

Supplement 8 | Clinical Evidence Profiles (GRADE tables)

Key question 1.1.

Clinical evidence profiles: clinical outcomes of early vs. late commencement of hemodialysis based on eGFR

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Early	Late	Relative (95% CI)	Absolute (95% CI)		
All-cause mortality: events - HD or PD												
1	randomized trials	serious ^a	not serious	not serious	not serious	none	152/404 (37.6%)	155/424 (36.6%)	RR 1.03 (0.86 to 1.23)	11 more per 1,000 (from 51 fewer to 84 more)	⊕⊕⊕○ MODERATE	CRITICAL
All-cause mortality: events - HD planned												
1	randomized trials	serious ^{a,b}	not serious	not serious	serious ^c	none	50/171 (29.2%)	59/191 (30.9%)	RR 0.95 (0.69 to 1.30)	15 fewer per 1,000 (from 96 fewer to 93 more)	⊕⊕○○ LOW	IMPORTANT
All-cause mortality: time to event - HD or PD												
1	randomized trials	serious ^a	not serious	not serious	serious ^c	none	152/404 (37.6%)	155/424 (36.6%)	HR 1.04 (0.83 to 1.30)	11 more per 1,000 (from 51 fewer to 81 more)	⊕⊕○○ LOW	IMPORTANT
All-cause mortality: time to event - HD planned												
1	randomized trials	serious ^{a,b}	not serious	not serious	serious ^c	none	50/171 (29.2%)	59/191 (30.9%)	HR 0.97 (0.66 to 1.43)	8 fewer per 1,000 (from 93 fewer to 0)	⊕⊕○○ LOW	IMPORTANT

										102 more)		
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All-cause mortality: events - HD

3	observational studies	serious ^a	serious ^b	not serious	serious ^c	none	6292/17965 (35.0%)	8829/31790 (27.8%)	RR 1.62 (0.97 to 2.69)	172 more per 1,000 (from 8 fewer to 469 more)	⊕○○○ VERY LOW	IMPORTANT
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All-cause mortality: time to event - HD

3	observational studies	serious ^a	serious ^b	not serious	not serious	none			HR 1.31 (1.05 to 1.63)	1 fewer per 1,000 (from 2 fewer to 1 fewer)	⊕○○○ VERY LOW	NOT IMPORTANT
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All-cause mortality: 1mL/min/1.73m² GFR greater - HD or PD

3	observational studies	serious ^a	not serious	not serious	not serious	dose response gradient			HR 0.99 (0.88 to 1.11)	1 fewer per 1,000 (from 1 fewer to 1 fewer)	⊕⊕○○ LOW	IMPORTANT
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Hospitalization: average days - HD or PD

1	randomized trials	serious ^a	not serious	not serious	not serious	none	307	335	-	MD 8 higher (1.2 lower to 17.2 higher)	⊕⊕⊕○ MODERATE	CRITICAL
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Hospitalization: average contacts - HD or PD

1	randomized trials	serious ^{a,b}	not serious	not serious	not serious	none	307	335	-	MD 0 (0.93)	⊕⊕⊕○ MODERATE	CRITICAL
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											lower to 0.93 higher)		
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Non-admitted hospital visits - HD or PD

1	randomized trials	very serious ^{a,b}	not serious	not serious	not serious	none	307	335	-	MD 0 (2.73 lower to 2.73 higher)	⊕⊕○○ LOW	IMPORTANT
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Visit to health care professional - HD or PD

1	randomized trials	very serious ^{a,b}	not serious	not serious	not serious	none	307	335	-	MD 0 (2.73 lower to 2.73 higher)	⊕⊕○○ LOW	IMPORTANT
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Composite cardiovascular events - HD or PD

1	randomized trials	serious ^a	not serious	not serious	serious ^b	none	139/404 (34.4%)	127/424 (30.0%)	RR 1.15 (0.94 to 1.40)	45 more per 1,000 (from 18 fewer to 120 more)	⊕⊕○○ LOW	CRITICAL
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Composite cardiovascular events - HD planned

