="checkbox"/>
1.4	The authors clearly state if or how they limited their review by publication type. ^{iv}	Yes <input type="checkbox"/>	No <input checked="" type="checkbox"/>
1.5	The included and excluded studies are listed. ^v K _{total} =9; k _{Vt} =4 (n=1149); ; k _{PEEP} =3 (n=2299) ; k _X =2 (n=148)	Yes <input type="checkbox"/>	No <input checked="" type="checkbox"/> (incl.only)
1.6	The characteristics of the included studies are provided. ^{vi}	Yes <input checked="" type="checkbox"/>	No <input type="checkbox"/>
1.7	The scientific quality of the included studies is assessed and documented. ^{vii}	Yes <input checked="" type="checkbox"/>	No <input type="checkbox"/>

1.8	The scientific quality of the included studies was assessed appropriately. ^{viii}	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.9	Appropriate methods are used to combine the individual study findings. ^{ix}	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.10	The likelihood of publication bias is assessed. ^x	Yes <input type="checkbox"/> No <input type="checkbox"/> Can't say <input checked="" type="checkbox"/>
1.11	Conflicts of interest are declared. ^{xi}	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/>
SECTION 2: OVERALL ASSESSMENT OF THE STUDY		
2.1	What is your overall assessment of the methodological quality of this review? ^{xii}	High quality (++) <input type="checkbox"/> Acceptable (+) <input checked="" type="checkbox"/> Unacceptable – reject <input type="checkbox"/>
2.2	Are the results of this study directly applicable to the patient group targeted by this guideline?	Yes <input type="checkbox"/> No <input type="checkbox"/>
2.3	Notes: ^{xiii} Ref. belongs rather to Chap. IV than VI	

ⁱ The research question and inclusion criteria should be established before the review is conducted. To score a 'yes' for this factor there must be reference to a protocol, ethics approval, or pre-determined/a priori published research objectives.

ⁱⁱ At least two people should select papers and extract data. There should be a consensus procedure to resolve any differences.

ⁱⁱⁱ At least two major electronic databases should be searched. The report must include years and databases searched (e.g., Central, EMBASE, MEDLINE, OpenGrey, 1999-2009). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found. In rare cases this may not apply where authors have carried out a meta analysis focusing on a specified range of major trials in their field.

^{iv} The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status or language. If searching sources that contains both grey and non-grey literature, must specify that they were searching for both.

^v A list of included and excluded studies should be provided. Limiting the excluded studies to references is acceptable.

^{vi} In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analyzed e.g., age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported. (**Note** that a format other than a table is acceptable, as long as the information noted here is provided).

^{vii} This relates to the scientific quality of the studies included in the review. I can include use of a quality scoring tool or checklist, e.g., Jadad scale, risk of bias, sensitivity analysis, or a description of quality items, with some kind of result for EACH study (“low” or “high” is fine, as long as it is clear which studies scored “low” and which scored “high”; a summary score/range for all studies is not acceptable).

^{viii} The methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations. (**Note**: The review might say something like “the results should be interpreted with caution due to poor quality of included studies.” Cannot score “yes” for this question if scored “no” for question 7).

^{ix} For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e., Chi-squared test for homogeneity, I^2). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e., is it sensible to combine?). Indicate “yes” where the authors mention or describe heterogeneity or variability between results and discuss the consequences (eg where authors declare they cannot pool results because of heterogeneity).

^x An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test, Hedges-Olken). (**Note**: Score “Can’t say” if there were fewer than 10 included studies).

^{xi} Potential sources of support should be clearly acknowledged in both the systematic review and the included studies.

^{xii} Rate the overall methodological quality of the study, using the following as a guide: **High quality** (++) : Majority of criteria met. Little or no risk of bias. Results unlikely to be changed by further research. **Acceptable** (+) : Most criteria met. Some flaws in the study with an associated risk of bias, Conclusions may change in the light of further studies. **Low quality** (0) : Either most criteria not met, or significant flaws relating to key aspects of study design. Conclusions likely to change in the light of further studies.

^{xiii} Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above. This is a very important part of the evaluation and will feature in the evidence table. PLEASE FILL IN.



Methodology Checklist 1: Systematic Reviews and Meta-analyses

SIGN

SIGN gratefully acknowledges the permission received from the authors of the AMSTAR tool to base this checklist on their work: *Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C, et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Medical Research Methodology 2007, 7:10 doi:10.1186/1471-2288-7-10. Available from <http://www.biomedcentral.com/1471-2288/7/10> [cited 10 Sep 2012]*

Study identification (Include author, title, year of publication, journal title, pages)

< SantaCruzR_2013 > Cochrane DB syst rev 2013(6)

Guideline topic: AG IV

Key Question No: 4.1

Before completing this checklist, consider:

1. Is the paper a systematic review or meta-analysis? IF NO reject. IF **YES** continue.
2. Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO reject. IF **YES** complete the checklist.

