## **Supplement 9**| Forest Plots

# **Key question 1.1.**

#### 1.1. All-cause mortality: RCTs

### 1.1.1. All-cause mortality: events

	Earl	y	Late	•	Risk Ratio	Risk Ratio
Study or Subgroup	<b>Events</b>	Total	<b>Events</b>	Total	M-H, Fixed, 95% CI Year	M-H, Fixed, 95% CI
1.1.1 HD or PD						
Cooper 2010 (IDEAL trial)_HD or PD	152	404	155	424	1.03 [0.86, 1.23] 2010	+
1.1.2 HD planned Collins 2011 (IDEAL substudy)_HD planned	50	171	59	191	0.95 [0.69, 1.30] 2010	
						0.1 0.2 0.5 1 2 5 10 Favours [early] Favours [late]

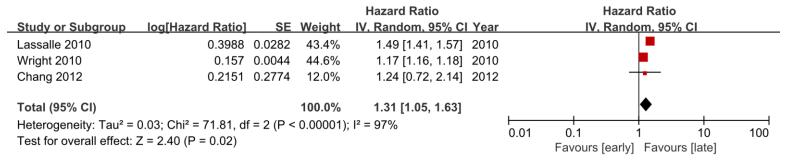
#### 1.1.2. All-cause mortality: time to event

			Early	Late	Hazard Ratio		H	lazard Ration	)	
Study or Subgroup	log[Hazard Ratio]	SE	Total	Total	IV, Fixed, 95% CI		IV,	Fixed, 95%	CI	
1.2.1 HD or PD										
Cooper 2010 (IDEAL trial)_HD or PD	0.0392	0.1151	404	424	1.04 [0.83, 1.30]			<b>†</b>		
1.2.2 HD planned										
Collins 2011 (IDEAL substudy)_HD planned	-0.0305	0.1965	171	191	0.97 [0.66, 1.43]			+		
						<u> </u>	-			—
						0.01	0.1	1	10	100
							Favours [	early] Favo	urs [late]	

**1.2. All-cause mortality: non-RCTs** 1.2.1. All-cause mortality: events (HD)

	Earl	y	Late	е		Risk Ratio		Risk	Ratio	
Study or Subgroup	<b>Events</b>	Total	<b>Events</b>	Total	Weight I	M-H, Random, 95% CI Yea	r	M-H, Rand	lom, 95% CI	
Hwang 2010	1761	9406	1184	14145	35.6%	2.24 [2.09, 2.40] 201	0		•	
Clark 2011	4498	8441	7613	17469	35.8%	1.22 [1.19, 1.26] 201	1		•	
Zhang 2018	33	118	32	176	28.6%	1.54 [1.00, 2.36] 201	8		-	
Total (95% CI)		17965		31790	100.0%	1.62 [0.97, 2.69]			<b>◆</b>	
Total events	6292		8829							
Heterogeneity: Tau <sup>2</sup> = Test for overall effect:				(P < 0.0	0001); I <sup>2</sup> = 9	9%	0.01	0.1 Favours [early]	1 10 Favours [late]	100

#### 1.2.2. All-cause mortality: time to event (HD)



#### 1.2.3. All-cause mortality: 1 mL/min/1.73m2 GFR greater (HD or PD)

				Hazard Ratio		Haza	rd Ratio	
Study or Subgroup	log[Hazard Ratio]	SE	Weight	IV, Random, 95% CI Yea	ar	IV, Rand	lom, 95% CI	
Korevaar 2001	-0.1985	0.0664	27.3%	0.82 [0.72, 0.93] 200	)1	1	•	
Traynor 2002	0.0953	0.0486	32.2%	1.10 [1.00, 1.21] 200	)2		•	
Kazmi 2005	0.0296	0.0049	40.5%	1.03 [1.02, 1.04] 200	)5		•	
Total (95% CI)			100.0%	0.99 [0.88, 1.11]			<b>†</b> .	
Heterogeneity: Tau <sup>2</sup> = Test for overall effect:		= 2 (P =	0.001); I <sup>2</sup>	= 85%	0.01	0.1 Favours [early	1 10 1 Tavours [lat	

#### 1.3. Cost effectiveness: use of resource by group over duration of trial

#### 1.3.1. Hospitalization: average days

	E	Early		L	_ate		Mean Difference		Mea	n Differenc	e	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI		IV,	Fixed, 95%	CI	
3.1.1 HD or PD												
Harris 2010 (IDEAL substudy)_HD or PD	48	64	307	40	54	335	8.00 [-1.20, 17.20]			-		
3.1.2 HD planned												
Collins 2011 (IDEAL substudy)_HD planned	0	0	0	0	0	0	Not estimable					
								<u> </u>	-			——
								-100	-50	0	50	100
									Favours [e	arly] Favou	rs [late]	

