CQ6-1 (GRADE)

P: Patients with sepsis/ septic shock
I: Use of echocardiography
C: Not use of echocardiography
O: Mortality (28-day), length of ICU stay

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Treatment	Placebo	Relative (95% CI)	Absolute (95% CI)		
Mortality (28-day)												
1	randomised trials	serious	not serious	not serious	very serious	none	5/15 (33.3%)	3/15 (20.0%)	**RR 1.67** (0.48 to 5.76)	**134 fewer per 1,000** (from 104 fewer to 952 more)	⨁◯◯◯ Very low	CRITICAL
Length of ICU stay												
1	randomised trials	serious	not serious	not serious	very serious	none	15	15	-	**MD 0.3 day fewer** (from 4.46 fewer to 3.86 more)	⨁◯◯◯ Very low	CRITICAL

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	**Don't know**
UNDESIRABLE EFFECTS	Large	Moderate	Small	Trivial		Varies	**Don't know**
CERTAINTY OF EVIDENCE	**Very low**	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	**Don't know**
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

CQ6-2 (GRADE)

P: Patients with sepsis/ septic shock
I: Use of EGDT
C: Not use of EGDT
O: Mortality (28 or 30-day, 90-day), length of ICU stay, serious adverse events

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Treatment	Placebo	Relative (95% CI)	Absolute (95% CI)		
Mortality (28 or 30 day)												
4	randomised trials	not serious	serious	not serious	not serious	none	403/1986 (20.3%)	425/2007 (21.2%)	**RR 0.96** (0.85 to 1.08)	**8 fewer per 1,000** (from 32 fewer to 17 more)	⨁⨁⨁◯ Moderate	CRITICAL
Mortality (90-day)												
3	randomised trials	not serious	not serious	not serious	not serious	none	461/1820 (25.3%)	470/1828 (25.7%)	**RR 0.98** (0.88 to 1.10)	**5 fewer per 1,000** (from 31 fewer to 26 more)	⨁⨁⨁⨁ High	CRITICAL
Length of ICU stay												
3	randomised trials	not serious	serious	not serious	not serious	none	1857	1880	-	**MD 0.22 day more** (from 0.13 fewer to 0.58 more)	⨁⨁⨁◯ Moderate	CRITICAL
Serious adverse events												
3	randomised trials	not serious	serious	not serious	serious	none	109/1856 (5.9%)	105/1878 (5.6%)	**RR 1.02** (0.66 to 1.57)	**1 more per 1,000** (from 19 fewer to 32 more)	⨁⨁◯◯ Low	CRITICAL

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	**Trivial**	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	**Trivial**		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	**Low**	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	**Does not favor either the intervention or the comparison**	Probably favors the intervention	Favors the intervention	Varies	Don't know
ACCEPTABILITY	No	**Probably no**	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

CQ6-3 (GRADE)

P: Patients with sepsis/ septic shock
I: Early use of vasopressor with initial fluid resuscitation
C: Only initial fluid resuscitation
O: Mortality (28 day, 90-day or longest observational period), serious adverse events (pulmonary edema, myocardial ischemia)

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Treatment	Placebo	Relative (95% CI)	Absolute (95% CI)		
Mortality (28 day)												
2	randomised trials	not serious	serious	not serious	serious	none	27/204 (13.2%)	35/204 (17.2%)	**RR 0.77** (0.49 to 1.22)	**39 fewer per 1,000** (from 88 fewer to 38 more)	⨁⨁◯◯ Low	CRITICAL
Mortality (90-day or longest observational period)												
2	randomised trials	not serious	not serious	not serious	serious	none	39/203 (19.2%)	41/202 (20.3%)	**RR 0.95** (0.64 to 1.40)	**10 fewer per 1,000** (from 73 fewer to 81 more)	⨁⨁◯◯ Low	CRITICAL
Pulmonary edema												
2	randomised trials	not serious	not serious	not serious	serious	none	23/205 (11.2%)	44/204 (21.6%)	**RR 0.52** (0.33 to 0.82)	**104 fewer per 1,000** (from 145 fewer to 39 fewer)	⨁⨁⨁◯ Moderate	CRITICAL
Myocardial ischemia												
2	randomised trials	not serious	not serious	not serious	very serious	none	7/205 (3.4%)	4/204 (2.0%)	**RR 1.74** (0.52 to 5.86)	**15 more per 1,000** (from 9 fewer to 95 more)	⨁⨁◯◯ Low	CRITICAL