Checklist completed by: **AF, ZKLS**

Section 1: Internal validity

In a well conducted systematic review:

Does this study do it?

1.1	The study addresses a clearly defined research question. ⁱ	Yes X	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	
1.2	At least two people should select studies and extract data. ⁱⁱ	Yes X	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	
1.3	A comprehensive literature search is carried out. ⁱⁱⁱ	Yes X	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	Does not apply <input type="checkbox"/>
1.4	The authors clearly state if or how they limited their review by publication type. ^{iv}	Yes X	No <input type="checkbox"/>
1.5	The included and excluded studies are listed. ^v	Yes X	No <input type="checkbox"/>
1.6	The characteristics of the included studies are provided. ^{vi}	Yes X	No <input type="checkbox"/>
1.7	The scientific quality of the included studies is assessed and documented. ^{vii}	Yes X	No <input type="checkbox"/>

1.8	The scientific quality of the included studies was assessed appropriately. ^{viii}	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.9	Appropriate methods are used to combine the individual study findings. ^{ix}	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.10	The likelihood of publication bias is assessed. ^x Stated but not presented (although not necessarily essential due to k=7)	Yes <input type="checkbox"/> No <input type="checkbox"/> Can't say <input checked="" type="checkbox"/>
1.11	Conflicts of interest are declared. ^{xi}	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/>
SECTION 2: OVERALL ASSESSMENT OF THE STUDY		
2.1	What is your overall assessment of the methodological quality of this review? ^{xii}	High quality (++) Acceptable (+) <input checked="" type="checkbox"/> Unacceptable – reject
2.2	Are the results of this study directly applicable to the patient group targeted by this guideline?	Yes <input type="checkbox"/> No <input type="checkbox"/>
2.3	Notes: ^{xiii} 95%-CI rather near to significance regarding relevant outcomes like hospital/ 28d-mortality; Too rigorous rejection of higher PEEP's value with respect to the overall results	

ⁱ The research question and inclusion criteria should be established before the review is conducted. To score a 'yes' for this factor there must be reference to a protocol, ethics approval, or pre-determined/a priori published research objectives.

ⁱⁱ At least two people should select papers and extract data. There should be a consensus procedure to resolve any differences.

ⁱⁱⁱ At least two major electronic databases should be searched. The report must include years and databases searched (e.g., Central, EMBASE, MEDLINE, OpenGrey, 1999-2009). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found. In rare cases this may not apply where authors have carried out a meta analysis focusing on a specified range of major trials in their field.

^{iv} The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status or language. If searching sources that contains both grey and non-grey literature, must specify that they were searching for both.

^v A list of included and excluded studies should be provided. Limiting the excluded studies to references is acceptable.

^{vi} In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analyzed e.g., age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported. (**Note** that a format other than a table is acceptable, as long as the information noted here is provided).

^{vii} This relates to the scientific quality of the studies included in the review. I can include use of a quality scoring tool or checklist, e.g., Jadad scale, risk of bias, sensitivity analysis, or a description of quality items, with some kind of result for EACH study (“low” or “high” is fine, as long as it is clear which studies scored “low” and which scored “high”; a summary score/range for all studies is not acceptable).

^{viii} The methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations. (**Note:** The review might say something like “the results should be interpreted with caution due to poor quality of included studies.” Cannot score “yes” for this question if scored “no” for question 7).

^{ix} For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e., Chi-squared test for homogeneity, I^2). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e., is it sensible to combine?). Indicate “yes” where the authors mention or describe heterogeneity or variability between results and discuss the consequences (eg where authors declare they cannot pool results because of heterogeneity).

^x An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test, Hedges-Olken). (**Note:** Score “Can’t say” if there were fewer than 10 included studies).

^{xi} Potential sources of support should be clearly acknowledged in both the systematic review and the included studies.

^{xii} Rate the overall methodological quality of the study, using the following as a guide: **High quality** (++) : Majority of criteria met. Little or no risk of bias. Results unlikely to be changed by further research. **Acceptable** (+) : Most criteria met. Some flaws in the study with an associated risk of bias, Conclusions may change in the light of further studies. **Low quality** (0) : Either most criteria not met, or significant flaws relating to key aspects of study design. Conclusions likely to change in the light of further studies.