#### 1.3.2. Hospitalization: average contacts

	E	arly		L	ate		Mean Difference		Me	an Differen	ce	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% C		IV	Fixed, 95%	CI	
3.2.1 HD or PD												
Harris 2010 (IDEAL substudy)_HD or PD	8	6	307	8	6	335	0.00 [-0.93, 0.93]			†		
3.2.2 HD planned												
Collins 2011 (IDEAL substudy)_HD planned	0	0	0	0	0	0	Not estimable					
								-100	-50	0	50	100
									Favours [	early] Favo	urs [late]	

### 1.3.3. Non-admitted hospital visits

	E	arly		L	.ate		Mean Difference		Me	an Differen	ce	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% C		IV	Fixed, 95%	CI	
3.3.1 HD or PD												
Harris 2010 (IDEAL substudy)_HD or PD	15	19	307	15	16	335	0.00 [-2.73, 2.73]			†		
3.3.2 HD planned												
Collins 2011 (IDEAL substudy)_HD planned	0	0	0	0	0	0	Not estimable					
								<u> </u>				———
								-100	-50 Favours [	0 early] Favo	50 urs [late]	100

#### 1.3.4. Visit to health care professional

	E	arly		L	ate		Mean Difference		Mea	n Differen	ce	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% C	<u> </u>	IV,	Fixed, 95%	CI	
3.4.1 HD or PD												
Harris 2010 (IDEAL substudy)_HD or PD	15	19	307	15	16	335	0.00 [-2.73, 2.73]			†		
3.4.2 HD planned Collins 2011 (IDEAL substudy)_HD planned	0	0	0	0	0	0	Not estimable					
								-100	-50 Favours [e	0 arly] Favou	50 urs [late]	100

#### 1.4. Adverse events

### 1.4.1. Composite cardiovascular events

vents	Total	Events	Total	M-H, Fixed, 95% CI		M H Fixed 0E% CL	
				IN TIL I IXCUL DO 70 OI		M-H, Fixed, 95% CI	
139	404	127	424	1.15 [0.94, 1.40]		†	
50	171	51	191	1.10 [0.79, 1.52]		+	
					<u> </u>		+
					0.01	• • • • • • • • • • • • • • • • • • • •	10 100
						· · · · · · · · · · · · · · · · · · ·	50 171 51 191 1.10 [0.79, 1.52]

#### 1.4.2. Composite infectious events (death or hospitalization from infection)

	Experim	ental	Contr	ol	Risk Ratio			Risk Ratio		
Study or Subgroup	Events	Total	<b>Events</b>	Total	M-H, Fixed, 95% C	<u> </u>	M-	H. Fixed, 95	% CI	
4.2.1 HD or PD										
Cooper 2010 (IDEAL trial)_HD or PD	148	404	174	424	0.89 [0.75, 1.06]			*		
4.2.2 HD planned										
Collins 2011 (IDEAL substudy)_HD planned	60	171	72	191	0.93 [0.71, 1.22]			+		
						<u> </u>				
						0.01	0.1	1	10	100
							Favours	[early] Favo	ours [late]	

#### 1.4.3. Complications of dialysis (need for access revision)

	Earl	у	Late	•	Risk Ratio		R	isk Ratio		
Study or Subgroup	<b>Events</b>	Total	<b>Events</b>	Total	M-H, Fixed, 95% C	1	M-H, I	Fixed, 95°	% CI	
4.3.1 HD or PD										
Cooper 2010 (IDEAL trial)_HD or PD	145	404	147	424	1.04 [0.86, 1.25]			†		
4.3.2 HD planned										
Collins 2011 (IDEAL substudy)_HD planned	73	171	75	191	1.09 [0.85, 1.39]			†		
						-			+	
						0.01	_0.1	1 _	10	100
							Favours [ea	rly  Favo	urs [late]	

#### 1.4.4. Complication of dialysis (access site infection)

	Earl	У	Late	•	Risk Ratio		Risk Ratio	
Study or Subgroup	Events	Total	<b>Events</b>	Total	M-H, Fixed, 95% CI		M-H, Fixed, 95% CI	
4.4.1 HD or PD								
Cooper 2010 (IDEAL trial)_HD or PD	47	404	50	424	0.99 [0.68, 1.43]		+	
4.4.2 HD planned								
Collins 2011 (IDEAL substudy)_HD planned	20	171	27	191	0.83 [0.48, 1.42]		+	
						<u> </u>		———
						0.01	0.1 1 10	100
							Favours [early] Favours [late	]

### 1.4.5. Complication of dialysis (serious fluid or electrolytes disorder)

	Earl	у	Late	•	Risk Ratio		Risk Ratio	
Study or Subgroup	Events	Total	<b>Events</b>	Total	M-H, Fixed, 95% C		M-H, Fixed, 95% CI	
4.5.1 HD or PD								
Cooper 2010 (IDEAL trial)_HD or PD	146	404	175	424	0.88 [0.74, 1.04]		+	
4.5.2 HD planned								
Collins 2011 (IDEAL substudy)_HD planned	44	171	73	191	0.67 [0.49, 0.92]		+	
						<u> </u>		——
						0.01	0.1 1 10	100
							Favours [early] Favours [late	el

