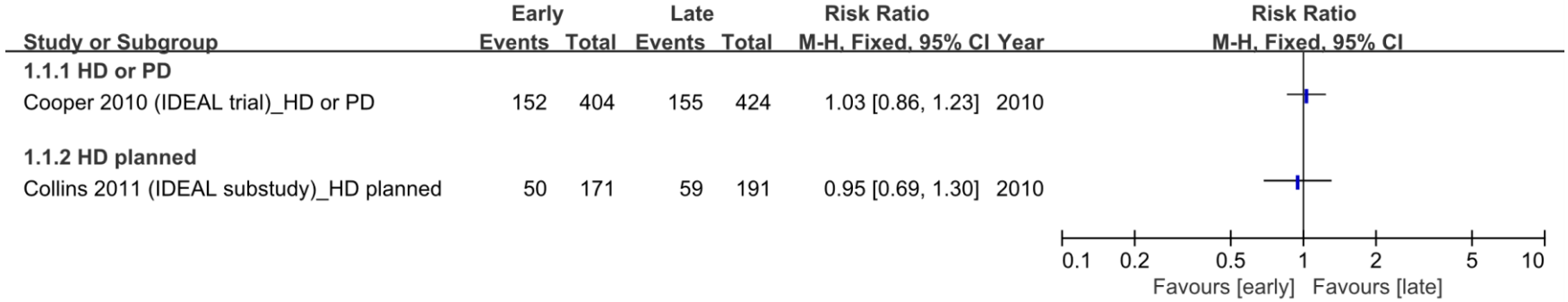
Supplement 9| Forest Plots

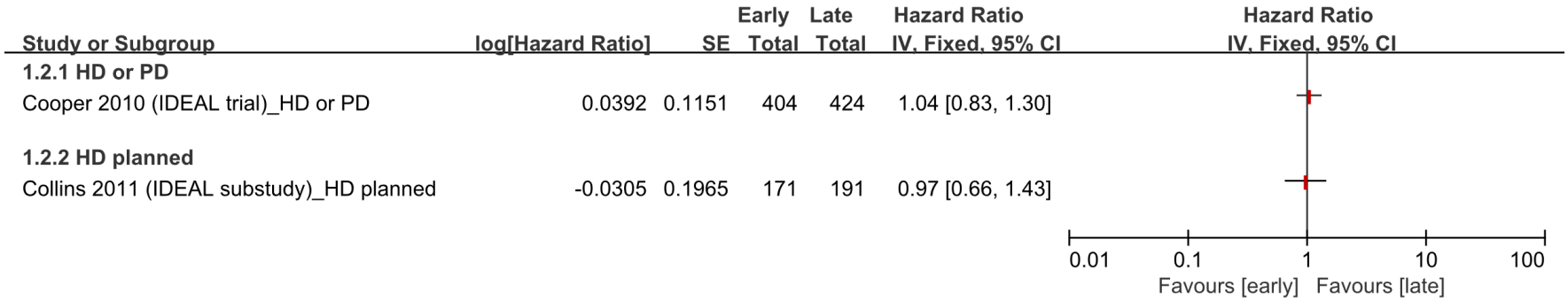
Key question 1.1.

1.1. All-cause mortality: RCTs

1.1.1. All-cause mortality: events



1.1.2. All-cause mortality: time to event

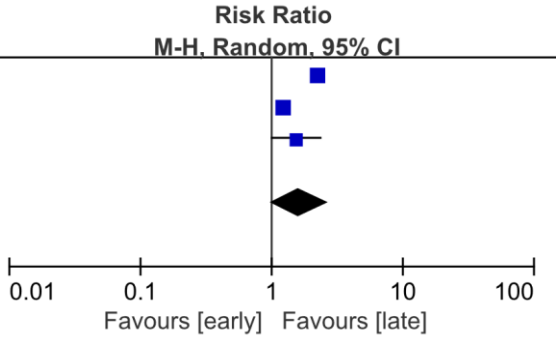


1.2. All-cause mortality: non-RCTs

1.2.1. All-cause mortality: events (HD)

Study or Subgroup	Early Events	Early Total	Late Events	Late Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Hwang 2010	1761	9406	1184	14145	35.6%	2.24 [2.09, 2.40]	2010
Clark 2011	4498	8441	7613	17469	35.8%	1.22 [1.19, 1.26]	2011
Zhang 2018	33	118	32	176	28.6%	1.54 [1.00, 2.36]	2018
Total (95% CI)		**17965**		**31790**	**100.0%**	**1.62 [0.97, 2.69]**	
Total events	6292		8829				

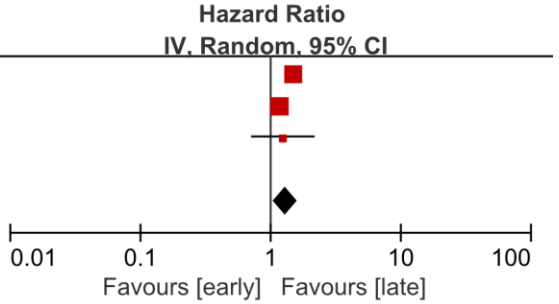
Heterogeneity: Tau² = 0.19; Chi² = 273.76, df = 2 (P < 0.00001); I² = 99%
Test for overall effect: Z = 1.86 (P = 0.06)



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

Study or Subgroup	log[Hazard Ratio]	SE	Weight	Hazard Ratio IV, Random, 95% CI	Year
Lassalle 2010	0.3988	0.0282	43.4%	1.49 [1.41, 1.57]	2010
Wright 2010	0.157	0.0044	44.6%	1.17 [1.16, 1.18]	2010
Chang 2012	0.2151	0.2774	12.0%	1.24 [0.72, 2.14]	2012
Total (95% CI)			**100.0%**	**1.31 [1.05, 1.63]**	

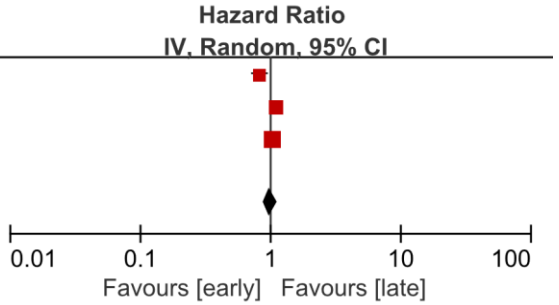
Heterogeneity: Tau² = 0.03; Chi² = 71.81, df = 2 (P < 0.00001); I² = 97%
Test for overall effect: Z = 2.40 (P = 0.02)