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	**Moderate**	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	**Trivial**		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	**Low**	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	**Probably favors the comparison**	**Does not favor either the intervention or the comparison**	**Probably favors the intervention**	Favors the intervention	Varies	Don't know
ACCEPTABILITY	No	**Probably no**	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

CQ6-4 (GRADE)

P: Patients with sepsis/ septic shock
I: Use of lactate or lactate clearance
C: Not use of lactate or lactate clearance
O: Mortality (28 or 30 day, 90-day), length of ICU stay, serious adverse events

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Treatment	Placebo	Relative (95% CI)	Absolute (95% CI)		
Mortality (28 or 30 day)												
5	randomised trials	not serious	serious	not serious	serious	none	204/738 (27.6%)	230/741 (31.0%)	**RR 0.80** (0.57 to 1.14)	**62 fewer per 1,000** (from 133 fewer to 43 more)	⨁⨁◯◯ Low	CRITICAL
Mortality (90-day)												
2	randomised trials	not serious	serious	not serious	serious	none	156/383 (40.7%)	163/389 (41.9%)	**RR 0.95** (0.65 to 1.38)	**21 fewer per 1,000** (from 147 fewer to 159 more)	⨁⨁◯◯ Low	CRITICAL
Length of ICU stay												
3	randomised trials	not serious	not serious	not serious	serious	none	542	542	-	**MD 0.03 day more** (from 0.66 fewer to 0.72 more)	⨁⨁⨁◯ Moderate	CRITICAL
Serious adverse event (SOFA score after 72 hours)												
3	randomised trials	not serious	serious	not serious	serious	none	487	492	-	**MD 0.04 more** (from 0.88 fewer to 0.96 more)	⨁⨁◯◯ Low	CRITICAL

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	**Small**	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	**Trivial**		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	**Low**	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	**Probably favors the comparison**	**Does not favor either the intervention or the comparison**	**Probably favors the intervention**	Favors the intervention	Varies	Don't know
ACCEPTABILITY	No	**Probably no**	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

CQ6-7 (GRADE)

P: Patients with sepsis/ septic shock
I: Use of crystalloid solution and albumin
C: Use of only crystalloid solution
O: Mortality (28 or 30 day), length of ICU stay, serious adverse events (lung injury score)

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Treatment	Placebo	Relative (95% CI)	Absolute (95% CI)		
Mortality (28 or 30 day)												
3	randomised trials	not serious	not serious	not serious	serious	none	187/622 (30.1%)	220/631 (34.9%)	**RR 0.87** (0.74 to 1.02)	**45 fewer per 1,000** (from 91 fewer to 7 more)	⨁⨁⨁◯ Moderate	CRITICAL
Length of ICU stay												
1	randomised trials	not serious	not serious	not serious	very serious	none	603	615	-	**MD 0.7 day more** (from 0.1 fewer to 1.5 more)	⨁⨁◯◯ Low	CRITICAL
Serious adverse event (Lung injury score)												
1	randomised trials	not serious	not serious	not serious	serious	none	12	12	-	**MD 0.75 more** (from 0.22 more to 1.28 more)	⨁⨁⨁◯ Moderate	CRITICAL

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	**Trivial**	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	**Trivial**		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	**Low**	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	**Probably favors the comparison**	**Does not favor either the intervention or the comparison**	Probably favors the intervention	Favors the intervention	Varies	Don't know
ACCEPTABILITY	No	**Probably no**	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

CQ6-8 (GRADE)

P: Patients with sepsis/ septic shock
I: Use of colloid solution and albumin
C: Use of only crystalloid solution
O: Mortality (28 or 30 day, 90 day or longest observational period), length of ICU stay, serious adverse events (use of dialysis, bleeding)