### 1.4.6. Complication of dialysis (placement of temporary dialysis catheter)

	Earl	y	Late	•	Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	<b>Events</b>	Total	M-H, Fixed, 95% C	I M-H, Fixed, 95% CI
4.6.1 HD or PD						
Cooper 2010 (IDEAL trial)_HD or PD	118	404	124	424	1.00 [0.81, 1.23]	†
4.6.2 HD planned Collins 2011 (IDEAL substudy)_HD planned	39	171	41	191	1.06 [0.72, 1.56]	+
						0.01 0.1 1 10 100  Favours [early] Favours [late]

#### 1.5. Echocardiographic data

1.5.1. Echocardiographic endpoint: Left ventricular ejection fraction (%)

	E	Early		- 1	Late		Mean Difference		Me	an Differen	ce	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI		IV.	<b>Fixed, 95%</b>	CI	
Whalley 2013 (IDEAL substudy)_HD or PD	61.8	10.5	91	61.8	23.2	91	0.00 [-5.23, 5.23]			+		
								-100	-50	Ó	50	100
									Favours [	early] Fayor	ırs [late]	

1.5.2. Echocardiographic endpoint: Left ventricular mass index (g/m²)

	-	Early		- 1	Late		Mean Difference		M	ean Differen	ce	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI		IV	, Fixed, 95%	CI	
Whalley 2013 (IDEAL substudy)_HD or PD	126.3	32.2	91	137.7	46.9	91	-11.40 [-23.09, 0.29]			-		
								-100	-50	0	50	100
									Favours I	earlyl Favo	urs [late]	

1.5.3. Echocardiographic endpoint: Left atrial volume index (mL/m<sup>2</sup>)

	E	arly			Late		Mean Difference		Me	an Differen	ce	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI		IV.	Fixed, 95%	CI	
Whalley 2013 (IDEAL substudy)_HD or PD	52.7	24	91	53.3	20.1	91	-0.60 [-7.03, 5.83]		ı	+		
								-100	-50	0	50	100
									Favours [	earlyl Fayou	ırs [late]	

# **Key question 1.2.**

Not applicable

## **Key question 2.1.**

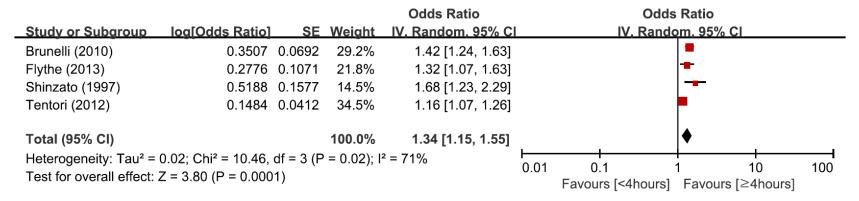
1.1. All-cause mortality of <4 hours vs ≥4 hours dialysis time per sessions: RCT

	<4hou	ırs	≥4hoι	ırs		Odds Ratio		Odd	s Ratio	
Study or Subgroup	<b>Events</b>	Total	<b>Events</b>	Total	Weight	M-H, Random, 95% CI		M-H, Ran	dom, 95% CI	
Dember (2019)	565	2532	425	1938	99.7%	1.02 [0.89, 1.18]				
Lowrie (1981)	1	78	2	73	0.3%	0.46 [0.04, 5.20]		<u> </u>	†	
Total (95% CI)		2610		2011	100.0%	1.02 [0.88, 1.18]			<b>\( \)</b>	
Total events	566		427							
Heterogeneity: Tau <sup>2</sup> = Test for overall effect:				P = 0.52	$(2); I^2 = 0\%$		0.01	0.1 Favours [<4hours]	1 10 Favours [≥4hours	100

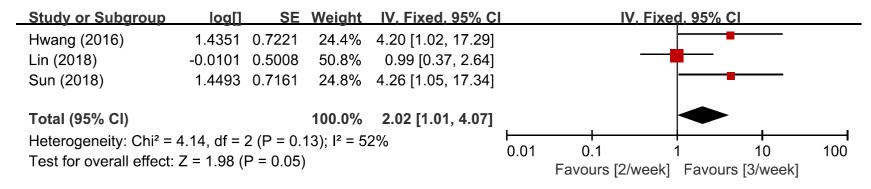
1.2. Hospitalization of <4 hours vs ≥4 hours dialysis time per sessions: RCT