^{xiii} Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above. This is a very important part of the evaluation and will feature in the evidence table. PLEASE FILL IN.



Methodology Checklist 1: Systematic Reviews and Meta-analyses

SIGN

SIGN gratefully acknowledges the permission received from the authors of the AMSTAR tool to base this checklist on their work: *Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C, et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Medical Research Methodology 2007, 7:10 doi:10.1186/1471-2288-7-10. Available from <http://www.biomedcentral.com/1471-2288/7/10> [cited 10 Sep 2012]*

Study identification (Include author, title, year of publication, journal title, pages)

< TokmajiG_ 2015 > Cochrane review 2015;8

Guideline topic: AG II (?)

Key Question No: 2.4.1 (?; 11.04.16 –Nachtrag)

Before completing this checklist, consider:

1. Is the paper a systematic review or meta-analysis? IF NO reject. IF **YES** continue.
2. Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO reject. IF YES complete the checklist.

Checklist completed by: AF, ZKSL

Section 1: Internal validity

In a well conducted systematic review:

Does this study do it?

1.1	The study addresses a clearly defined research question. ⁱ	Yes <input type="checkbox"/>	No <input type="checkbox"/>	Can't say <input type="checkbox"/>	
1.2	At least two people should select studies and extract data. ⁱⁱ	Yes <input type="checkbox"/>	No <input type="checkbox"/>	Can't say <input type="checkbox"/>	
1.3	A comprehensive literature search is carried out. ⁱⁱⁱ	Yes <input type="checkbox"/>	No <input type="checkbox"/>	Can't say <input type="checkbox"/>	Does not apply <input type="checkbox"/>
1.4	The authors clearly state if or how they limited their review by publication type. ^{iv}	Yes <input type="checkbox"/>	No <input type="checkbox"/>		
1.5	The included and excluded studies are listed. ^v	Yes <input type="checkbox"/>	No <input type="checkbox"/>		
1.6	The characteristics of the included studies are provided. ^{vi}	Yes <input type="checkbox"/>	No <input type="checkbox"/>		
1.7	The scientific quality of the included studies is assessed and documented. ^{vii}	Yes <input type="checkbox"/>	No <input type="checkbox"/>		

1.8	The scientific quality of the included studies was assessed appropriately. ^{viii}	Yes <input type="checkbox"/>	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	
1.9	Appropriate methods are used to combine the individual study findings. ^{ix}	Yes <input type="checkbox"/>	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	
1.10	The likelihood of publication bias is assessed. ^x	Yes <input type="checkbox"/>	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	
1.11	Conflicts of interest are declared. ^{xi}	Yes <input type="checkbox"/>	No <input type="checkbox"/>
SECTION 2: OVERALL ASSESSMENT OF THE STUDY			
2.1	What is your overall assessment of the methodological quality of this review? ^{xii}	High quality (++) <input type="checkbox"/> Acceptable (+) <input checked="" type="checkbox"/> (at least) Unacceptable – reject 0 <input type="checkbox"/>	
2.2	Are the results of this study directly applicable to the patient group targeted by this guideline?	Yes <input type="checkbox"/>	No <input type="checkbox"/>
2.3	Notes: ^{xiii} Acc. to convention Cochrane rev. are not to be methodologically reviewed in detail;		

ⁱ The research question and inclusion criteria should be established before the review is conducted. To score a 'yes' for this factor there must be reference to a protocol, ethics approval, or pre-determined/a priori published research objectives.

ⁱⁱ At least two people should select papers and extract data. There should be a consensus procedure to resolve any differences.

ⁱⁱⁱ At least two major electronic databases should be searched. The report must include years and databases searched (e.g., Central, EMBASE, MEDLINE, OpenGrey, 1999-2009). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found. In rare cases this may not apply where authors have carried out a meta analysis focusing on a specified range of major trials in their field.

^{iv} The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status or language. If searching sources that contains both grey and non-grey literature, must specify that they were searching for both.

^v A list of included and excluded studies should be provided. Limiting the excluded studies to references is acceptable.

^{vi} In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analyzed e.g., age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported. (**Note** that a format other than a table is acceptable, as long as the information noted here is provided).

^{vii} This relates to the scientific quality of the studies included in the review. I can include use of a quality scoring tool or checklist, e.g., Jadad scale, risk of bias, sensitivity analysis, or a description of quality items, with some kind of result for EACH study (“low” or “high” is fine, as long as it is clear which studies scored “low” and which scored “high”; a summary score/range for all studies is not acceptable).