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Treatment	Placebo	Relative (95% CI)	Absolute (95% CI)		
Mortality (28 or 30 day)												
4	randomised trials	serious	not serious	not serious	not serious	none	409/1293 (31.6%)	400/1293 (30.9%)	**RR 1.03** (0.92 to 1.15)	**9 more per 1,000** (from 25 fewer to 46 more)	⨁⨁⨁◯ Moderate	CRITICAL
Mortality (90 day or longest observational period)												
3	randomised trials	serious	serious	not serious	not serious	none	498/1271 (38.8%)	490/1274 (38.5%)	**RR 1.05** (0.84 to 1.32)	**19 more per 1,000** (from 62 fewer to 123 more)	⨁⨁◯◯ Low	CRITICAL
Length of ICU stay												
2	randomised trials	not serious	serious	not serious	very serious	none	109	105	-	**MD 1.13 day fewer** (from 8.28 fewer to 6.03 more)	⨁◯◯◯ Very low	CRITICAL
Serious adverse event (Use of dialysis)												
4	randomised trials	not serious	not serious	serious	not serious	none	268/1933 (13.9%)	264/1958 (13.5%)	**RR 1.12** (0.82 to 1.53)	**16 more per 1,000** (from 24 fewer to 71 more)	⨁⨁⨁◯ Moderate	CRITICAL
Serious adverse event (Bleeding)												
2	randomised trials	not serious	not serious	serious	very serious	none	67/498 (13.5%)	45/496 (9.1%)	**RR 1.46** (1.03 to 2.07)	**42 more per 1,000** (from 3 more to 97 more)	⨁◯◯◯ Very low	CRITICAL

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	**Trivial**	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	**Moderate**	Small	Trivial		Varies	Don't know
CERTAINTY OF EVIDENCE	**Very low**	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	**Probably favors the comparison**	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Don't know
ACCEPTABILITY	No	**Probably no**	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

CQ6-9-1 (GRADE)

P: Septic shock patients without vasopressor (initial fluid resuscitation did not archive target mean blood pressure)
I: Use of noradrenaline as the first line drug
C: Use of dopamine as the first line drug
O: Mortality (28 or 30 day, 90 day or longest observational period), length of ICU stay, time to resolution of shock, organ ischemia, arrythmia

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Treatment	Placebo	Relative (95% CI)	Absolute (95% CI)		
Mortality (28 or 30 day)												
5	randomised trials	serious	not serious	not serious	serious	none	326/670 (48.7%)	390/727 (53.6%)	**RR 0.90** (0.81 to 1.00)	**54 fewer per 1,000** (from 102 fewer to 0 fewer)	⨁⨁◯◯ Low	CRITICAL
arrythmia												
2	randomised trials	serious	not serious	serious	not serious	none	153/939 (16.3%)	274/992 (27.6%)	**RR 0.60** (0.50 to 0.71)	**110 fewer per 1,000** (from 138 fewer to 80 fewer)	⨁⨁◯◯ Low	CRITICAL
Myocardial ischemia												
1	randomised trials	not serious	not serious	serious	very serious	none	25/821 (3.0%)	19/858 (2.2%)	**RR 1.38** (0.76 to 2.48)	**8 more per 1,000** (from 5 fewer to 33 more)	⨁◯◯◯ Very low	IMORTANT
Limb ischemia												
1	randomised trials	not serious	not serious	serious	very serious	none	14/821 (1.7%)	12/858 (1.4%)	**RR 1.22** (0.57 to 2.62)	**3 more per 1,000** (from 6 fewer to 23 more)	⨁◯◯◯ Very low	IMORTANT
Mesenteric ischemia												
1	randomised trials	not serious	not serious	serious	very serious	none	6/821 (0.7%)	11/858 (1.3%)	**RR 0.57** (0.21 to 1.53)	**6 fewer per 1,000** (from 10 fewer to 7 more)	⨁◯◯◯ Very low	IMORTANT

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	**Moderate**	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	**Trivial**		Varies	Don't know
CERTAINTY OF EVIDENCE	**Very low**	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	**Favors the intervention**	Varies	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

CQ6-9-2 (GRADE)