	<4hou	ırs	≥4hou	ırs		Odds Ratio		Odd	s Ratio	Ratio			
Study or Subgroup	<b>Events</b>	Total	<b>Events</b>	Total	Weight	M-H, Random, 95% CI		M-H, Ran	dom, 95% CI				
Dember (2019)	1792	2532	1364	1938	59.6%	1.02 [0.90, 1.16]			•				
Lowrie (1981)	39	78	23	73	40.4%	2.17 [1.12, 4.22]			-				
Total (95% CI)		2610		2011	100.0%	1.38 [0.67, 2.87]		-					
Total events	1831		1387										
Heterogeneity: Tau <sup>2</sup> =	0.23; Chi <sup>2</sup>	= 4.82	, df = 1 (F	P = 0.03	3); I <sup>2</sup> = 79%	<b>6</b>	0.01	0.1	<del>1 1</del>	<u> </u>	100		
Test for overall effect:	Z = 0.87 (	P = 0.3	8)				0.01	Favours [<4hours]		-	100		

1.3. All-cause mortality of <4 hours vs ≥4 hours dialysis time per sessions: non-RCT



1.4. All-cause mortality of 2/week vs 3/week dialysis session: non-RCT



#### **Key question 2.2.**

Not applicable

#### **Key question 3.1.**

# 1.1. High vs. low flux hemodialysis: meta-analysis result on all-cause mortality

	High-f	lux				Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Chazot 2015	5	32	13	38	2.1%	0.46 [0.18, 1.14]	<del></del>
EGE Study 2013	75	352	97	352	19.2%	0.77 [0.59, 1.01]	•
HEMO 2002	429	921	442	925	52.3%	0.97 [0.89, 1.07]	•
Kuchle 1996	1	12	1	12	0.3%	1.00 [0.07, 14.21]	
Lang 2001	0	15	0	15		Not estimable	
Li 2010	0	21	1	24	0.2%	0.38 [0.02, 8.83]	
Locatelli 1996	1	51	5	104	0.4%	0.41 [0.05, 3.40]	
Locatelli 2000	0	35	0	39		Not estimable	
MPO 2009	74	318	88	329	18.6%	0.87 [0.67, 1.14]	*
Simon 1993	14	32	15	22	6.9%	0.64 [0.39, 1.04]	7
Total (95% CI)		1789		1860	100.0%	0.87 [0.76, 0.99]	•
Total events	599		662				
Heterogeneity: Tau <sup>2</sup> = 6	0.01; Chi²	= 8.45	df = 7 (P	= 0.29	); I <sup>2</sup> = 17%	6	0.01 0.1 1 10 100
Test for overall effect: 2	Z = 2.06 (	P = 0.0	4)				0.01 0.1 1 10 100 High-flux better Low-flux better

### 1.2. High vs. low flux hemodialysis: meta-analysis result on cardiovascular death

	High-f	lux	Low-fl	ux		Risk Ratio		Risk	Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% C		IV, Rando	m, 95% CI	
Li 2010	0	21	1	24	0.3%	0.38 [0.02, 8.83]	_	•		
Simon 1993	5	32	6	22	2.2%	0.57 [0.20, 1.65]			<del> </del>	
MPO 2009	34	318	41	329	13.6%	0.86 [0.56, 1.32]		-	<b>-</b>	
EGE Study 2013	39	352	53	352	16.6%	0.74 [0.50, 1.08]		-	t	
HEMO 2002	156	921	187	925	67.3%	0.84 [0.69, 1.02]				
Total (95% CI)		1644		1652	100.0%	0.81 [0.70, 0.95]		<b>*</b>		
Total events	234		288							
Heterogeneity: Tau <sup>2</sup> =	0.00; Chi2	= 1.06	, df = 4 (F	P = 0.90	); I <sup>2</sup> = 0%		-		10	100
Test for overall effect:							0.01	0.1 High-flux better	1 10 Low-flux better	100

### 1.3. High vs. low flux hemodialysis: meta-analysis result on hospitalization

	High-f	lux	Low-fl	lux		Risk Ratio		Risk	Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	IV. Random, 95% CI		IV. Rando	m. 95% Cl	
1.4.1 Any cause										
Chazot 2015	3	32	3	38	7.4%	1.19 [0.26, 5.48]			<del></del>	
Simon 1993	17	32	15	22	92.6%	0.78 [0.51, 1.20]		1	-	
Subtotal (95% CI)		64		60	100.0%	0.80 [0.53, 1.22]		•	<b>•</b>	
Total events	20		18							
Heterogeneity: Tau <sup>2</sup> =	0.00; Chi2	= 0.27	, df = 1 (F	P = 0.60	)); I <sup>2</sup> = 0%					
Test for overall effect:	Z = 1.03 (	P = 0.3	0)							
						H	0.01	0.1	1 10	100
						,	0.01	High-flux better		100