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

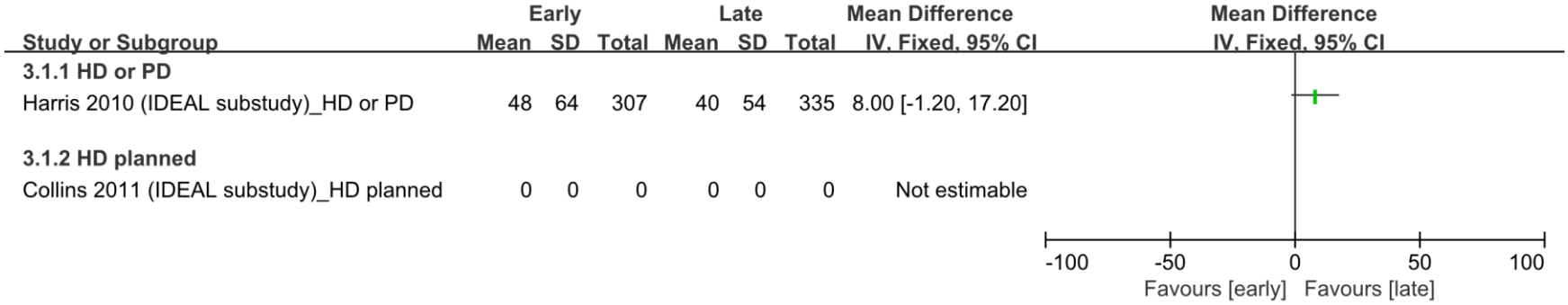
Study or Subgroup	log[Hazard Ratio]	SE	Weight	Hazard Ratio IV, Random, 95% CI	Year
Korevaar 2001	-0.1985	0.0664	27.3%	0.82 [0.72, 0.93]	2001
Traynor 2002	0.0953	0.0486	32.2%	1.10 [1.00, 1.21]	2002
Kazmi 2005	0.0296	0.0049	40.5%	1.03 [1.02, 1.04]	2005
Total (95% CI)			**100.0%**	**0.99 [0.88, 1.11]**	

Heterogeneity: Tau² = 0.01; Chi² = 13.61, df = 2 (P = 0.001); I² = 85%
Test for overall effect: Z = 0.19 (P = 0.85)

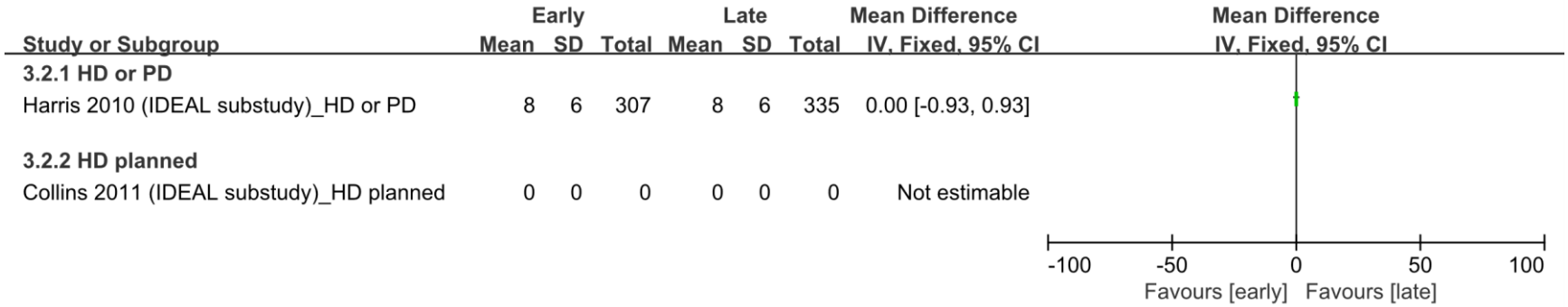


1.3. Cost effectiveness: use of resource by group over duration of trial

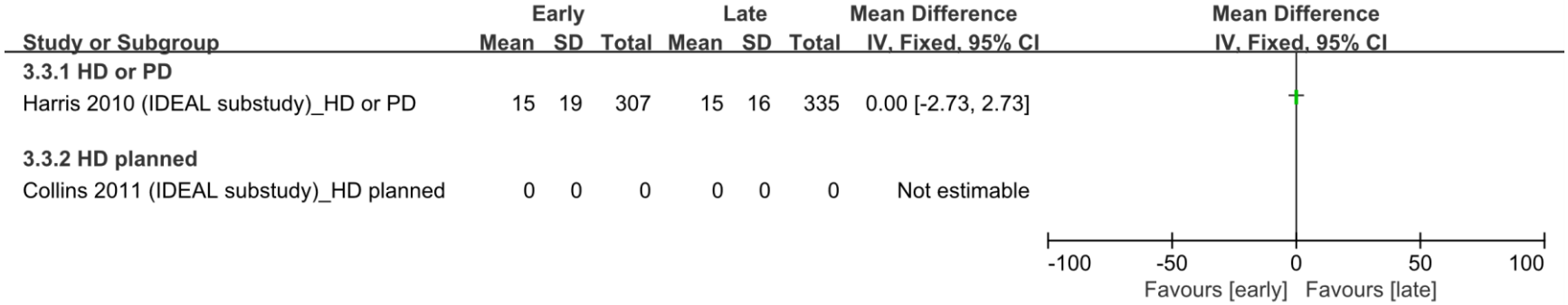
1.3.1. Hospitalization: average days



1.3.2. Hospitalization: average contacts

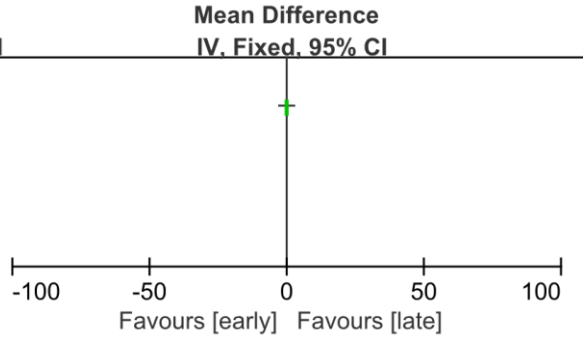


1.3.3. Non-admitted hospital visits



1.3.4. Visit to health care professional

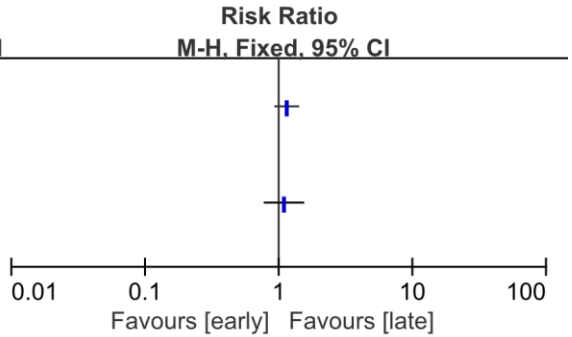
Study or Subgroup	Early Mean	SD	Total	Late Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
3.4.1 HD or PD							
Harris 2010 (IDEAL substudy)_HD or PD	15	19	307	15	16	335	0.00 [-2.73, 2.73]
3.4.2 HD planned							
Collins 2011 (IDEAL substudy)_HD planned	0	0	0	0	0	0	Not estimable