P: Septic shock patients without vasopressor (initial fluid resuscitation did not archive target mean blood pressure)
I: Use of noradrenaline as the first line drug
C: Use of phenylephrine as the first line drug
O: Mortality (28 or 30 day, 90 day or longest observational period), length of ICU stay, time to resolution of shock, organ ischemia, arrythmia

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Treatment	Placebo	Relative (95% CI)	Absolute (95% CI)		
Mortality (28 or 30 day)												
3	randomised trials	serious	not serious	not serious	very serious	none	27/52 (51.9%)	28/51 (54.9%)	**RR 0.95** (0.67 to 1.36)	**27 fewer per 1,000** (from 181 fewer to 198 more)	⨁◯◯◯ Very low	CRITICAL
arrythmia												
1	randomised trials	serious	not serious	not serious	very serious	none	2/9 (22.2%)	1/8 (12.5%)	**RR 1.78** (0.20 to 16.10)	**98 more per 1,000** (from 100 fewer to 1000 more)	⨁◯◯◯ Very low	CRITICAL

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	**Trivial**	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	Trivial		Varies	**Don't know**
CERTAINTY OF EVIDENCE	**Very low**	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	**Does not favor either the intervention or the comparison**	Probably favors the intervention	Favors the intervention	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		**Varies**	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

CQ6-10-1 (GRADE)

P: Septic shock patients (initial fluid resuscitation and the first line vasopressor did not archive target mean blood pressure)
I: Use of adrenaline as the second line drug
C: Not use of adrenaline as the second line drug
O: Mortality (28 day, 90 day), time to resolution of shock, organ ischemia, arrythmia

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Treatment	Placebo	Relative (95% CI)	Absolute (95% CI)		
Mortality (28 day)												
2	randomised trials	not serious	not serious	serious	very serious	none	80/191 (41.9%)	73/199 (36.7%)	**RR 1.13** (0.89 to 1.45)	**48 more per 1,000** (from 40 fewer to 165 more)	⨁◯◯◯ Very low	CRITICAL
Mortality (90 day)												
1	randomised trials	not serious	not serious	serious	very serious	none	84/161 (52.2%)	85/169 (50.3%)	**RR 1.04** (0.84 to 1.28)	**20 more per 1,000** (from 80 fewer to 141 more)	⨁◯◯◯ Very low	CRITICAL
Length of ICU stay												
2	randomised trials	not serious	not serious	very serious	serious	none	191	199	-	**MD 1 day fewer** (from 2.98 fewer to 0.98 more)	⨁◯◯◯ Very low	CRITICAL
Arrythmia												
2	randomised trials	not serious	not serious	serious	very serious	none	37/191 (19.4%)	34/199 (17.1%)	**RR 1.13** (0.74 to 1.73)	**22 more per 1,000** (from 44 fewer to 125 more)	⨁◯◯◯ Very low	CRITICAL
Limb ischemia												
2	randomised trials	not serious	not serious	serious	very serious	none	5/191 (2.6%)	8/199 (4.0%)	**RR 0.70** (0.17 to 2.91)	**12 fewer per 1,000** (from 33 fewer to 77 more)	⨁◯◯◯ Very low	IMORTANT

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	**Trivial**	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	**Small**	Trivial		Varies	Don't know
CERTAINTY OF EVIDENCE	**Very low**	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	**Probably favors the comparison**	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Don't know
ACCEPTABILITY	No	**Probably no**	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

CQ6-10-2 (GRADE)

P: Septic shock patients (initial fluid resuscitation and the first line vasopressor did not archive target mean blood pressure)
I: Use of vasopressin as the second line drug
C: Not use of vasopressin as the second line drug
O: Mortality (28 day, 90 day), time to resolution of shock, organ ischemia, arrythmia