Test for subgroup differences: Not applicable

1.4. High vs. low flux hemodialysis: meta-analysis result on serum  $\beta_2$ -microglobulin concentration

	High-flux Low-flux				w-flux			Mean Difference	Mea	Difference	
Study or Subgroup	Mean [mg/L]	SD [mg/L]	Total	Mean [mg/L]	SD [mg/L]	Total	Weight	IV, Random, 95% CI	IV. Ra	ndom, 95% CI	
Klemm 2004	41.1	12.4	13	57.1	16.7	13	3.5%	-16.00 [-27.31, -4.69]		-	
Kuchle 1996	37	14	10	55	7	10	4.7%	-18.00 [-27.70, -8.30]			
Locatelli 1996	28.8	14.2	51	43.4	9.6	54	14.0%	-14.60 [-19.26, -9.94]	-		
Ayli 2005	31.6	5.3	24	42	9.1	24	15.7%	-10.40 [-14.61, -6.19]	-	-	
EGE Study 2013	25.3	9.9	352	32.9	13.1	352	29.2%	-7.60 [-9.32, -5.88]	1		
HEMO 2002	33.6	9.1	921	41.5	13	925	32.8%	-7.90 [-8.92, -6.88]		•	
Total (95% CI)			1371			1378	100.0%	-9.90 [-12.14, -7.65]	•		
Heterogeneity: Tau <sup>2</sup> =	3.72; Chř = 14.	81, df = 5 (P	= 0.01	); I <sup>2</sup> = 66%					-50 -25	0 25	50
Test for overall effect:	Z = 8.64 (P < 0.	00001)								ter Low-flux bett	

1.5. High vs. low flux hemodialysis: meta-analysis result on eKt/V

	Hill	gh-flux				κ		Mean Difference	erence Mean Difference				
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV. Random, 95% CI		IV, Random, 95	i% CI		
Ayli 2005	1.24	2	24	1.21	1.8	24	0.0%	0.03 [-1.05, 1.11]					
Locatelli 2000	1.26	0.21	35	1.33	0.2	39	2.9%	-0.07 [-0.16, 0.02]		<del>-</del> †			
EGE Study 2013	1.47	0.21	352	1.47	0.21	352	26.8%	0.00 [-0.03, 0.03]		<u>.</u>			
HEMO 2002	1.34	0.21	921	1.34	0.21	925	70.2%	0.00 [-0.02, 0.02]		<b>-</b>			
Total (95% CI)			1332			1340	100.0%	-0.00 [-0.02, 0.01]					
Heterogeneity: Tau <sup>2</sup> =	0.00; Ct	$ni^2 = 2.5$	08, df =	3 (P =	0.56);	$ ^2 = 0\%$	5		-2	1 0			
Test for overall effect:	Z = 0.25	(P = 0	0.80)						-2	Low-flux better High-	-flux better	2	

# **Key question 3.2.**

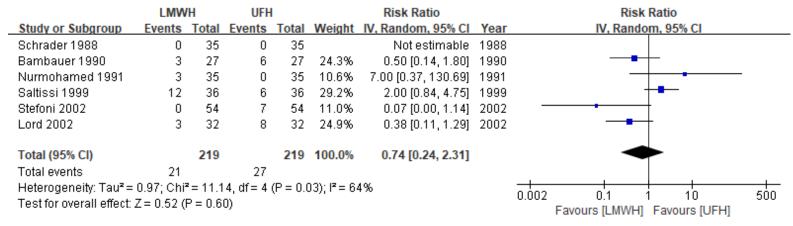
1.1. Impact of OL-HDF on participants with end-stage kidney disease on all-cause mortality.

	Online hemodiafil	tration	High-flux hemodi	iafiltrati		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
Morena 2017	36	190	43	191	38.2%	0.80 [0.49, 1.32]	<del>-</del>
Ok 2013	52	391	65	391	61.8%	0.77 [0.52, 1.14]	=
Total (95% CI)		581		582	100.0%	0.78 [0.57, 1.07]	•
Total events	88		108				
Heterogeneity: Chi²=		9); I² = 09	6				0.01 0.1 1 10 100
Test for overall effect:	Z = 1.55 (P = 0.12)						Favours OL-HDF Favours HF-HD

1.2. Impact of OL-HDF on participants with end-stage kidney disease on all-cause hospitalization.

	Online hemodiafi	tration	Hifh-flux hemod	lialysis		Risk Ratio		Risk	Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI		M-H, Fixe	ed, 95% CI	
Morena 2017	252	313	266	311	59.3%	0.94 [0.88, 1.01]				
Ok 2013	204	1000	183	1000	40.7%	1.11 [0.93, 1.33]		I	•	
Total (95% CI)		1313		1311	100.0%	1.01 [0.93, 1.10]			•	
Total events	456		449							
Heterogeneity: Chi <sup>z</sup> =	5.09, df = $1$ (P = $0.0$	(2);	%				0.01 0	1 .	<del>                                     </del>	100
Test for overall effect:	Z = 0.27 (P = 0.79)							OL-HDF	Favours H	