1.4. Adverse events

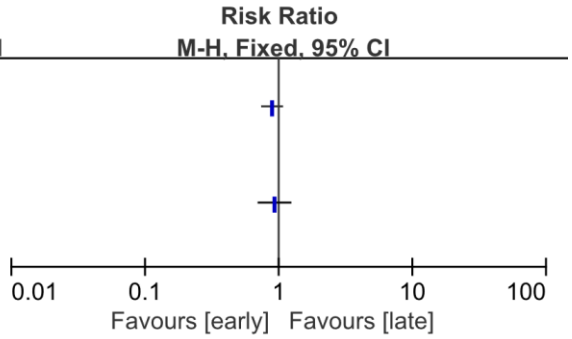
1.4.1. Composite cardiovascular events

Study or Subgroup	Early Events	Total	Late Events	Total	Risk Ratio M-H, Fixed, 95% CI
4.1.1 HD or PD					
Cooper 2010 (IDEAL trial)_HD or PD	139	404	127	424	1.15 [0.94, 1.40]
4.1.2 HD planned					
Collins 2011 (IDEAL substudy)_HD planned	50	171	51	191	1.10 [0.79, 1.52]



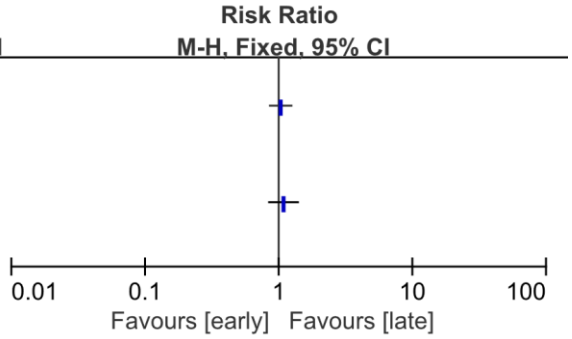
1.4.2. Composite infectious events (death or hospitalization from infection)

Study or Subgroup	Experimental Events	Total	Control Events	Total	Risk Ratio 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]



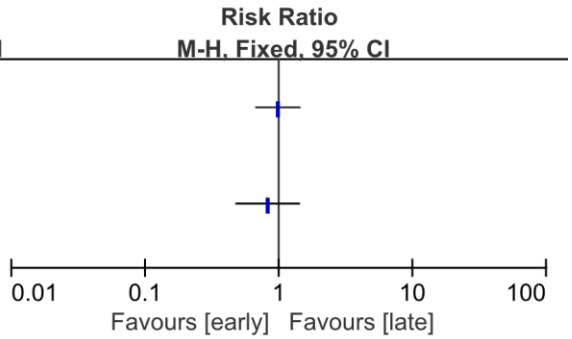
1.4.3. Complications of dialysis (need for access revision)

Study or Subgroup	Early Events	Total	Late Events	Total	Risk Ratio M-H, 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]



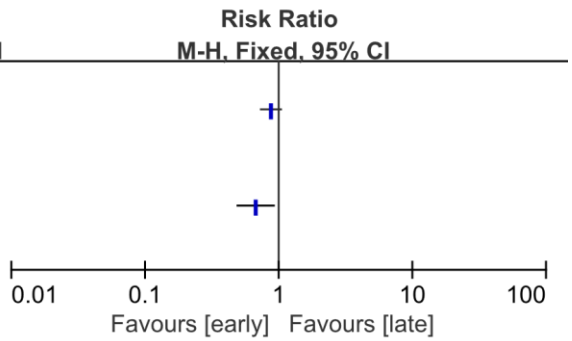
1.4.4. Complication of dialysis (access site infection)

Study or Subgroup	Early Events	Total	Late Events	Total	Risk Ratio 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]



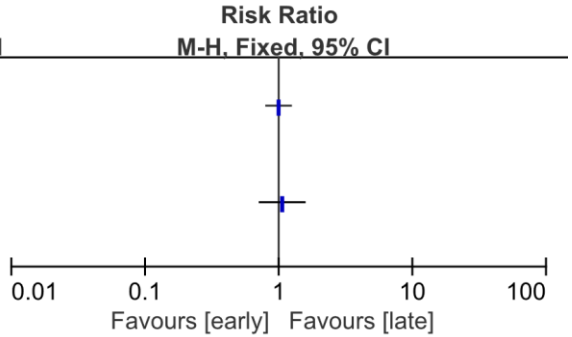
1.4.5. Complication of dialysis (serious fluid or electrolytes disorder)

Study or Subgroup	Early Events	Total	Late Events	Total	Risk Ratio 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]



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

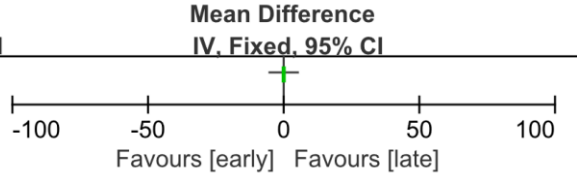
Study or Subgroup	Early Events	Early Total	Late Events	Late Total	Risk Ratio M-H, Fixed, 95% CI
4.6.1 HD or PD					
Cooper 2010 (IDEAL trial)_HD or PD	118	404	124	424	1.00 [0.81, 1.23]
4.6.2 HD planned					
Collins 2011 (IDEAL substudy)_HD planned	39	171	41	191	1.06 [0.72, 1.56]



1.5. Echocardiographic data

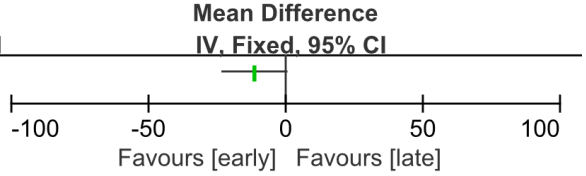
1.5.1. Echocardiographic endpoint: Left ventricular ejection fraction (%)

Study or Subgroup	Early Mean	Early SD	Early Total	Late Mean	Late SD	Late Total	Mean Difference IV, Fixed, 95% CI
Whalley 2013 (IDEAL substudy)_HD or PD	61.8	10.5	91	61.8	23.2	91	0.00 [-5.23, 5.23]