1	randomized trials	serious ^{a,b}	not serious	not serious	serious ^c	none	50/171 (29.2%)	51/191 (26.7%)	RR 1.10 (0.79 to 1.52)	27 more per 1,000 (from 56 fewer to 139 more)	⊕⊕○○ LOW	IMPORTANT
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Composite Infectious events (death or hospitalization from infection) - HD or PD

1	randomized	serious ^a	not serious	not serious	serious ^c	none	148/404	174/424	RR 0.89	45	⊕⊕○○	IMPORTANT
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	trials						(36.6%)	(41.0%)	(0.75 to 1.06)	fewer per 1,000 (from 103 fewer to 25 more)	LOW	
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Composite Infectious events (death or hospitalization from infection) - HD planned

1	randomized trials	serious ^{a,b}	not serious	not serious	serious ^c	none	60/171 (35.1%)	72/191 (37.7%)	RR 0.93 (0.71 to 1.22)	26 fewer per 1,000 (from 109 fewer to 83 more)	⊕⊕○○ LOW	IMPORTANT
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Complications of dialysis: need for access revision - HD or PD

1	randomized trials	serious ^a	not serious	not serious	serious ^c	none	145/404 (35.9%)	147/424 (34.7%)	RR 1.04 (0.86 to 1.25)	14 more per 1,000 (from 49 fewer to 87 more)	⊕⊕○○ LOW	IMPORTANT
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Complications of dialysis: need for access revision - HD planned

1	randomized trials	very serious ^{a,b}	not serious	not serious	serious ^c	none	73/171 (42.7%)	75/191 (39.3%)	RR 1.09 (0.85 to 1.39)	35 more per 1,000 (from 59 fewer to 153 more)	⊕○○○ VERY LOW	IMPORTANT
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Complication of dialysis: access site infection - HD or PD

1	randomized trials	serious ^a	not serious	not serious	serious ^c	none	47/404 (11.6%)	50/424 (11.8%)	RR 0.99 (0.68 to 1.43)	1 fewer per 1,000 (from 38 fewer to 51 more)	⊕⊕○○ LOW	IMPORTANT
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Complication of dialysis: access site infection - HD planned

1	randomized trials	serious ^{a,b}	not serious	not serious	serious ^c	none	20/171 (11.7%)	27/191 (14.1%)	RR 0.83 (0.48 to 1.42)	24 fewer per 1,000 (from 74 fewer to 59 more)	⊕⊕○○ LOW	IMPORTANT
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Complication of dialysis: serious fluid or electrolytes disorder - HD or PD

1	randomized trials	serious ^a	not serious	not serious	not serious	none	146/404 (36.1%)	175/424 (41.3%)	RR 0.88 (0.74 to 1.04)	50 fewer per 1,000 (from 107 fewer to 17 more)	⊕⊕⊕○ MODERATE	IMPORTANT
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Complication of dialysis: serious fluid or electrolytes disorder - HD planned

1	randomized trials	serious ^{a,b}	not serious	not serious	not serious	none	44/171 (25.7%)	73/191 (38.2%)	RR 0.67 (0.49 to 0.92)	126 fewer per 1,000 (from 195 fewer to 31 fewer)	⊕⊕⊕○ MODERATE	IMPORTANT
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Complication of dialysis: placement of temporary dialysis catheter - HD or PD

1	randomized trials	serious ^a	not serious	not serious	not serious	none	118/404 (29.2%)	124/424 (29.2%)	RR 1.00 (0.81 to 1.23)	0 fewer per 1,000 (from 56 fewer to 67 more)	⊕⊕⊕○ MODERATE	IMPORTANT
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Complication of dialysis: placement of temporary dialysis catheter - HD planned

1	randomized trials	serious ^{a,b}	not serious	not serious	serious ^c	none	39/171 (22.8%)	41/191 (21.5%)	RR 1.06 (0.72 to 1.56)	13 more per 1,000 (from 60 fewer to 120 more)	⊕⊕○○ LOW	IMPORTANT
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Echocardiographic endpoint: Left ventricular ejection fraction (%)

1	randomized trials	very serious ^{a,b}	not serious	not serious	serious ^c	none	91	91	-	MD 0 (5.23 lower to 5.23 higher)	⊕○○○ VERY LOW	IMPORTANT
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Echocardiographic endpoint: Left ventricular mass index (g/m²)

