CQ4-4 (UnGRADE)

P: Patients who suspected sepsis/ septic shock/ severe infection
I: Discontinuation of antimicrobial drugs when culture negative is found
C: Continuation of antimicrobial drugs after culture negative is found
O: Mortality, length of hospital stay, infection

	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

CQ4-6 (GRADE)

P: Patients with sepsis/ septic shock
I: Administration of antimicrobial drugs within 1 hour
C: Administration of antimicrobial drugs after 1 hour
O: Mortality

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												
7	Observational study	very serious	not serious	not serious	not serious	none	1994/6458 (30.9%)	5411/16556 (32.7%)	**RR 0.97** (0.93 to 1.02)	**10 fewer per 1,000** (from 23 fewer to 7 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

CQ4-7 (GRADE)

P: Patients with sepsis/ septic shock
I: Continuous infusion of beta-lactam antibiotic
C: Intermittent infusion of beta-lactam antibiotic
O: Mortality, clinical cure, side effect, drug-resistant bacterium, achieved target blood concentration

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												
9	randomised trials	serious	not serious	not serious	serious	none	88/420 (21.0%)	112/424 (26.4%)	**RR 0.74** (0.49 to 1.12)	**69 fewer per 1,000** (from 135 fewer to 32 more)	⨁⨁◯◯ Low	CRITICAL
Clinical cure												
9	randomised trials	serious	not serious	not serious	not serious	Publication bias was suggested	245/443 (55.3%)	209/443 (47.2%)	**RR 1.24** (1.02 to 1.51)	**113 more per 1,000** (from 9 more to 241 more)	⨁⨁◯◯ Low	CRITICAL
Side effect												
3	randomised trials	serious	not serious	not serious	not serious	none	42/342 (12.3%)	43/349 (12.3%)	**RR 1.00** (0.67 to 1.48)	**0 fewer per 1,000** (from 41 fewer to 59 more)	⨁⨁⨁◯ Moderate	CRITICAL
Drug-resistant bacterium												
1	randomised trials	serious	not serious	not serious	serious	none	2/96 (2.1%)	4/102 (3.9%)	**RR 0.53** (0.10 to 2.83)	**18 fewer per 1,000** (from 35 fewer to 72 more)	⨁⨁◯◯ Low	CRITICAL
Achieved target blood concentration												
2	randomised trials	serious	not serious	not serious	not serious	none	71/90 (78.9%)	29/87 (33.3%)	**RR 2.35** (1.71 to 3.22)	**450 more per 1,000** (from 237 more to 740 more)	⨁⨁⨁◯ Moderate	IMPORTANT

	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

CQ4-8 (GRADE)

P: Patients with sepsis/ septic shock
I: De-escalation
C: Not de-escalation
O: Mortality (90-day, 28-day, longest observation period), superinfection

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 (90-day)												
1	randomised trials	serious	not serious	not serious	very serious	none	18/59 (30.5%)	13/57 (22.8%)	**RR 1.34** (0.72 to 2.47)	**78 more per 1,000** (from 64 fewer to 335 more)	⨁◯◯◯ Very low	CRITICAL
Superinfection												
1	randomised trials	serious	not serious	not serious	serious	none	6/57 (27.1%)	6/57 (10.5%)	**RR 2.58** (1.08 to 6.12)	**166 more per 1,000** (from 8 more to 539 more)	⨁⨁◯◯ Low	CRITICAL
Mortality (longest observation period)												
13	observational study	serious	serious	not serious	not serious	none	229/1337 (17.1%)	544/2298 (23.7%)	**RR 0.66** (0.52 to 0.83)	**80 fewer per 1,000** (from 114 fewer to 40 fewer)	⨁◯◯◯ Very low	CRITICAL
Mortality (28-day)												
2	observational study	serious	serious	not serious	serious	none	15/244 (6.1%)	45/261 (17.2%)	**RR 0.48** (0.12 to 1.84)	**90 fewer per 1,000** (from 152 fewer to 145 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

CQ4-9 (GRADE)

P: Patients with sepsis/ septic shock
I: Procalcitonin guided discontinuation
C: Not use procalcitonin guide
O: Mortality (28-day, hospital), recurrence of sepsis, duration of administration of antibacterial drugs

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)												
5	randomised trials	serious	not serious	not serious	not serious	none	320/1434 (22.3%)	379/1433 (26.4%)	**RR 0.84** (0.74 to 0.96)	**42 fewer per 1,000** (from 69 fewer to 11 fewer)	⨁⨁⨁◯ Moderate	CRITICAL
Mortality (Hospital)												
9	randomised trials	serious	not serious	not serious	not serious	none	256/1197 (21.4%)	321/1225 (26.2%)	**RR 0.81** (0.70 to 0.93)	**50 fewer per 1,000** (from 79 fewer to 18 fewer)	⨁⨁⨁◯ Moderate	CRITICAL
Recurrence of sepsis												
4	randomised trials	serious	not serious	not serious	serious	none	7/126 (5.6%)	6/135 (4.4%)	**RR 1.19** (0.40 to 3.55)	**8 more per 1,000** (from 27 fewer to 113 more)	⨁⨁◯◯ Low	CRITICAL
Duration of administration of antibacterial drugs												
3	randomised trials	serious	serious	not serious	serious	none	120	111	-	**MD 1.16 day fewer** (from 2.33 fewer to 0 fewer)	⨁◯◯◯ 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

CQ4-10 (GRADE)

P: Patients with sepsis/ septic shock, Infectious patients who treated in ICU
I: Short-term antibiotic therapy (1 week)
C: Long-term antibiotic therapy (more than 1 week)
O: Mortality (28-day, longest observational period), clinical cure, recurrence of sepsis, drug-resistant bacterium

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	not serious	not serious	not serious	serious	none	63/396 (15.9%)	61/408 (15.0%)	**RR 1.08** (0.77 to 1.52)	**12 more per 1,000** (from 34 fewer to 78 more)	⨁⨁⨁◯ Moderate	CRITICAL
Mortality (Longest observational period)												
4	randomised trials	serious	not serious	not serious	serious	none	73/512 (14.3%)	70/517 (13.5%)	**RR 1.08** (0.80 to 1.46)	**11 more per 1,000** (from 27 fewer to 62 more)	⨁⨁◯◯ Low	CRITICAL
Clinical cure												
2	randomised trials	serious	not serious	not serious	serious	none	135/195 (69.2%)	142/197 (72.1%)	**RR 0.93** (0.72 to 1.20)	**50 fewer per 1,000** (from 202 fewer to 144 more)	⨁⨁◯◯ Low	CRITICAL
Recurrence of sepsis												
3	randomised trials	serious	serious	not serious	serious	none	120/433 (27.7%)	89/429 (20.7%)	**RR 1.37** (1.00 to 1.89)	**77 more per 1,000** (from 0 fewer to 185 more)	⨁◯◯◯ Very low	CRITICAL
Drug-resistant bacterium												
2	randomised trials	serious	not serious	not serious	serious	none	49/127 (38.6%)	58/119 (48.7%)	**RR 0.73** (0.40 to 1.34)	**132 fewer per 1,000** (from 292 fewer to 166 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