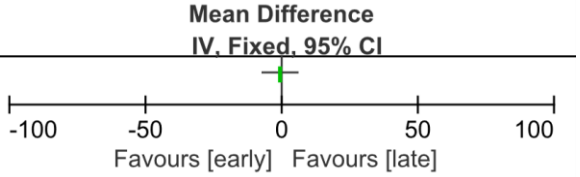
1.5.2. Echocardiographic endpoint: Left ventricular mass index (g/m^2)

Study or Subgroup	Early Mean	Early SD	Early Total	Late Mean	Late SD	Late Total	Mean Difference 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]



1.5.3. Echocardiographic endpoint: Left atrial volume index (mL/m^2)

Study or Subgroup	Early Mean	Early SD	Early Total	Late Mean	Late SD	Late Total	Mean Difference 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]

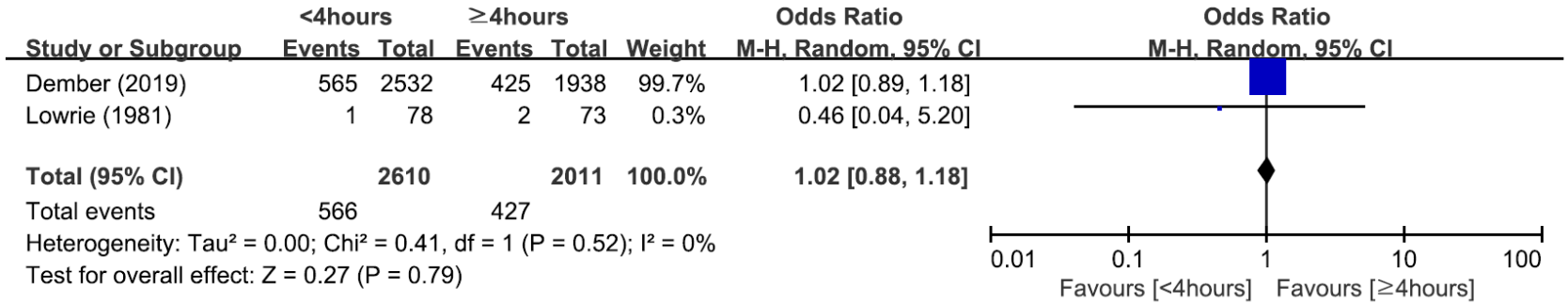


Key question 1.2.

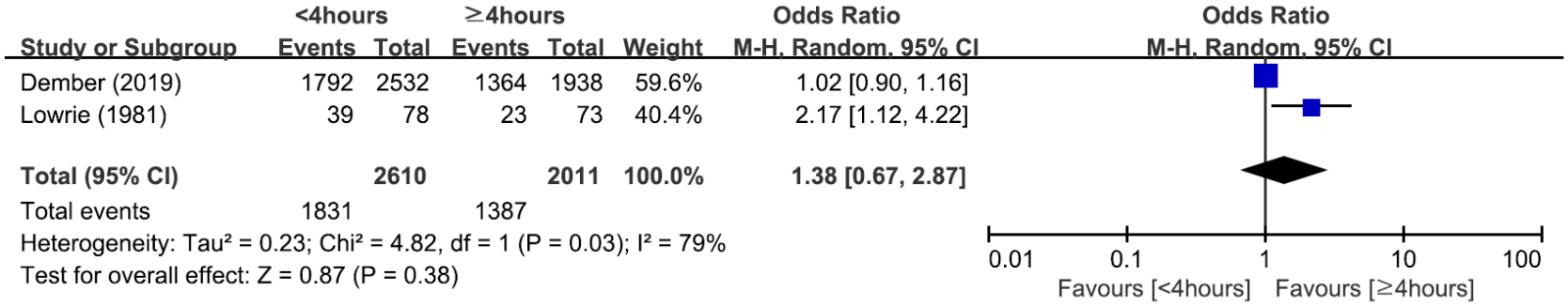
Not applicable

Key question 2.1.

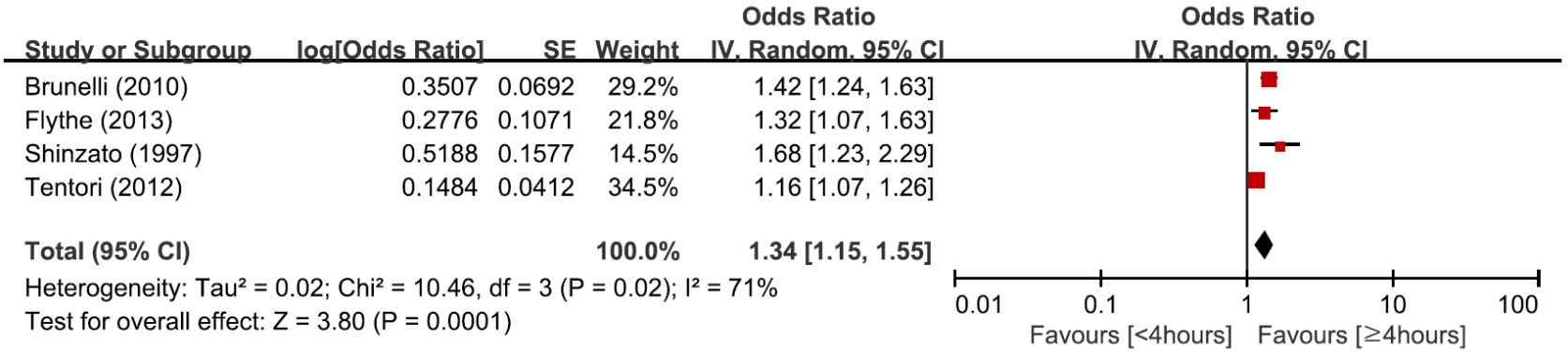
1.1. All-cause mortality of <4 hours vs ≥4 hours dialysis time per sessions: RCT