# **Key question 4.1.**



#### 1.1. Meta-analysis result for bleeding

#### 1.2. Meta-analysis result for hemodialysis circuit thrombosis

	LMW	/H	UFH	ł		Risk Ratio			Risl	( Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	Year		IV, Rand	om, 95%	CI	
Schrader 1988	80	5045	69	5197	38.1%	1.19 [0.87, 1.64]	1988			<b>-</b>		
Saltissi 1999	17	1111	35	1141	30.3%	0.50 [0.28, 0.89]	1999		-	-		
Lord 2002	32	378	21	382	31.6%	1.54 [0.90, 2.62]	2002			+		
Total (95% CI)		6534		6720	100.0%	0.99 [0.56, 1.77]			-	•		
Total events	129		125									
Heterogeneity: Tau² =	0.20; Ch	i² = 9.01	6, df = 2 (	P = 0.0	1); I²= 78°	%		0.01	0.1	+	10	100
Test for overall effect:	Z = 0.02	(P = 0.9)	38)					0.01	Favours [LMWH	Favou		100

### **Key question 4.2.**

Not applicable

#### **Key question 5.1.**

Not applicable

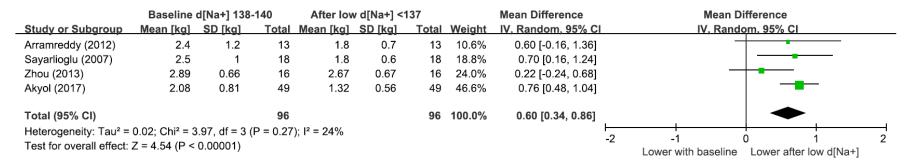
#### Key question 5.2.

#### 1.1. Interdialytic weight gain

1.1.1. Low dialysate [Na<sup>+</sup>] (<138 mEq/L) vs. conventional dialysate [Na<sup>+</sup>] (138 -140 mEq/L): RCT

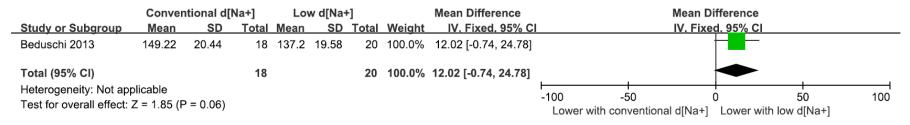
	conven	tional d[Na	a+]	Low	d[Na+]			Mean Difference	Mean Difference
Study or Subgroup	Mean [kg]	SD [kg]	Total	Mean [kg]	SD [kg]	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Beduschi 2013	2.79	1.92	18	2.5	0.63	20	7.6%	0.29 [-0.64, 1.22]	<u> </u>
Boquin 1977	2.52	0.85	37	1.95	0.85	37	43.6%	0.57 [0.18, 0.96]	
Liu 2016	3	0.8	29	2.8	0.6	28	48.8%	0.20 [-0.17, 0.57]	<del>  •</del>
Total (95% CI)			84			85	100.0%	0.37 [0.11, 0.62]	•
Heterogeneity: Tau <sup>2</sup> = Test for overall effect			? (P = 0.3	39); I² = 0%					-2 -1 0 1 2  Lower with conventional d[Na+] Lower with low d[Na+]

1.1.2. Low dialysate [Na<sup>+</sup>] (<138 mEq/L) vs. conventional dialysate [Na<sup>+</sup>] (138 -140 mEq/L): non-RCT



#### 1.2. Predialysis BP

1.2.1. Low dialysate [Na<sup>+</sup>] (<138 mEq/L) vs. conventional dialysate [Na<sup>+</sup>] (138 -140 mEq/L): RCT



#### 1.2.2. Low dialysate [Na<sup>+</sup>] (<138 mEq/L) vs. conventional dialysate [Na<sup>+</sup>] (138 -140 mEq/L): non-RCT

	Baseline o	d[Na+] 138	3-140	After lov	v d[Na+]	<137		Mean Difference		Mean D	ifference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI		IV, Fixe	d, 95% CI		
Arramreddy (2012)	144.5	31.4	13	143.6	32.4	13	20.4%	0.90 [-23.63, 25.43]			•		
Kooman (2000)	144	19	6	155	27	6	17.6%	-11.00 [-37.42, 15.42]			<u> </u>		
Sayarlioglu (2007)	179.7	24.8	18	151.7	17.7	18	62.0%	28.00 [13.92, 42.08]			-		
Total (95% CI)			37			37	100.0%	15.60 [4.52, 26.69]			•		
Heterogeneity: Chi <sup>2</sup> = 8 Test for overall effect: 2	,	,.	l <sup>2</sup> = 76%						-100	-50 Lower with baseline	0 Lower aft	50 er low d[Na+]	100