1	randomized trials	very serious ^{a,b}	not serious	not serious	serious ^c	none	91	91	-	MD 11.4 lower (23.09 lower to 0.29 higher)	⊕○○○ VERY LOW	IMPORTANT
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Echocardiographic endpoint: Left atrial volume index (mL/m²)

1	randomized trials	very serious ^{a,b}	not serious	not serious	serious ^c	none	91	91	-	MD 0.6 lower	⊕○○○ VERY LOW	IMPORTANT
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										(7.03 lower to 5.83 higher)		
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CI: Confidence interval; MD: Mean difference

Explanations

a. High risk of bias in blinding, b. High risk of bias in the selection, c. Confidence interval crossed minimally important difference

Key question 1.2.

Not applicable

Key question 2.1.

Clinical evidence profiles: clinical outcomes of <4 hours vs. ≥4 hours dialysis time per sessions

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	<4hour per session	4hours per session	Relative (95% CI)	Absolute (95% CI)		

Overall Mortality_RCT

2	randomized trials	not serious	not serious	not serious	serious	none	566/2610 (21.7%)	427/2011 (21.2%)	OR 1.02 (0.88 to 1.18)	3 more per 1,000 (from 21 fewer to 29 more)	⊕⊕⊕○ MODERATE	CRITICAL
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Hospitalization

2	randomized trials	not serious	not serious	not serious	not serious	publication bias strongly suspected	1831/2610 (70.2%)	1387/2011 (69.0%)	OR 1.38 (0.67 to 2.87)	64 more per 1,000 (from 91 fewer to 175 more)	⊕⊕⊕○ MODERATE	CRITICAL
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Overall Mortality: Time to event

4	observational studies	not serious	not serious	not serious	not serious	none	-/0	-/0	OR 1.34 (1.15 to 1.55)	1 fewer per 1,000 (from 2 fewer to 1 fewer)	⊕⊕○○ LOW	IMPORTANT
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Overall Mortality: 2/week vs 3/week

3	observational studies	not serious	not serious	not serious	not serious	none	-/0	-/0	2.02 (1.01 to 4.07)	-- per 1,000 (from -- to --)	⊕⊕○○ LOW	IMPORTANT
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Key question 2.2.

Clinical evidence profiles: high-dose dialysis versus low-dose dialysis for ESRD patients

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	High dose	Low dose	Relative (95% CI)	Absolute (95% CI)		

Mortality

11	observational studies	not serious	not serious	serious ^a	not serious	dose response gradient	In total, 11 observational studies consistently reported that low dialysis dose, which was evaluated using spKt/V, eKt/V, or URR, was associated increased mortality in adult ESRD patients maintaining hemodialysis. However, the relationship between high-dose dialysis, eKt/V>1.4 or spKt/V>1.6, and mortality showed heterogeneity between studies.		⊕⊕○○ LOW	IMPORTANT
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Mortality

1	randomized trials	not serious	not serious	not serious	serious ^b	none	431/920 (46.8%)	440/926 (47.5%)	OR 0.97 (0.81 to 1.17)	8 fewer per 1,000 (from 52 fewer to 39 more)	⊕⊕⊕○ MODERATE	CRITICAL
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CI: Confidence interval; **OR:** Odds ratio

Explanations

- a. Some studies presented relationship between dialysis dose and mortality only in subgroups according to body mass index or sex, not for all cohort patients.
- b. There was a high risk of imprecision because only one randomized controlled trial was included for this issue.

Key question 3.1.

Clinical evidence profiles: high-flux compared to low-flux membranes for end-stage kidney disease

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	High-flux	low-flux membranes	Relative (95% CI)	Absolute (95% CI)		
All-cause mortality												
10	randomized trials	not serious	not serious	not serious	not serious	none	599/1789 (33.5%)	662/1860 (35.6%)	RR 0.87 (0.76 to 0.99)	46 fewer per 1,000 (from 85 fewer to 4 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Cardiovascular mortality												
5	randomized trials	not serious	not serious	not serious	not serious	none	234/1644 (14.2%)	288/1652 (17.4%)	RR 0.81 (0.70 to 0.95)	33 fewer per 1,000 (from 52 fewer to 9 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Hospitalization - Any cause												
2	randomized trials					none	20/64 (31.3%)	18/60 (30.0%)	RR 0.80 (0.53 to 1.22)	60 fewer per 1,000 (from 141 fewer to 66 more)	-	IMPORTANT

Predialysis β-2 microglobulin

6	randomized trials					none	1371	1378	-	MD 9.9 lower (12.14 lower to 7.65 lower)	-	IMPORTANT
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Equilibrated Kt/Vurea

4	randomized trials					none	1332	1340	-	MD 0 (0.02 lower to 0.01 higher)	-	IMPORTANT
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CI: Confidence interval; RR: Risk ratio; MD: Mean difference

Key question 3.2.