^{viii} The methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations. (**Note**: The review might say something like “the results should be interpreted with caution due to poor quality of included studies.” Cannot score “yes” for this question if scored “no” for question 7).

^{ix} For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e., Chi-squared test for homogeneity, I^2). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e., is it sensible to combine?). Indicate “yes” where the authors mention or describe heterogeneity or variability between results and discuss the consequences (eg where authors declare they cannot pool results because of heterogeneity).

^x An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test, Hedges-Olken). (**Note**: Score “Can’t say” if there were fewer than 10 included studies).

^{xi} Potential sources of support should be clearly acknowledged in both the systematic review and the included studies.

^{xii} Rate the overall methodological quality of the study, using the following as a guide: **High quality** (++) : Majority of criteria met. Little or no risk of bias. Results unlikely to be changed by further research. **Acceptable** (+) : Most criteria met. Some flaws in the study with an associated risk of bias, Conclusions may change in the light of further studies. **Low quality** (0) : Either most criteria not met, or significant flaws relating to key aspects of study design. Conclusions likely to change in the light of further studies.

^{xiii} Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above. This is a very important part of the evaluation and will feature in the evidence table. PLEASE FILL IN.



Methodology Checklist 1: Systematic Reviews and Meta-analyses

SIGN

SIGN gratefully acknowledges the permission received from the authors of the AMSTAR tool to base this checklist on their work: *Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C., et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Medical Research Methodology 2007, 7:10 doi:10.1186/1471-2288-7-10. Available from <http://www.biomedcentral.com/1471-2288/7/10> [cited 10 Sep 2012]*

Study identification (Include author, title, year of publication, journal title, pages)

Vital et al., Non-invasive positive pressure ventilation, 2013, Cochrane Review

Guideline topic: 7-02

Key Question No: 7-02

Before completing this checklist, consider:

1. Is the paper a systematic review or meta-analysis? IF NO reject. IF YES continue.
2. Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO reject. IF YES complete the checklist.

Checklist completed by: CP, IMISE

Section 1: Internal validity

In a well conducted systematic review:

Does this study do it?

1.1	The study addresses a clearly defined research question. ⁱ	Yes X	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	
1.2	At least two people should select studies and extract data. ⁱⁱ	Yes X	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	
1.3	A comprehensive literature search is carried out. ⁱⁱⁱ	Yes X	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	Does not apply <input type="checkbox"/>
1.4	The authors clearly state if or how they limited their review by publication type. ^{iv}	Yes X	No <input type="checkbox"/>
1.5	The included and excluded studies are listed. ^v Only included studies.	Yes X	No <input type="checkbox"/>
1.6	The characteristics of the included studies are provided. ^{vi}	Yes X	No <input type="checkbox"/>
1.7	The scientific quality of the included studies is assessed and documented. ^{vii}	Yes X	No <input type="checkbox"/>

1.8	The scientific quality of the included studies was assessed appropriately. ^{viii}	Yes X Can't say <input type="checkbox"/>	No <input type="checkbox"/>
1.9	Appropriate methods are used to combine the individual study findings. ^{ix}	Yes X Can't say <input type="checkbox"/>	No <input type="checkbox"/>
1.10	The likelihood of publication bias is assessed. ^x	Yes X Can't say <input type="checkbox"/>	No <input type="checkbox"/>
1.11	Conflicts of interest are declared. ^{xi}	Yes X	No <input type="checkbox"/>
SECTION 2: OVERALL ASSESSMENT OF THE STUDY			
2.1	What is your overall assessment of the methodological quality of this review? ^{xii}	High quality (++) X Acceptable (+) <input type="checkbox"/> Unacceptable – reject 0 <input type="checkbox"/>	
2.2	Are the results of this study directly applicable to the patient group targeted by this guideline?	Yes <input type="checkbox"/>	No <input type="checkbox"/>
2.3	Notes:^{xiii} Bei Heterogenität der Studien wurden Sensitivitätsanalysen ohne bestimmte Studien gemacht, aber kein Random Effects Model.		

ⁱ The research question and inclusion criteria should be established before the review is conducted. To score a 'yes' for this factor there must be reference to a protocol, ethics approval, or pre-determined/a priori published research objectives.

ⁱⁱ At least two people should select papers and extract data. There should be a consensus procedure to resolve any differences.

ⁱⁱⁱ At least two major electronic databases should be searched. The report must include years and databases searched (e.g., Central, EMBASE, MEDLINE, OpenGrey, 1999-2009). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found. In rare cases this may not apply where authors have carried out a meta analysis focusing on a specified range of major trials in their field.

^{iv} The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status or language. If searching sources that contains both grey and non-grey literature, must specify that they were searching for both.