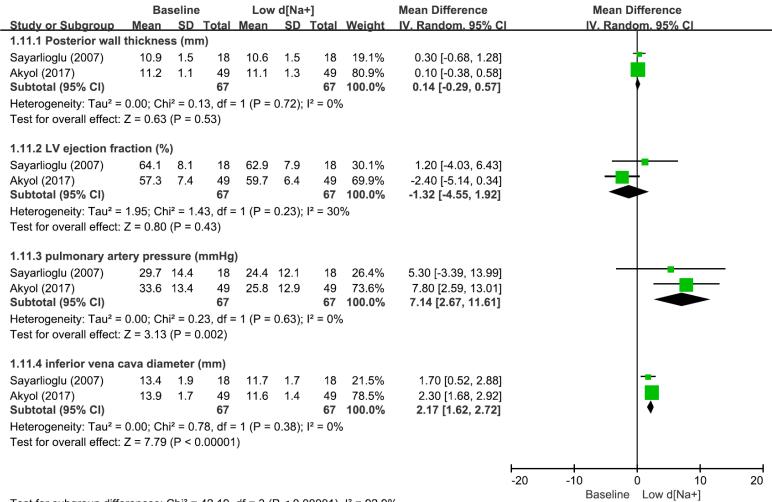
#### 1.3. Antihypertensive medication: Low dialysate [Na<sup>+</sup>] (<138 mEq/L) vs. conventional dialysate [Na<sup>+</sup>] (138 -140 mEq/L): RCT

	Conventi	ional d[l	Na+]	Low	d[Na	+]	;	Std. Mean Difference	Sto	d. Mean Differenc	e	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV	<mark>/, Random, 95% C</mark>	:	
Liu 2016 (1)	4.2	2.9	29	2.7	1.9	28	100.0%	0.60 [0.07, 1.13]				
Total (95% CI)			29			28	100.0%	0.60 [0.07, 1.13]				
Heterogeneity: Not app Test for overall effect: 2		= 0.03)							-2 -1 Less with conventional	0 d[Na+] Less with	1 n lower d[Na+]	2

#### <u>Footnotes</u>

(1) Aggregated equivalent dose units

#### 1.4. Echocardiographic parameter: Low dialysate [Na<sup>+</sup>] (<138 mEq/L) vs. conventional dialysate [Na<sup>+</sup>] (138 -140 mEq/L): non-RCT



Test for subgroup differences:  $Chi^2 = 42.19$ . df = 3 (P < 0.00001).  $I^2 = 92.9\%$ 

#### 1.5. Serum Na

1.5.1. Low dialysate [Na<sup>+</sup>] (<138 mEq/L) vs. conventional dialysate [Na<sup>+</sup>] (138 -140 mEq/L): RCT

	Conver	ntional d[Na	+]	Low	d[Na+]			Mean Difference			Mean Difference		
Study or Subgroup	Mean [mM]	SD [mM]	Total	Mean [mM]	SD [mM]	Total	Weight	IV, Random, 95% CI		IN IN	V, Random, 95% CI		
1.6.1 Predialysis													
Beduschi 2013	139.3	3.9	18	136.3	7.3	20	4.8%	3.00 [-0.67, 6.67]			<del>  -</del>	-	
Liu 2016	139.1	2.7	29	138.1	1.8	28	45.8%	1.00 [-0.19, 2.19]			<del>  -</del>		
Boquin 1977	137.1	2.51	37	135.1	2.51	37	49.4%	2.00 [0.86, 3.14]			📜		
Subtotal (95% CI)			84			85	100.0%	1.59 [0.78, 2.40]			•		
Heterogeneity: Tau <sup>2</sup> =	0.00; Chi <sup>2</sup> = 2	.01, df = 2 (F	P = 0.37	); I <sup>2</sup> = 0%									
Test for overall effect:	Z = 3.86 (P =	0.0001)											
									-20	-10	<del> </del>	10	20
										conventional	I d[Na+] Lower with	n low d[Na+]	20

# $1.5.2.\ Low\ dialysate\ [Na^+]\ (<138\ mEq/L)\ vs.\ conventional\ dialysate\ [Na^+]\ (138\ -140\ mEq/L):\ non-RCT$

	Baseline o	d[Na+] 13	8-140	After lov	v d[Na+]	<137		Mean Difference		Mean	Differen	ce	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Ran	dom, 95	% CI	
Arramreddy (2012)	135.5	3.7	13	134.9	3.9	13	9.5%	0.60 [-2.32, 3.52]			<u>+</u>		
Zhou (2013)	139.66	1.38	16	139.28	1.36	16	90.5%	0.38 [-0.57, 1.33]					
Total (95% CI)			29			29	100.0%	0.40 [-0.50, 1.30]			1		
Heterogeneity: Tau <sup>2</sup> = Test for overall effect:			1 (P = 0.8	39); I² = 0%	b				-100	-50 Lower with baseling	0 e Lowe	50 r after low d[N	100 la+]

## 1.6. Intradialytic hypotension: Low dialysate [Na<sup>+</sup>] (< 38 mEq/L) vs. conventional dialysate [Na<sup>+</sup>] (138 -140 mEq/L): RCT