Online hemodiafiltration compared to High-flux hemodialysis for outcomes

Certainty assessment							N ^o of patients		Effect		Certainty	Importance
N ^o of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Online hemodiafiltration	High-flux hemodialysis	Relative (95% CI)	Absolute (95% CI)		

Overall mortality

2	randomized trials	serious ^{1,a}	not serious	not serious	not serious	none	88/581 (15.1%)	108/582 (18.6%)	OR 0.78 (0.57 to 1.07)	35 fewer per 1,000 (from 71 fewer to 10 more)	⊕⊕⊕○ MODERATE	CRITICAL
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Hospitalization rate

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Online hemodiafiltration	High-flux hemodialysis	Relative (95% CI)	Absolute (95% CI)		
2	randomized trials	serious ^a	very serious ^b	not serious	not serious	none	456/1313 (34.7%)	449/1311 (34.2%)	RR 1.01 (0.93 to 1.10)	3 more per 1,000 (from 24 fewer to 34 more)	⊕○○○ VERY LOW	IMPORTANT

CI: Confidence interval; OR: Odds ratio; RR: Risk ratio

Key question 4.1.

Clinical evidence profiles: clinical outcomes of LMWH vs. UFH of hemodialysis

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	low molecular weight heparin (LMWH)	unfractionated heparin (UFH)	Relative (95% CI)	Absolute (95% CI)		

Outcome: bleeding complications

6	randomized trials	serious ^a	not serious	not serious	not serious	none	21/219 (9.6%)	27/219 (12.3%)	RR 0.74 (0.24 to 2.31)	32 fewer per 1,000 (from 94 fewer to 162 more)	⊕⊕⊕○ MODERATE	CRITICAL
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Outcome: circuit thrombosis

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	low molecular weight heparin (LMWH)	unfractionated heparin (UFH)	Relative (95% CI)	Absolute (95% CI)		
3	randomized trials	serious ^a	serious ^b	not serious	not serious	none	129/6534 (2.0%)	125/6720 (1.9%)	RR 0.99 (0.56 to 1.77)	0 fewer per 1,000 (from 8 fewer to 14 more)	⊕⊕○○ LOW	CRITICAL

CI: Confidence interval; **RR:** Risk ratio

Explanations

a. no description of randomization process and blinding of participants and/or researchers

b. significant heterogeneity within studies

Key question 4.2.

Not applicable

Key question 5.1.

Clinical evidence profiles: increased inter-dialytic weight gain (IDWG) of reference value as risk factor for mortality

Certainty assessment							Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations		

IDWG: Prospective observational study

Certainty assessment							Certainty	Importance
Nº of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations		
7	Prospective observational study	serious	not serious	not serious	not serious	none	⊕⊕⊕○ MODERATE	CRITICAL

IDWG: Retrospective study

5	Retrospective study	serious	not serious	not serious	serious	none	⊕⊕○○ LOW	CRITICAL
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Key question 5.2.

Clinical evidence profiles: clinical outcomes of low vs. conventional dialysate sodium levels for chronic hemodialysis

Certainty assessment							Nº of patients		Effect		Certainty	Importance
Nº of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Low dialysate	placebo	Relative (95% CI)	Absolute (95% CI)		
3	randomized trials	not serious	not serious	not serious	serious	none	84	85	-	MD 0.37 higher (0.11 higher to 0.62 higher)	⊕⊕⊕○ MODERATE	

Interdialytic weight gain

4	observational studies	not serious	not serious	not serious	not serious	publication bias strongly suspected	96	96	-	MD 0.6 higher (0.34 higher to 0.86 higher)	⊕○○○ VERY LOW	
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Predialysis BP