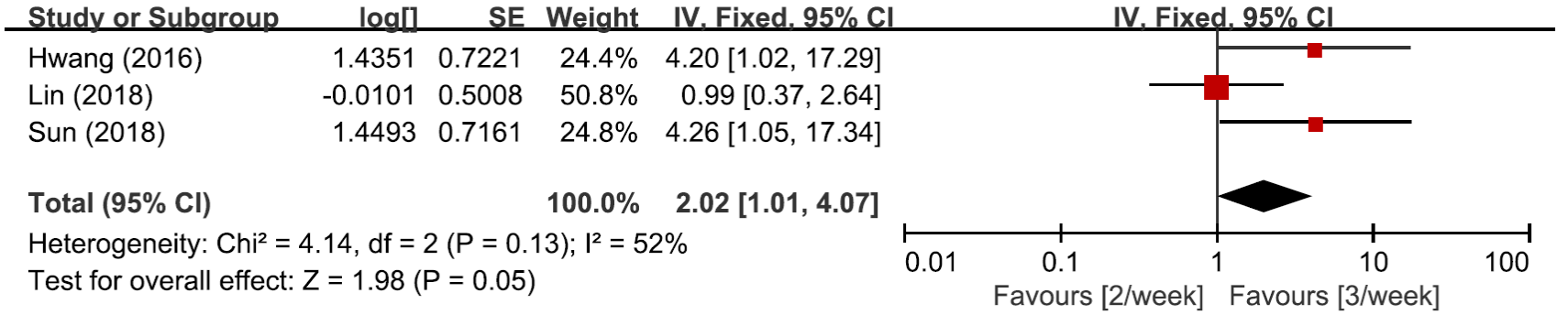
1.2. Hospitalization of <4 hours vs ≥4 hours dialysis time per sessions: RCT



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

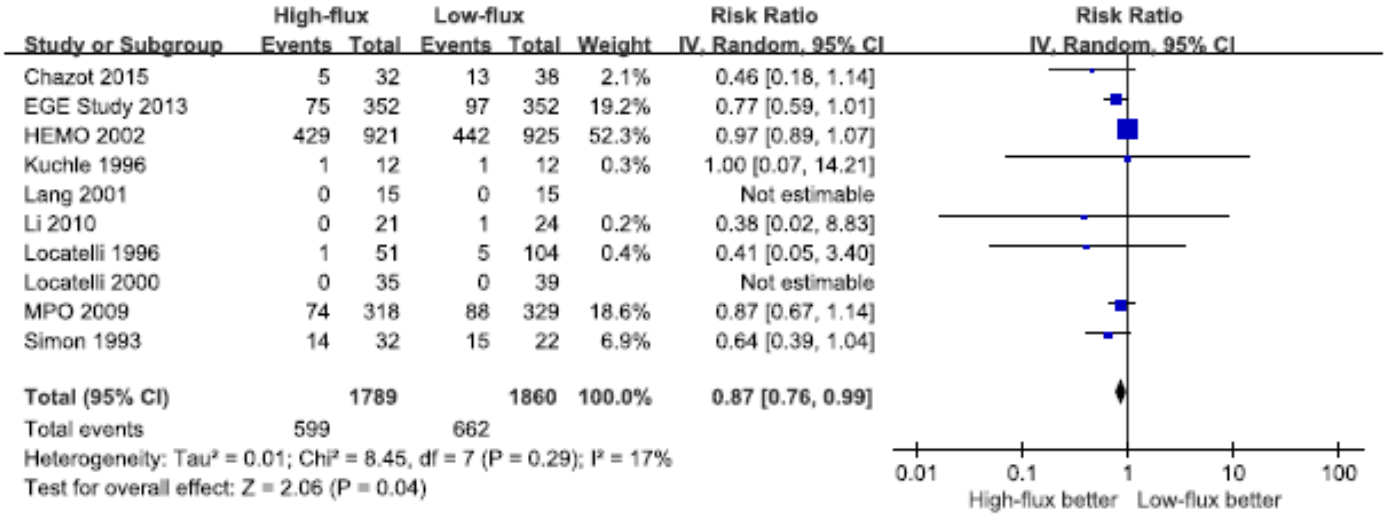


Key question 2.2.

Not applicable

Key question 3.1.

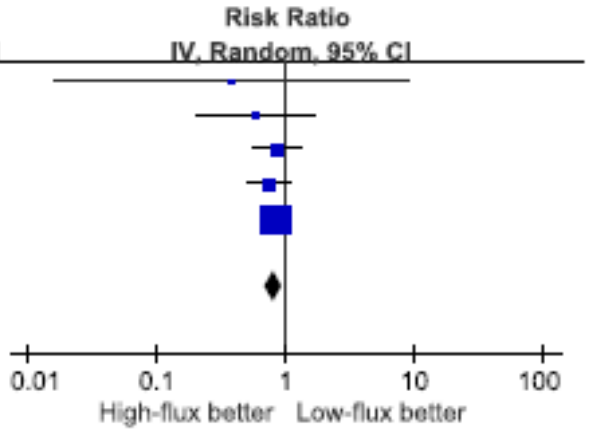
1.1. High vs. low flux hemodialysis: meta-analysis result on all-cause mortality



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

Study or Subgroup	High-flux Events	Total	Low-flux Events	Total	Weight	Risk Ratio IV, Random, 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]
MPO 2009	34	318	41	329	13.6%	0.86 [0.56, 1.32]
EGE Study 2013	39	352	53	352	16.6%	0.74 [0.50, 1.08]
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]**
Total events	234		288			

Heterogeneity: Tau² = 0.00; Chi² = 1.06, df = 4 (P = 0.90); I² = 0%
Test for overall effect: Z = 2.56 (P = 0.01)