^v A list of included and excluded studies should be provided. Limiting the excluded studies to references is acceptable.

^{vi} In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analyzed e.g., age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported. (**Note** that a format other than a table is acceptable, as long as the information noted here is provided).

^{vii} This relates to the scientific quality of the studies included in the review. I can include use of a quality scoring tool or checklist, e.g., Jadad scale, risk of bias, sensitivity analysis, or a description of quality items, with some kind of result for EACH study (“low” or “high” is fine, as long as it is clear which studies scored “low” and which scored “high”; a summary score/range for all studies is not acceptable).

^{viii} The methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations. (**Note:** The review might say something like “the results should be interpreted with caution due to poor quality of included studies.” Cannot score “yes” for this question if scored “no” for question 7).

^{ix} For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e., Chi-squared test for homogeneity, *I*²). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e., is it sensible to combine?). Indicate “yes” where the authors mention or describe heterogeneity or variability between results and discuss the consequences (eg where authors declare they cannot pool results because of heterogeneity).

^x An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test, Hedges-Olken). (**Note:** Score “Can’t say” if there were fewer than 10 included studies).

^{xi} Potential sources of support should be clearly acknowledged in both the systematic review and the included studies.

^{xii} Rate the overall methodological quality of the study, using the following as a guide: **High quality** (++) : Majority of criteria met. Little or no risk of bias. Results unlikely to be changed by further research. **Acceptable** (+) : Most criteria met. Some flaws in the study with an associated risk of bias, Conclusions may change in the light of further studies. **Low quality** (0) : Either most criteria not met, or significant flaws relating to key aspects of study design. Conclusions likely to change in the light of further studies.

^{xiii} Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above. This is a very important part of the evaluation and will feature in the evidence table. PLEASE FILL IN.



Methodology Checklist 1: Systematic Reviews and Meta-analyses

SIGN

SIGN gratefully acknowledges the permission received from the authors of the AMSTAR tool to base this checklist on their work: *Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C, et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Medical Research Methodology 2007, 7:10 doi:10.1186/1471-2288-7-10. Available from <http://www.biomedcentral.com/1471-2288/7/10> [cited 10 Sep 2012]*

Study identification (Include author, title, year of publication, journal title, pages)

< WangL_2016 >

Cochrane review 2016;1

Guideline topic: AG VI (?)

Key Question No: 6.2 (?; 11.04.16 –Nachtrag)

Before completing this checklist, consider:

1. Is the paper a systematic review or meta-analysis? IF NO reject. IF **YES** continue.
2. Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO reject. IF YES complete the checklist.

Checklist completed by: AF, ZKSL

Section 1: Internal validity

In a well conducted systematic review:

Does this study do it?

1.1	The study addresses a clearly defined research question. ⁱ	Yes <input type="checkbox"/>	No <input type="checkbox"/>	Can't say <input type="checkbox"/>	
1.2	At least two people should select studies and extract data. ⁱⁱ	Yes <input type="checkbox"/>	No <input type="checkbox"/>	Can't say <input type="checkbox"/>	
1.3	A comprehensive literature search is carried out. ⁱⁱⁱ	Yes <input type="checkbox"/>	No <input type="checkbox"/>	Can't say <input type="checkbox"/>	Does not apply <input type="checkbox"/>
1.4	The authors clearly state if or how they limited their review by publication type. ^{iv}	Yes <input type="checkbox"/>	No <input type="checkbox"/>		
1.5	The included and excluded studies are listed. ^v	Yes <input type="checkbox"/>	No <input type="checkbox"/>		
1.6	The characteristics of the included studies are provided. ^{vi}	Yes <input type="checkbox"/>	No <input type="checkbox"/>		
1.7	The scientific quality of the included studies is assessed and documented. ^{vii}	Yes <input type="checkbox"/>	No <input type="checkbox"/>		

1.8	The scientific quality of the included studies was assessed appropriately. ^{viii}	Yes <input type="checkbox"/>	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	
1.9	Appropriate methods are used to combine the individual study findings. ^{ix}	Yes <input type="checkbox"/>	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	
1.10	The likelihood of publication bias is assessed. ^x	Yes <input type="checkbox"/>	No <input type="checkbox"/>
		Can't say <input type="checkbox"/>	
1.11	Conflicts of interest are declared. ^{xi}	Yes <input type="checkbox"/>	No <input type="checkbox"/>
SECTION 2: OVERALL ASSESSMENT OF THE STUDY			
2.1	What is your overall assessment of the methodological quality of this review? ^{xii}	High quality (++) <input type="checkbox"/> Acceptable (+) <input checked="" type="checkbox"/> (at least) Unacceptable – reject 0 <input type="checkbox"/>	
2.2	Are the results of this study directly applicable to the patient group targeted by this guideline?	Yes <input type="checkbox"/>	No <input type="checkbox"/>
2.3	Notes: ^{xiii} Acc. to convention Cochrane rev. are not to be methodologically reviewed in detail;		

ⁱ The research question and inclusion criteria should be established before the review is conducted. To score a 'yes' for this factor there must be reference to a protocol, ethics approval, or pre-determined/a priori published research objectives.