	Conventional	d[Na+]	Low d[l	Na+]		Risk Ratio			Risk	Ratio			
Study or Subgroup	Events	Total	<b>Events</b>	Total	Weight	M-H, Random, 95% Cl			M-H, Ran	<u>dom, 95</u>	5% CI		
Beduschi 2013	36	864	113	960	29.4%	0.35 [0.25, 0.51]			-				
Boquin 1977	132	444	174	444	34.7%	0.76 [0.63, 0.91]			-				
Liu 2016	430	4524	428	4368	35.9%	0.97 [0.85, 1.10]			_	-			
Total (95% CI)		5832		5772	100.0%	0.66 [0.43, 1.02]				-			
Total events	598		715										
Heterogeneity: Tau <sup>2</sup> =			P < 0.000	)01); l² :	= 93%		0.1	0.2	0.5	<del>                                     </del>	2	<del>   </del> 5	10
Test for overall effect:	Z = 1.86 (P = 0.0	6)						•	entional d[Na+]	Less	with low d	Na+]	

# **Key question 6.1.**

Not applicable

## Key question 6.2.

Not applicable

## Key question 7.1.

Not applicable

# **Key question 8.1.**

1.1. Meta-analysis of dialysis treatment compared with supportive care for mortality in elderly ESRD patients.

	Dialysi	is	Conservative treati	nent		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	M-H, Fixed, 95% CI
Brown 2015	28	273	68	122	11.4%	0.09 [0.05, 0.15]	<del>-</del>
Carson 2009	100	173	25	29	2.4%	0.22 [0.07, 0.66]	<del></del>
Joly 2003	60	101	37	43	2.9%	0.24 [0.09, 0.61]	<del></del>
Murtagh 2007	12	52	51	77	4.3%	0.15 [0.07, 0.34]	<del></del>
Pyart 2020	420	841	262	375	24.6%	0.43 [0.33, 0.56]	<b>-</b>
Raman 2017	72	123	67	81	4.5%	0.29 [0.15, 0.58]	<del></del>
Smith 2003	41	258	34	63	6.2%	0.16 [0.09, 0.29]	<del></del>
Tam-Tham 2018	305	500	285	338	18.0%	0.29 [0.21, 0.41]	
Tam-Tham 2020	221	557	163	411	15.3%	1.00 [0.77, 1.30]	<u></u>
van Loon 2019	31	192	31	89	4.8%	0.36 [0.20, 0.64]	<del></del>
Verberne 2016	111	204	69	107	5.6%	0.66 [0.41, 1.06]	
Total (95% CI)		3274		1735	100.0%	0.42 [0.37, 0.47]	•
Total events	1401		1092				
Heterogeneity: Chi <sup>2</sup> =	102.60, df =	= 10 (F	P < 0.00001); I <sup>2</sup> = 90%	,			
Test for overall effect:		,	, .				0.01

1.2. Subgroup meta-analysis of dialysis treatments for mortality in prospective observational studies.

	Dialys	is	Conservative trea	atment		Odds Ratio		Odds	Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C		M-H, Fix	ed, 95% CI	
Brown 2015	28	273	68	122	49.2%	0.09 [0.05, 0.15]		-		
Carson 2009	100	173	25	29	10.5%	0.22 [0.07, 0.66]		-		
Raman 2017	72	123	67	81	19.5%	0.29 [0.15, 0.58]		_		
van Loon 2019	31	192	31	89	20.7%	0.36 [0.20, 0.64]		-		
Total (95% CI)		761		321	100.0%	0.20 [0.15, 0.28]		•		
Total events	231		191							
Heterogeneity: Chi2 =	13.77, df =	3 (P =	: 0.003); I <sup>2</sup> = 78%				0.04		+ +	400
Test for overall effect:		-	, .				0.01 Fa	0.1 vours [Dialysisl]	1 10 Favours [CTI]	100

1.3. Subgroup meta-analysis of dialysis treatments for mortality in retrospective studies only.

	Dialys	sis	Conservative treat	ment		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	M-H, Fixed, 95% CI
Joly 2003	60	101	37	43	3.7%	0.24 [0.09, 0.61]	
Murtagh 2007	12	52	51	77	5.6%	0.15 [0.07, 0.34]	
Pyart 2020	420	841	262	375	32.0%	0.43 [0.33, 0.56]	-
Smith 2003	41	258	34	63	8.1%	0.16 [0.09, 0.29]	
Tam-Tham 2018	305	500	285	338	23.4%	0.29 [0.21, 0.41]	-
Tam-Tham 2020	221	557	163	411	20.0%	1.00 [0.77, 1.30]	+
Verberne 2016	111	204	69	107	7.3%	0.66 [0.41, 1.06]	-
Total (95% CI)		2513		1414	100.0%	0.48 [0.42, 0.56]	<b>•</b>
Total events	1170		901				
Heterogeneity: Chi2 = 6	63.79, df =	6 (P <	0.00001); I <sup>2</sup> = 91%				
Test for overall effect:	Z = 10.10	(P < 0.	00001)				0.01 0.1 1 10 100 Favours [experimental] Favours [control]

# **Key question 8.2.**

Not applicable