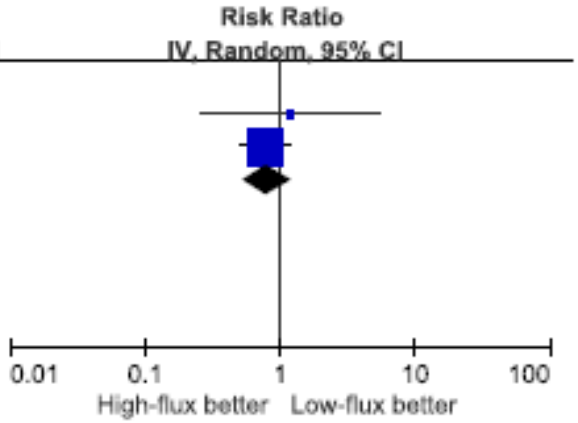


1.3. High vs. low flux hemodialysis: meta-analysis result on hospitalization

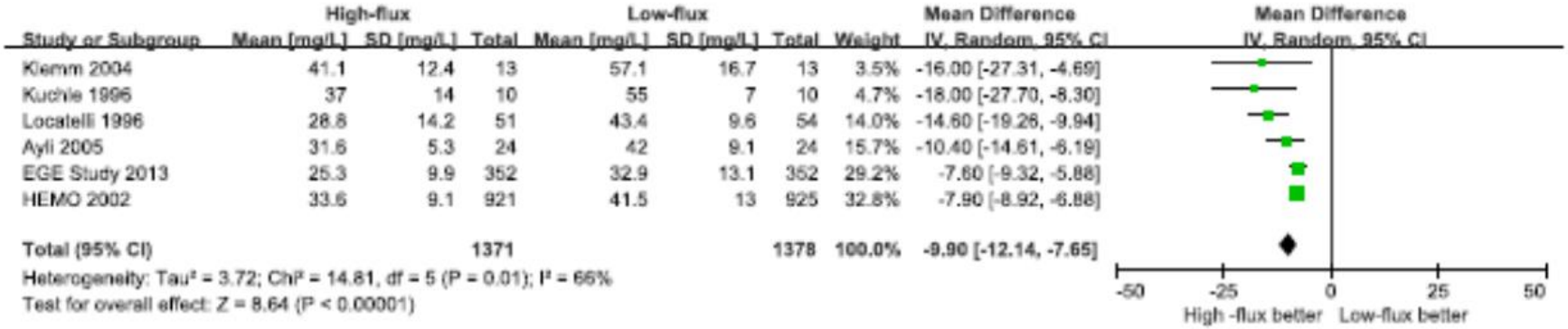
Study or Subgroup	High-flux Events	Total	Low-flux Events	Total	Weight	Risk Ratio IV, Random, 95% CI
1.4.1 Any cause						
Chazot 2015	3	32	3	38	7.4%	1.19 [0.26, 5.48]
Simon 1993	17	32	15	22	92.6%	0.78 [0.51, 1.20]
Subtotal (95% CI)		**64**		**60**	**100.0%**	**0.80 [0.53, 1.22]**
Total events	20		18			

Heterogeneity: Tau² = 0.00; Chi² = 0.27, df = 1 (P = 0.60); I² = 0%
Test for overall effect: Z = 1.03 (P = 0.30)

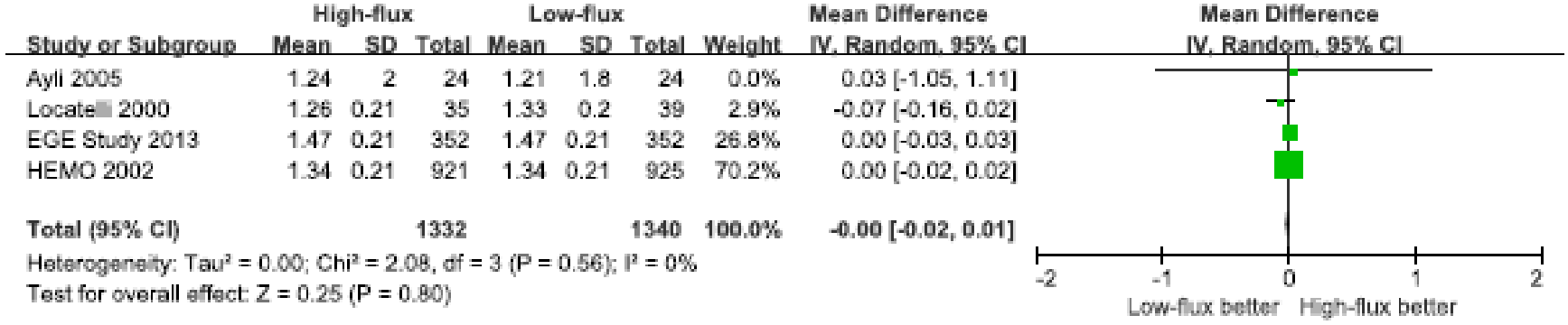
Test for subgroup differences: Not applicable



1.4. High vs. low flux hemodialysis: meta-analysis result on serum β_2-microglobulin concentration



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

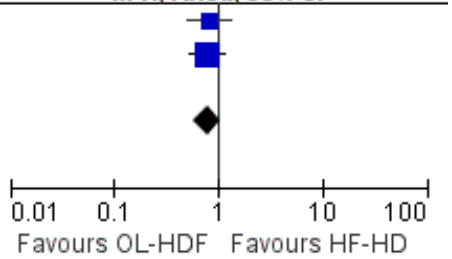


Key question 3.2.

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

	Online hemodiafiltration		High-flux hemodiafiltrati			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]	
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				

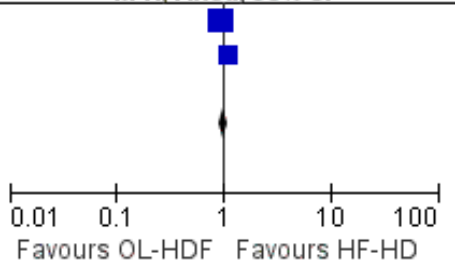
Heterogeneity: Chi² = 0.02, df = 1 (P = 0.89); I² = 0%
Test for overall effect: Z = 1.55 (P = 0.12)



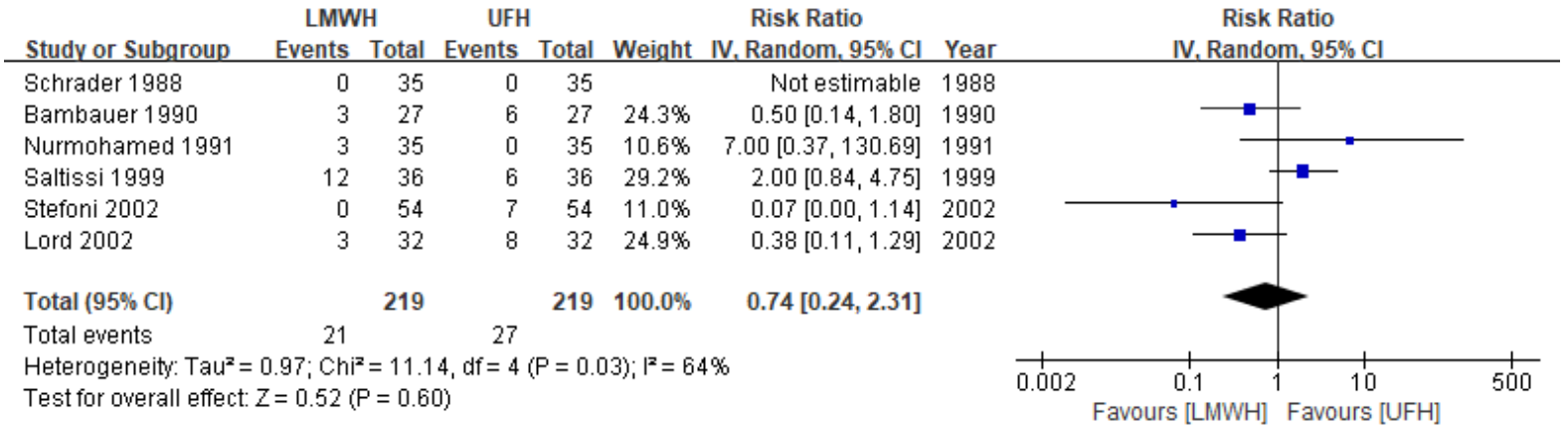
1.2. Impact of OL-HDF on participants with end-stage kidney disease on all-cause hospitalization.