1	randomized trials	not serious	not serious	not serious	serious	publication bias strongly suspected	18	20	-	MD 12.02 higher (0.74 lower to 24.78 higher)	⊕⊕○○ LOW	
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Predialysis BP

3	observational studies	not serious	not serious	not serious	not serious	publication bias strongly suspected	37	37	-	MD 15.6 higher (4.52 higher to 26.69 higher)	⊕○○○ VERY LOW	
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Antihypertensive medication

1	randomized trials	not serious	not serious	not serious	serious	publication bias strongly suspected	29	28	-	MD 1.5 higher (0.23 higher to 2.77 higher)	⊕⊕○○ LOW	
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Echocardiographic parameter - Posterior wall thickness (mm)

2	observational studies	not serious	not serious	not serious	not serious	publication bias strongly suspected	67	67	-	MD 0.14 higher (0.29 lower to 0.57 higher)	⊕○○○ VERY LOW	
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Echocardiographic parameter - LV ejection fraction (%)

2	observational studies	not serious	not serious	not serious	not serious	publication bias strongly suspected	67	67	-	MD 1.32 lower (4.55 lower to 1.92 higher)	⊕○○○ VERY LOW	
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Echocardiographic parameter - pulmonary artery pressure (mmHg)

2	observational studies	not serious	not serious	not serious	not serious	publication bias strongly suspected	67	67	-	MD 7.14 higher (2.67 higher to 11.61 higher)	⊕○○○ VERY LOW	
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Echocardiographic parameter - inferior vena cava diameter (mm)

2	observational studies	not serious	not serious	not serious	not serious	publication bias strongly suspected	67	67	-	MD 2.17 higher (1.62 higher to 2.72 higher)	⊕○○○ VERY LOW	
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Predialysis serum [Na⁺]

2	observational studies	not serious	not serious	not serious	not serious	publication bias strongly suspected	29	29	-	MD 0.4 higher (0.5 lower to 1.3 higher)	⊕○○○ VERY LOW	
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Key question 6.1.

Not applicable

Key question 6.2.

Clinical evidence profiles: cool dialysate compared to Standard dialysate for Hemodialysis patients

Certainty assessment							Impact	Certainty	Importance
Nº of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			

Intradialytic hypotension: RCT

4	Randomized trials	serious	not serious	not serious	not serious	none	In total 4 randomized crossover trial, cool dialysate reduced intradialytic hypotension compared with standard dialysate.	⊕⊕⊕○ MODERATE	CRITICAL
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Intradialytic hypotension: non-RCT

2	Observational studies	serious	not serious	not serious	not serious	none	In total 2 observational studies, cool dialysate reduced intradialytic hypotension compared with standard dialysate.	⊕⊕⊕○ MODERATE	CRITICAL
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Key question 7.1.

Not applicable

Key question 8.1.

Clinical evidence profiles: dialysis vs. conservative treatment for elderly ESRD patients.

Certainty assessment							Nº of patients		Effect		Certainty	Importance
Nº of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Dialysis	conservative treatment	Relative (95% CI)	Absolute (95% CI)		

Mortality

11	observational studies	not serious	not serious	serious	not serious	none	1401/3274 (42.8%)	1092/1735 (62.9%)	OR 0.42 (0.37 to 0.47)	213 fewer per 1,000 (from 244 fewer to 186 fewer)	⊕⊕⊕○ MODERATE	CRITICAL
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Prospective cohort data only

4	observational studies	not serious	not serious	serious	not serious	none	231/761 (30.4%)	191/321 (59.5%)	OR 0.20 (0.15 to 0.28)	368 fewer per 1,000 (from 414 fewer to 304 fewer)	⊕⊕⊕○ MODERATE	CRITICAL
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Retrospective data only

7	observational studies	not serious	not serious	serious	not serious	none	1170/2513 (46.6%)	901/1414 (63.7%)	OR 0.48 (0.42 to 0.56)	180 fewer per 1,000 (from 213 fewer to 141 fewer)	⊕⊕⊕○ MODERATE	IMPORTANT
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CI: Confidence interval; **OR:** Odds ratio

Key question 8.2.

Not applicable