ⁱⁱ At least two people should select papers and extract data. There should be a consensus procedure to resolve any differences.

ⁱⁱⁱ At least two major electronic databases should be searched. The report must include years and databases searched (e.g., Central, EMBASE, MEDLINE, OpenGrey, 1999-2009). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found. In rare cases this may not apply where authors have carried out a meta analysis focusing on a specified range of major trials in their field.

^{iv} The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status or language. If searching sources that contains both grey and non-grey literature, must specify that they were searching for both.

^v A list of included and excluded studies should be provided. Limiting the excluded studies to references is acceptable.

^{vi} In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analyzed e.g., age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported. (**Note** that a format other than a table is acceptable, as long as the information noted here is provided).

^{vii} This relates to the scientific quality of the studies included in the review. I can include use of a quality scoring tool or checklist, e.g., Jadad scale, risk of bias, sensitivity analysis, or a description of quality items, with some kind of result for EACH study (“low” or “high” is fine, as long as it is clear which studies scored “low” and which scored “high”; a summary score/range for all studies is not acceptable).

^{viii} The methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations. (**Note:** The review might say something like “the results should be interpreted with caution due to poor quality of included studies.” Cannot score “yes” for this question if scored “no” for question 7).

^{ix} For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e., Chi-squared test for homogeneity, I^2). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e., is it sensible to combine?). Indicate “yes” where the authors mention or describe heterogeneity or variability between results and discuss the consequences (eg where authors declare they cannot pool results because of heterogeneity).

^x An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test, Hedges-Olken). (**Note:** Score “Can’t say” if there were fewer than 10 included studies).

^{xi} Potential sources of support should be clearly acknowledged in both the systematic review and the included studies.

^{xii} Rate the overall methodological quality of the study, using the following as a guide: **High quality** (++) : Majority of criteria met. Little or no risk of bias. Results unlikely to be changed by further research. **Acceptable** (+) : Most criteria met. Some flaws in the study with an associated risk of bias, Conclusions may change in the light of further studies. **Low quality** (0) : Either most criteria not met, or significant flaws relating to key aspects of study design. Conclusions likely to change in the light of further studies.

^{xiii} Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above. This is a very important part of the evaluation and will feature in the evidence table. PLEASE FILL IN.



Methodology Checklist 1: Systematic Reviews and Meta-analyses

SIGN

SIGN gratefully acknowledges the permission received from the authors of the AMSTAR tool to base this checklist on their work: *Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C, et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Medical Research Methodology 2007, 7:10 doi:10.1186/1471-2288-7-10. Available from <http://www.biomedcentral.com/1471-2288/7/10> [cited 10 Sep 2012]*

Study identification (Include author, title, year of publication, journal title, pages)

< ZampieriF_2013 > J Crit Care 2013;28:998ff

Guideline topic: AG VI

Key Question No: 6.4.1 (28.10.15.ff)

Before completing this checklist, consider:

1. Is the paper a systematic review or meta-analysis? IF NO reject. IF YES continue.
2. Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO reject. IF YES complete the checklist.

Checklist completed by: AF, ZKSL

Section 1: Internal validity

<i>In a well conducted systematic review:</i>		<i>Does this study do it?</i>	
1.1	The study addresses a clearly defined research question. ⁱ	Yes <input checked="" type="checkbox"/>	No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.2	At least two people should select studies and extract data. ⁱⁱ	Yes <input checked="" type="checkbox"/>	No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.3	A comprehensive literature search is carried out. ⁱⁱⁱ	Yes <input checked="" type="checkbox"/>	No <input type="checkbox"/> Does not apply <input type="checkbox"/>
1.4	The authors clearly state if or how they limited their review by publication type. ^{iv}	Yes <input checked="" type="checkbox"/>	No <input type="checkbox"/>
1.5	The included and excluded studies are listed. ^v K=3 (1 RCT & 2 CCs w. Propensity adjustment)	Yes <input checked="" type="checkbox"/>	No <input type="checkbox"/> k _{ex} =2 (old)
1.6	The characteristics of the included studies are provided. ^{vi}	Yes <input checked="" type="checkbox"/>	No <input type="checkbox"/>
1.7	The scientific quality of the included studies is assessed and documented. ^{vii}	Yes <input checked="" type="checkbox"/>	No <input type="checkbox"/>

