

CQ11-1 (GRADE)

P: Septic AKI patients/ Critically ill patients with AKI

I: Furosemide

C: Placebo or standard treatment, no intervention

O: Mortality, renal replacement therapy, resolution of AKI, duration of AKI

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 (hospital)												
6	randomised trials	not serious	not serious	serious	serious	none	124/338 (36.7%)	100/311 (32.2%)	RR 1.12 (0.92 to 1.38)	39 more per 1,000 (from 26 fewer to 122 more)	⊕⊕○○ Low	CRITICAL
Renal replacement therapy												
3	randomised trials	not serious	serious	serious	very serious	none	35/105 (33.3%)	29/101 (28.7%)	RR 1.14 (0.64 to 2.04)	40 more per 1,000 (from 103 fewer to 299 more)	⊕○○○ Very low	CRITICAL
Resolution of AKI												
5	randomised trials	not serious	not serious	serious	serious	none	146/304 (48.0%)	158/298 (53.0%)	RR 0.91 (0.78 to 1.05)	48 fewer per 1,000 (from 117 fewer to 27 more)	⊕⊕○○ Low	IMPORTANT
Duration of AKI (duration of renal replacement therapy)												
3	randomised trials	not serious	not serious	serious	serious	none	234	229	-	MD 0.67 day lower (from 2.36 lower to 1.01 higher)	⊕⊕○○ Low	IMPORTANT
Hearing impairment												
3	randomised trials	not serious	not serious	serious	very serious	none	4/235 (1.7%)	2/230 (0.9%)	RR 1.68 (0.34 to 8.22)	6 more per 1,000 (from 6 fewer to 63 more)	⊕○○○ Very low	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

CQ11-2 (GRADE)

P: Septic AKI patients/ Critically ill patients with AKI

I: ANP

C: Placebo or standard treatment, no intervention

O: Mortality, renal replacement therapy, length of ICU stay, resolution of AKI, complication (hypotension)

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 (hospital)												
3	randomised trials	not serious	not serious	serious	serious	none	143/386 (37.0%)	139/393 (35.4%)	RR 1.05 (0.84 to 1.31)	18 more per 1,000 (from 57 fewer to 110 more)	⊕⊕○○ Low	CRITICAL
Renal replacement therapy												
3	randomised trials	not serious	serious	serious	serious	none	188/386 (48.7%)	206/393 (52.4%)	RR 0.89 (0.70 to 1.14)	58 fewer per 1,000 (from 157 fewer to 73 more)	⊕○○○ Very low	CRITICAL
Resolution of AKI												
2	randomised trials	not serious	serious	serious	serious	none	130/357 (36.4%)	138/371 (37.2%)	RR 1.05 (0.70 to 1.59)	19 more per 1,000 (from 112 fewer to 219 more)	⊕○○○ Very low	IMPORTANT
Hypotension												
3	randomised trials	not serious	serious	serious	not serious	none	217/386 (56.2%)	109/393 (27.7%)	RR 2.06 (1.37 to 3.09)	294 more per 1,000 (from 103 more to 580 more)	⊕⊕○○ Low	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





CQ11-3 (GRADE)

P: Septic AKI patients/ Critically ill patients with AKI

I: Dopamine

C: Placebo or standard treatment, no intervention

O: Mortality, renal replacement therapy, resolution of AKI, complication (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 (hospital)												
1	randomised trials	not serious	not serious	not serious	serious	none	69/161 (42.9%)	66/163 (40.5%)	RR 1.06 (0.82 to 1.37)	24 more per 1,000 (from 73 fewer to 150 more)	 Moderate	CRITICAL
Mortality (ICU)												
1	randomised trials	not serious	not serious	not serious	serious	none	53/161 (32.9%)	58/163 (35.6%)	RR 0.93 (0.68 to 1.25)	25 fewer per 1,000 (from 114 fewer to 89 more)	 Moderate	CRITICAL
Renal replacement therapy												
1	randomised trials	not serious	not serious	not serious	very serious	none	35/161 (21.7%)	40/163 (24.5%)	RR 0.89 (0.60 to 1.32)	27 fewer per 1,000 (from 98 fewer to 79 more)	 Low	CRITICAL
Arrythmia												
1	randomised trials	not serious	not serious	not serious	very serious	none	53/161 (32.9%)	54/163 (33.1%)	RR 0.99 (0.73 to 1.35)	3 fewer per 1,000 (from 89 fewer to 116 more)	 Low	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

CQ11-4 (GRADE)

P: Septic AKI patients/ Critically ill patients with AKI

I: Continuous renal replacement therapy

C: Intermittent renal replacement therapy

O: Mortality, dialysis dependence, composite outcome (mortality and dialysis dependence), complication

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												
4	randomised trials	serious	not serious	serious	not serious	none	256/419 (61.1%)	262/419 (62.5%)	RR 0.99 (0.89 to 1.10)	6 fewer per 1,000 (from 69 fewer to 63 more)	⊕⊕○○ Low	CRITICAL
Dialysis dependence												
2	randomised trials	serious	not serious	serious	very serious	none	5/98 (5.1%)	8/103 (7.8%)	RR 0.64 (0.22 to 1.87)	28 fewer per 1,000 (from 61 fewer to 68 more)	⊕○○○ Very low	CRITICAL
Composite outcome (mortality and dialysis dependence)												
1	randomised trials	serious	not serious	serious	very serious	none	34/70 (48.6%)	29/55 (52.7%)	RR 0.92 (0.65 to 1.30)	42 fewer per 1,000 (from 185 fewer to 158 more)	⊕○○○ Very low	CRITICAL
Bleeding												
2	randomised trials	serious	not serious	serious	very serious	none	16/297 (5.4%)	18/312 (5.8%)	RR 0.94 (0.49 to 1.80)	3 fewer per 1,000 (from 29 fewer to 46 more)	⊕○○○ Very low	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