	Online hemodiafiltration		Hifh-flux hemodialysis			Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 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]	
Total (95% CI)		**1313**		**1311**	**100.0%**	**1.01 [0.93, 1.10]**	
Total events	456		449				

Heterogeneity: Chi² = 5.09, df = 1 (P = 0.02); I² = 80%
Test for overall effect: Z = 0.27 (P = 0.79)

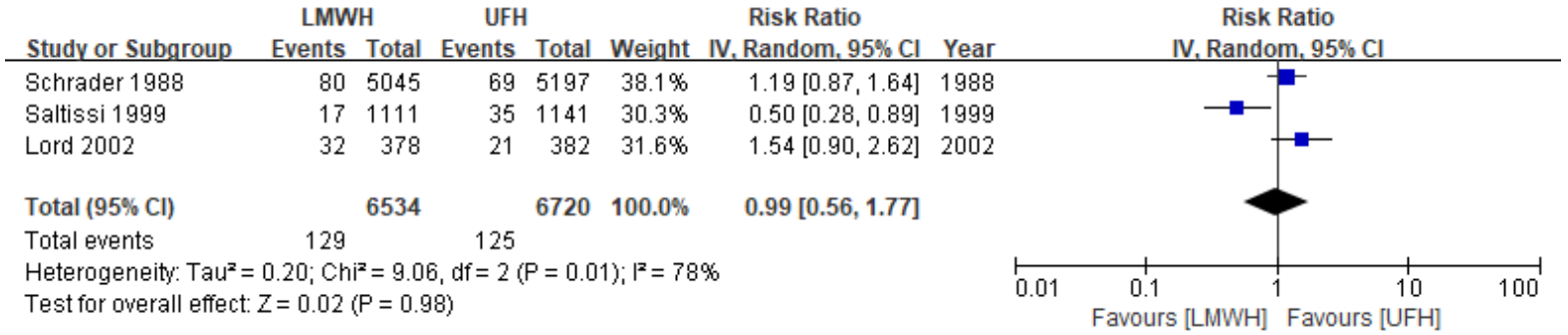


Key question 4.1.



1.1. Meta-analysis result for bleeding

1.2. Meta-analysis result for hemodialysis circuit thrombosis



Key question 4.2.

Not applicable

Key question 5.1.

Not applicable

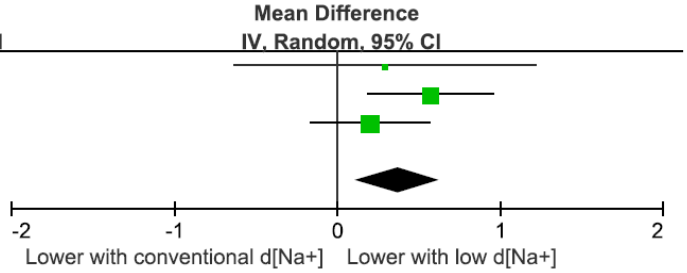
Key question 5.2.

1.1. Interdialytic weight gain

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

	conventional d[Na+]			Low d[Na+]				Mean Difference
Study or Subgroup	Mean [kg]	SD [kg]	Total	Mean [kg]	SD [kg]	Total	Weight	IV, Random, 95% CI
Beduschi 2013	2.79	1.92	18	2.5	0.63	20	7.6%	0.29 [-0.64, 1.22]
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]
Total (95% CI)			**84**			**85**	**100.0%**	**0.37 [0.11, 0.62]**

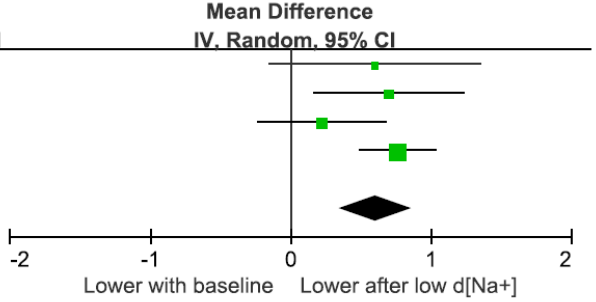
Heterogeneity: Tau² = 0.00; Chi² = 1.88, df = 2 (P = 0.39); I² = 0%
Test for overall effect: Z = 2.82 (P = 0.005)



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

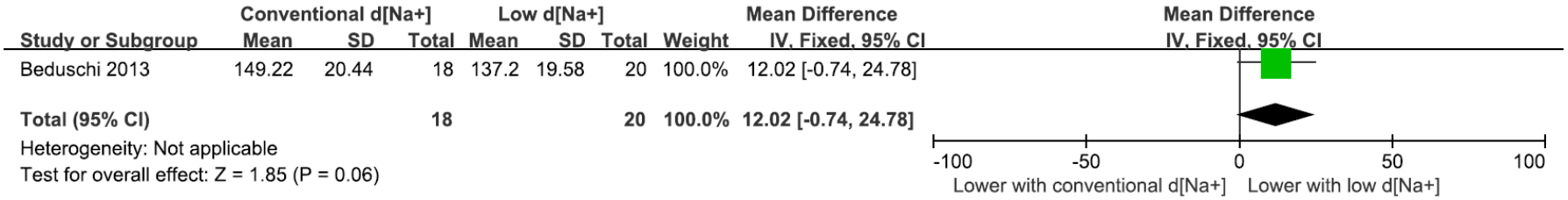
	Baseline d[Na+] 138-140			After low d[Na+] <137				Mean Difference
Study or Subgroup	Mean [kg]	SD [kg]	Total	Mean [kg]	SD [kg]	Total	Weight	IV, Random, 95% CI
Arramreddy (2012)	2.4	1.2	13	1.8	0.7	13	10.6%	0.60 [-0.16, 1.36]
Sayarlioglu (2007)	2.5	1	18	1.8	0.6	18	18.8%	0.70 [0.16, 1.24]
Zhou (2013)	2.89	0.66	16	2.67	0.67	16	24.0%	0.22 [-0.24, 0.68]
Akyol (2017)	2.08	0.81	49	1.32	0.56	49	46.6%	0.76 [0.48, 1.04]
Total (95% CI)			**96**			**96**	**100.0%**	**0.60 [0.34, 0.86]**

Heterogeneity: Tau² = 0.02; Chi² = 3.97, df = 3 (P = 0.27); I² = 24%
Test for overall effect: Z = 4.54 (P < 0.00001)