1.8	The scientific quality of the included studies was assessed appropriately. ^{viii}	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.9	Appropriate methods are used to combine the individual study findings. ^{ix}	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.10	The likelihood of publication bias is assessed. ^x since K small → not suitable	Yes <input type="checkbox"/> No <input type="checkbox"/> Can't say <input checked="" type="checkbox"/>
1.11	Conflicts of interest are declared. ^{xi}	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/>
SECTION 2: OVERALL ASSESSMENT OF THE STUDY		
2.1	What is your overall assessment of the methodological quality of this review? ^{xii}	High quality (++) <input type="checkbox"/> Acceptable (+) <input checked="" type="checkbox"/> Unacceptable – reject <input type="checkbox"/>
2.2	Are the results of this study directly applicable to the patient group targeted by this guideline?	Yes <input type="checkbox"/> No <input type="checkbox"/>
2.3	Notes: ^{xiii} No definite evidence found that ECMO supports Survival; more studies needed;	

ⁱ The research question and inclusion criteria should be established before the review is conducted. To score a 'yes' for this factor there must be reference to a protocol, ethics approval, or pre-determined/a priori published research objectives.

ⁱⁱ At least two people should select papers and extract data. There should be a consensus procedure to resolve any differences.

ⁱⁱⁱ At least two major electronic databases should be searched. The report must include years and databases searched (e.g., Central, EMBASE, MEDLINE, OpenGrey, 1999-2009). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found. In rare cases this may not apply where authors have carried out a meta analysis focusing on a specified range of major trials in their field.

^{iv} The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status or language. If searching sources that contains both grey and non-grey literature, must specify that they were searching for both.

^v A list of included and excluded studies should be provided. Limiting the excluded studies to references is acceptable.

^{vi} In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analyzed e.g., age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported. (**Note** that a format other than a table is acceptable, as long as the information noted here is provided).

^{vii} This relates to the scientific quality of the studies included in the review. I can include use of a quality scoring tool or checklist, e.g., Jadad scale, risk of bias, sensitivity analysis, or a description of quality items, with some kind of result for EACH study (“low” or “high” is fine, as long as it is clear which studies scored “low” and which scored “high”; a summary score/range for all studies is not acceptable).

^{viii} The methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations. (**Note**: The review might say something like “the results should be interpreted with caution due to poor quality of included studies.” Cannot score “yes” for this question if scored “no” for question 7).

^{ix} For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e., Chi-squared test for homogeneity, I^2). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e., is it sensible to combine?). Indicate “yes” where the authors mention or describe heterogeneity or variability between results and discuss the consequences (eg where authors declare they cannot pool results because of heterogeneity).

^x An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test, Hedges-Olken). (**Note**: Score “Can’t say” if there were fewer than 10 included studies).

^{xi} Potential sources of support should be clearly acknowledged in both the systematic review and the included studies.

^{xii} Rate the overall methodological quality of the study, using the following as a guide: **High quality** (++) : Majority of criteria met. Little or no risk of bias. Results unlikely to be changed by further research. **Acceptable** (+) : Most criteria met. Some flaws in the study with an associated risk of bias, Conclusions may change in the light of further studies. **Low quality** (0) : Either most criteria not met, or significant flaws relating to key aspects of study design. Conclusions likely to change in the light of further studies.

^{xiii} Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above. This is a very important part of the evaluation and will feature in the evidence table. PLEASE FILL IN.



Methodology Checklist 1: Systematic Reviews and Meta-analyses

SIGN

SIGN gratefully acknowledges the permission received from the authors of the AMSTAR tool to base this checklist on their work: *Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C., et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Medical Research Methodology 2007, 7:10 doi:10.1186/1471-2288-7-10. Available from <http://www.biomedcentral.com/1471-2288/7/10> [cited 10 Sep 2012]*

Study identification (Include author, title, year of publication, journal title, pages)

< ZhangLN_2013 >

Exp Ther Med 2013;5:237ff

Guideline topic: AG V

Key Question No: 5.8.3 (25.05.16ff)

Before completing this checklist, consider:

1. Is the paper a systematic review or meta-analysis? IF NO reject. IF **YES** continue.
2. Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO reject. IF YES complete the checklist.

