

CQ7-1 (GRADE)

P: Septic shock patients (initial fluid resuscitation and vasopressor did not archive target mean blood pressure)

I: Use of steroid (hydrocortisone)

C: Not use of hydrocortisone

O: Mortality, resolution of shock, serious adverse events, 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 day)												
9	randomised trials	not serious	not serious	very serious	not serious	none	917/3208 (28.6%)	982/3216 (30.5%)	RR 0.93 (0.87 to 1.01)	21 fewer per 1,000 (from 40 fewer to 3 more)	⊕⊕○○ Low	CRITICAL
Mortality (more than 90 day)												
5	randomised trials	not serious	not serious	serious	not serious	none	1019/2859 (35.6%)	1079/2857 (37.8%)	RR 0.94 (0.88 to 1.01)	23 fewer per 1,000 (from 45 fewer to 4 more)	⊕⊕⊕○ Moderate	CRITICAL
Resolution of shock												
5	randomised trials	not serious	very serious	serious	not serious	none	2323	2338	-	MD 31.53 hour fewer (from 36.6 fewer to 26.46 fewer)	⊕○○○ Very low	CRITICAL
Serious adverse events												
3	randomised trials	not serious	not serious	serious	not serious	none	350/2651 (13.2%)	384/2662 (14.4%)	RR 0.93 (0.84 to 1.03)	10 fewer per 1,000 (from 23 fewer to 4 more)	⊕⊕⊕○ Moderate	CRITICAL
Infection												
7	randomised trials	not serious	not serious	serious	not serious	none	584/2914 (20.0%)	559/2911 (19.2%)	RR 1.04 (0.94 to 1.16)	8 more per 1,000 (from 12 fewer to 31 more)	⊕⊕⊕○ Moderate	CRITICAL
Gastrointestinal bleeding												
6	randomised trials	not serious	not serious	serious	not serious	none	80/1079 (7.4%)	73/1082 (6.7%)	RR 1.09 (0.80 to 1.48)	6 more per 1,000 (from 13 fewer to 32 more)	⊕⊕⊕○ Moderate	CRITICAL
Hyperglycemia												
4	randomised trials	not serious	not serious	serious	not serious	none	773/2722 (28.4%)	709/2723 (26.0%)	RR 1.10 (1.05 to 1.15)	26 more per 1,000 (from 13 more to 39 more)	⊕⊕⊕○ Moderate	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

CQ7-2 (GRADE)

P: Septic shock patients (initial fluid resuscitation and vasopressor did not archive target mean blood pressure)

I: Use of hydrocortisone and fludrocortisone

C: Use of only hydrocortisone or placebo

O: Mortality, resolution of shock, serious adverse events, 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 day)												
2	randomised trials	not serious	not serious	not serious	not serious	none	289/764 (37.8%)	335/776 (43.2%)	RR 0.88 (0.78 to 0.99)	52 fewer per 1,000 (from 4 fewer to 95 fewer)	⊕⊕⊕⊕ High	CRITICAL
Mortality (Long-term)												
3	randomised trials	not serious	not serious	not serious	not serious	none	478/1009 (47.4%)	548/1040 (52.7%)	RR 0.90 (0.83 to 0.98)	53 fewer per 1,000 (from 11 fewer to 90 fewer)	⊕⊕⊕⊕ High	CRITICAL
Resolution of shock												
1	randomised trials	not serious	not serious	not serious	serious	none	83/150 (55.3%)	64/149 (43.0%)	RR 1.29 (1.02 to 1.63)	124 more per 1,000 (from 9 more to 271 more)	⊕⊕⊕○ Moderate	CRITICAL
Superinfection												
3	randomised trials	not serious	serious	not serious	serious	none	266/1009 (26.4%)	242/1039 (23.3%)	RR 1.14 (0.85 to 1.51)	33 more per 1,000 (from 35 fewer to 119 more)	⊕⊕○○ Low	CRITICAL
Gastrointestinal bleeding												
2	randomised trials	not serious	not serious	not serious	very serious	none	50/764 (6.5%)	53/775 (6.8%)	RR 0.96 (0.66 to 1.39)	3 fewer per 1,000 (from 23 fewer to 27 more)	⊕⊕○○ Low	CRITICAL
Hyperglycemia												
3	randomised trials	not serious	not serious	not serious	not serious	none	547/614 (89.1%)	520/626 (83.1%)	RR 1.07 (1.03 to 1.12)	58 more per 1,000 (from 25 more to 100 more)	⊕⊕⊕⊕ High	IMORTANT
Mental disorder												
3	randomised trials	not serious	not serious	not serious	very serious	none	0/150 (0%)	1/149 (0.7%)	RR 0.33 (0.01 to 8.06)	4 fewer per 1,000 (from 6 fewer to 47 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

CQ7-3 (GRADE)

P: Septic patients without shock

I: Use of hydrocortisone

C: Not use of hydrocortisone or use of placebo

O: Mortality, progress to shock, serious adverse events, 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 day)												
3	randomised trials	serious	not serious	not serious	very serious	none	25/217 (11.5%)	26/220 (11.8%)	RR 0.98 (0.59 to 1.63)	2 fewer per 1,000 (from 48 fewer to 74 more)	⊕○○○ Very low	CRITICAL
Mortality (Long-term)												
2	randomised trials	not serious	not serious	not serious	serious	none	38/191 (19.9%)	33/191 (17.3%)	RR 1.15 (0.76 to 1.76)	26 more per 1,000 (from 42 fewer to 131 more)	⊕⊕⊕○ Moderate	CRITICAL
Progress to shock												
1	randomised trials	not serious	not serious	not serious	very serious	none	36/179 (20.1%)	39/170 (22.9%)	RR 0.88 (0.59 to 1.31)	27 fewer per 1,000 (from 94 fewer to 71 more)	⊕⊕○○ Low	CRITICAL
Infection												
1	randomised trials	not serious	not serious	not serious	serious	none	40/186 (21.5%)	32/189 (16.9%)	RR 1.27 (0.84 to 1.93)	46 more per 1,000 (from 27 fewer to 157 more)	⊕⊕⊕○ Moderate	CRITICAL
Gastrointestinal bleeding												
1	randomised trials	not serious	not serious	not serious	very serious	none	3/186 (1.6%)	2/189 (1.1%)	RR 1.52 (0.26 to 9.02)	6 more per 1,000 (from 8 fewer to 85 more)	⊕⊕○○ Low	CRITICAL
Hypnatremia												
1	randomised trials	not serious	not serious	not serious	very serious	none	10/186 (5.4%)	10/189 (5.3%)	RR 1.02 (0.43 to 2.38)	1 more per 1,000 (from 30 fewer to 73 more)	⊕⊕○○ Low	CRITICAL
Hyperglycemia												
1	randomised trials	not serious	not serious	not serious	not serious	none	169/186 (90.9%)	154/189 (81.5%)	RR 1.12 (1.03 to 1.21)	98 more per 1,000 (from 24 fewer to 171 more)	⊕⊕⊕⊕ High	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