CQ11-5-1 (GRADE)

P: Septic AKI patients/ Critically ill patients with AKI

I: Stage 2

C: Stage 3 or classic absolute indications

O: Mortality, dialysis dependence, composite outcome (mortality and dialysis dependence)

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 (Longest observational period)												
1	randomised trials	not serious	not serious	serious	serious	none	56/111 (50.5%)	83/119 (69.7%)	RR 0.72 (0.58 to 0.90)	195 fewer per 1,000 (from 293 fewer to 70 fewer)	⊕⊕○○ Low	CRITICAL
Dialysis dependence (Longest observational period)												
1	randomised trials	not serious	not serious	serious	very serious	none	4/55 (7.3%)	4/36 (11.1%)	RR 0.65 (0.17 to 2.45)	39 fewer per 1,000 (from 92 fewer to 161 more)	⊕○○○ Very low	IMPORTANT
Mortality or dialysis dependence (Longest observational period)												
1	randomised trials	not serious	not serious	serious	serious	none	60/111 (54.1%)	87/119 (73.1%)	RR 0.74 (0.60 to 0.91)	190 fewer per 1,000 (from 292 fewer to 66 fewer)	⊕⊕○○ 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

CQ11-5-2 (GRADE)

P: Septic AKI patients/ Critically ill patients with AKI

I: Stage 3

C: Classic absolute indications

O: Mortality, dialysis dependence, composite outcome (mortality and dialysis dependence), complication

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												
2	randomised trials	not serious	not serious	not serious	not serious	none	293/547 (53.6%)	287/543 (52.9%)	RR 1.02 (0.91 to 1.14)	11 more per 1,000 (from 48 fewer to 74 more)	⊕⊕⊕⊕ High	CRITICAL
Bleeding												
2	randomised trials	very serious	not serious	not serious	serious	none	39/557 (7.0%)	51/550 (9.3%)	RR 0.76 (0.51 to 1.13)	22 fewer per 1,000 (from 45 fewer to 12 more)	⊕○○○ Very low	CRITICAL
Dialysis dependence												
2	randomised trials	very serious	not serious	not serious	very serious	none	5/258 (1.9%)	11/265 (4.2%)	RR 0.47 (0.16 to 1.34)	22 fewer per 1,000 (from 35 fewer to 14 more)	⊕○○○ Very low	IMPORTANT
Mortality or dialysis dependence												
2	randomised trials	very serious	not serious	not serious	not serious	none	293/550 (53.3%)	292/546 (53.5%)	RR 1.00 (0.89 to 1.13)	0 fewer per 1,000 (from 59 fewer to 70 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

CQ11-6 (GRADE)

P: Septic AKI patients/ Critically ill patients with AKI

I: High dose renal replacement therapy

C: Low dose renal replacement therapy

O: Mortality, dialysis dependence, composite outcome (mortality and dialysis dependence), complication

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												
3	randomised trials	not serious	not serious	serious	not serious	none	644/1385 (46.5%)	623/1404 (44.4%)	RR 1.05 (0.97 to 1.13)	22 more per 1,000 (from 13 fewer to 58 more)	⊕⊕○○ Low	CRITICAL
Dialysis dependence												
3	randomised trials	serious	not serious	serious	not serious	none	494/1032 (47.9%)	468/1064 (44.0%)	RR 1.05 (0.98 to 1.13)	22 more per 1,000 (from 9 fewer to 57 more)	⊕⊕○○ Low	CRITICAL
Composite outcome (mortality and dialysis dependence)												
3	randomised trials	serious	not serious	serious	not serious	none	889/1382 (64.3%)	868/1404 (61.8%)	RR 1.02 (0.98 to 1.07)	12 more per 1,000 (from 12 fewer to 43 more)	⊕⊕○○ Low	CRITICAL
Hypophosphatemia												
2	randomised trials	serious	not serious	serious	not serious	none	560/1271 (44.1%)	457/1294 (35.3%)	RR 1.35 (1.01 to 1.81)	124 more per 1,000 (from 4 more to 286 more)	⊕⊕○○ Low	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

CQ11-7 (GRADE)

P: Septic patients

I: PMX-DHP

C: Not use of PMX-DHP, standard treatment

O: Mortality, adverse events, organ injury score (72 hours), catecholamine free days

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												
3	randomised trials	not serious	very serious	not serious	serious	none	167/373 (44.8%)	138/359 (38.4%)	RR 1.03 (0.68 to 1.58)	12 more per 1,000 (from 123 fewer to 223 more)	⊕○○○ Very low	CRITICAL
Adverse events												
2	randomised trials	not serious	not serious	serious	not serious	none	93/343 (27.1%)	82/339 (24.2%)	RR 1.07 (0.92 to 1.24)	17 more per 1,000 (from 19 fewer to 58 more)	⊕⊕⊕○ Moderate	CRITICAL
Organ injury score												
2	randomised trials	not serious	not serious	not serious	not serious	none	343	339	-	MD 0.01 higher (from 0.37 lower to 0.4 higher)	⊕⊕⊕⊕ High	IMPORTANT
Catecholamine free days												
1	randomised trials	serious	not serious	not serious	serious	none	119	113	-	MD 1.8 day lower (from 4.14 lower to 0.54 higher)	⊕⊕○○ Low	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