Checklist completed by: AF, ZKSL

Section 1: Internal validity

In a well conducted systematic review:

Does this study do it?

1.1	The study addresses a clearly defined research question. ⁱ	Yes X	No <input type="checkbox"/>	Can't say <input type="checkbox"/>
1.2	At least two people should select studies and extract data. ⁱⁱ	Yes X	No <input type="checkbox"/>	Can't say <input type="checkbox"/>
1.3	A comprehensive literature search is carried out. ⁱⁱⁱ	Yes X	No <input type="checkbox"/>	Can't say <input type="checkbox"/> Does not apply <input type="checkbox"/>
1.4	The authors clearly state if or how they limited their review by publication type. ^{iv} Engl. only	Yes X	No <input type="checkbox"/>	
1.5	The included and excluded studies are listed. ^v	Yes <input type="checkbox"/>	No X	
1.6	The characteristics of the included studies are provided. ^{vi}	Yes X	No <input type="checkbox"/>	
1.7	The scientific quality of the included studies is assessed and documented. ^{vii}	Yes X	No <input type="checkbox"/>	

1.8	The scientific quality of the included studies was assessed appropriately. ^{viii} Unknown assessment but statements are OK	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.9	Appropriate methods are used to combine the individual study findings. ^{ix}	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.10	The likelihood of publication bias is assessed. ^x	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Can't say <input type="checkbox"/>
1.11	Conflicts of interest are declared. ^{xi}	Yes <input type="checkbox"/> No <input checked="" type="checkbox"/>
SECTION 2: OVERALL ASSESSMENT OF THE STUDY		
2.1	What is your overall assessment of the methodological quality of this review? ^{xii}	High quality (++) <input checked="" type="checkbox"/> Acceptable (+) <input type="checkbox"/> Unacceptable – reject <input type="checkbox"/>
2.2	Are the results of this study directly applicable to the patient group targeted by this guideline?	Yes <input type="checkbox"/> No <input type="checkbox"/>
2.3	Notes: ^{xiii} No hints on therapeutic efficacy regarding reduced mortality 2 RCTs aus Mengh 2012 not included → reasons I/E-crit/ syst. Lit search?	

ⁱ The research question and inclusion criteria should be established before the review is conducted. To score a 'yes' for this factor there must be reference to a protocol, ethics approval, or pre-determined/a priori published research objectives.

ⁱⁱ At least two people should select papers and extract data. There should be a consensus procedure to resolve any differences.

ⁱⁱⁱ At least two major electronic databases should be searched. The report must include years and databases searched (e.g., Central, EMBASE, MEDLINE, OpenGrey, 1999-2009). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found. In rare cases this may not apply where authors have carried out a meta analysis focusing on a specified range of major trials in their field.

^{iv} The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status or language. If searching sources that contains both grey and non-grey literature, must specify that they were searching for both.

^v A list of included and excluded studies should be provided. Limiting the excluded studies to references is acceptable.

^{vi} In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analyzed e.g., age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported. (**Note** that a format other than a table is acceptable, as long as the information noted here is provided).

^{vii} This relates to the scientific quality of the studies included in the review. I can include use of a quality scoring tool or checklist, e.g., Jadad scale, risk of bias, sensitivity analysis, or a description of quality items, with some kind of result for EACH study (“low” or “high” is fine, as long as it is clear which studies scored “low” and which scored “high”; a summary score/range for all studies is not acceptable).

^{viii} The methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations. (**Note**: The review might say something like “the results should be interpreted with caution due to poor quality of included studies.” Cannot score “yes” for this question if scored “no” for question 7).

^{ix} For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e., Chi-squared test for homogeneity, *I*²). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e., is it sensible to combine?). Indicate “yes” where the authors mention or describe heterogeneity or variability between results and discuss the consequences (eg where authors declare they cannot pool results because of heterogeneity).

^x An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test, Hedges-Olken). (**Note**: Score “Can’t say” if there were fewer than 10 included studies).

^{xi} Potential sources of support should be clearly acknowledged in both the systematic review and the included studies.

^{xii} Rate the overall methodological quality of the study, using the following as a guide: **High quality** (++) : Majority of criteria met. Little or no risk of bias. Results unlikely to be changed by further research. **Acceptable** (+) : Most criteria met. Some flaws in the study with an associated risk of bias, Conclusions may change in the light of further studies. **Low quality** (0) : Either most criteria not met, or significant flaws relating to key aspects of study design. Conclusions likely to change in the light of further studies.

^{xiii} Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above. This is a very important part of the evaluation and will feature in the evidence table. PLEASE FILL IN.