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Treatment	Placebo	Relative (95% CI)	Absolute (95% CI)		
Mortality (28 day)												
4	randomised trials	serious	not serious	serious	serious	none	217/636 (34.1%)	218/624 (34.9%)	**RR 0.97** (0.84 to 1.13)	**10 fewer per 1,000** (from 56 fewer to 45 more)	⨁◯◯◯ Very low	CRITICAL
Mortality (90 day)												
1	randomised trials	not serious	not serious	serious	serious	none	177/400 (44.3%)	194/392 (49.5%)	**RR 0.89** (0.77 to 1.04)	**54 fewer per 1,000** (from 114 fewer to 20 more)	⨁⨁◯◯ Low	CRITICAL
Length of ICU stay												
3	randomised trials	not serious	not serious	serious	serious	none	602	615	-	**MD 0.16 day more** (from 1.84 fewer to 2.17 more)	⨁⨁◯◯ Low	CRITICAL
Arrythmia												
3	randomised trials	not serious	not serious	serious	very serious	none	11/616 (1.8%)	14/601 (2.3%)	**RR 0.77** (0.33 to 1.81)	**5 fewer per 1,000** (from 16 fewer to 19 more)	⨁◯◯◯ Very low	CRITICAL
Myocardial **ischemia**												
2	randomised trials	not serious	not serious	serious	very serious	none	15/601 (2.5%)	9/586 (1.5%)	**RR 1.67** (0.56 to 4.96)	**10 more per 1,000** (from 7 fewer to 61 more)	⨁◯◯◯ Very low	IMORTANT
Limb ischemia												
3	randomised trials	not serious	not serious	serious	serious	none	20/616 (3.2%)	5/601 (0.8%)	**RR 3.66** (1.44 to 9.30)	**22 more per 1,000** (from 4 more to 69 more)	⨁⨁◯◯ Low	IMORTANT

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	**Small**	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	**Trivial**		Varies	Don't know
CERTAINTY OF EVIDENCE	**Very low**	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	**Probably favors the intervention**	Favors the intervention	Varies	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

CQ6-11 (UnGRADE)

P: Septic shock patients with depression of cardiac function
I: Use of inotropic agents
C: Not use of inotropic agents
O: Mortality (28 day, 90 day), time to resolution of shock, complication (organ dysfunction, arrythmia)

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	**Moderate**	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	**Small**	Trivial		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			**No included studies**
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	**Probably favors the intervention**	Favors the intervention	Varies	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	**Yes**		Varies	Don't know

CQ6-12 (GRADE)

P: Patients with sepsis/ septic shock
I: Use of beta-blocker for rate control
C: Standard medication
O: Mortality (28 or 30 day, 90 day), length of ICU stay, length of hospital stay, serious adverse events (bradycardia, hypotension, arrythmia, organ dysfunction)

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Treatment	Placebo	Relative (95% CI)	Absolute (95% CI)		
Mortality (28 day)												
2	randomised trials	serious	not serious	very serious	serious	none	50/107 (46.7%)	104/137 (75.9%)	**RR 0.60** (0.48 to 0.75)	**304 fewer per 1,000** (from 395 fewer to 190 fewer)	⨁◯◯◯ Very low	CRITICAL
Length of ICU stay												
1	randomised trials	serious	not serious	not serious	serious	none	33	9	-	**MD 4 day fewer** (from 18.06 fewer to 10.06 more)	⨁⨁◯◯ Low	CRITICAL
Length of ICU treatment												
1	randomised trials	serious	not serious	serious	serious	none	30	30	-	**MD 4.1 day more** (from 1.8 more to 6.4 more)	⨁◯◯◯ Very low	CRITICAL
Serious adverse events (bradycardia)												
1	randomised trials	serious	not serious	serious	very serious	none	2/30 (6.7%)	0/30 (0.0%)	**RR 5.00** (0.25 to 99.95)	**0 fewer per 1,000** (from 0 fewer to 0 fewer)	⨁◯◯◯ Very low	CRITICAL
Serious adverse events (Use of renal replacement therapy)												
1	randomised trials	serious	not serious	not serious	very serious	none	31/77 (40.3%)	32/77 (41.6%)	**RR 0.97** (0.66 to 1.42)	**12 fewer per 1,000** (from 141 fewer to 175 more)	⨁◯◯◯ Very low	CRITICAL

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	**Large**		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	**Trivial**		Varies	Don't know
CERTAINTY OF EVIDENCE	**Very low**	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	**Favors the intervention**	Varies	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know