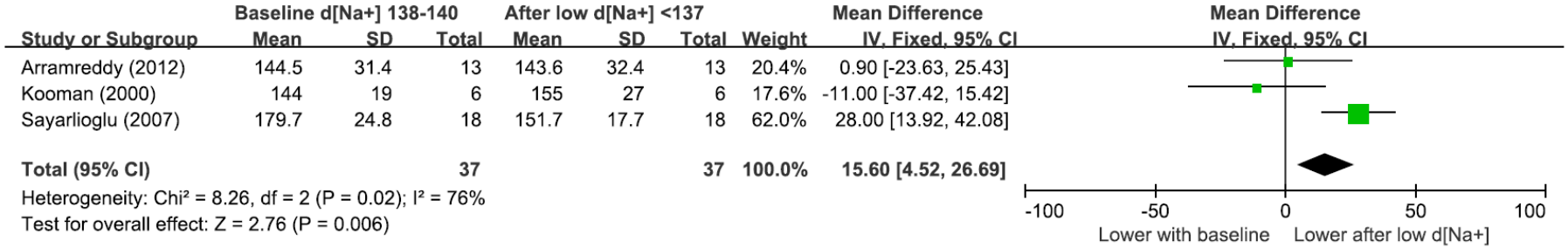


1.2. Predialysis BP

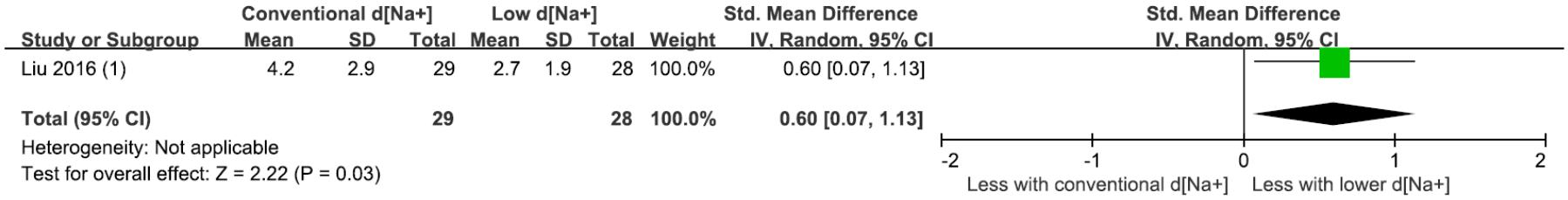
1.2.1. Low dialysate [Na^+] (<138 mEq/L) vs. conventional dialysate [Na^+] (138 -140 mEq/L): RCT



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

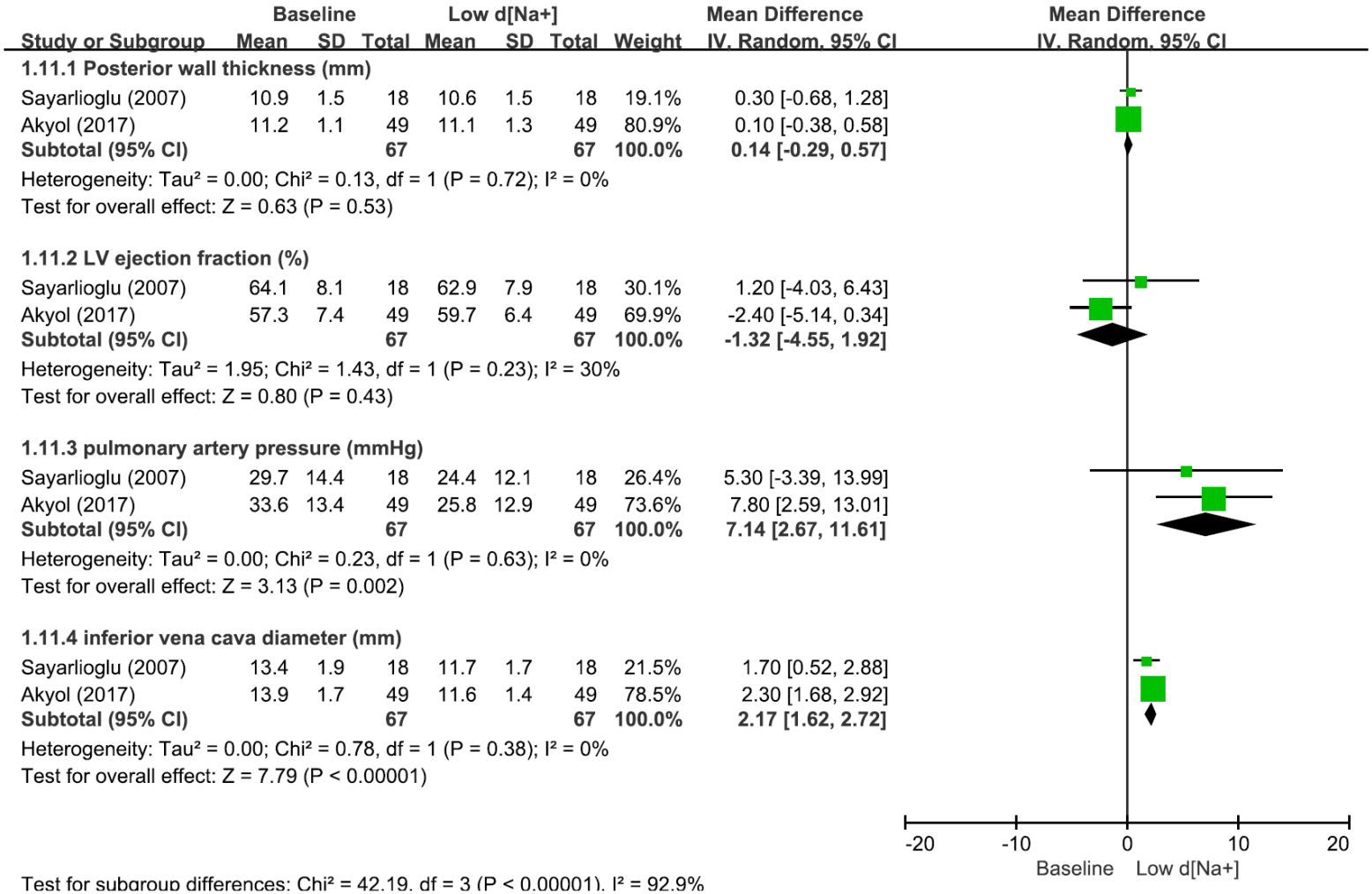


1.3. Antihypertensive medication: Low dialysate [Na^+] (<138 mEq/L) vs. conventional dialysate [Na^+] (138 -140 mEq/L): RCT



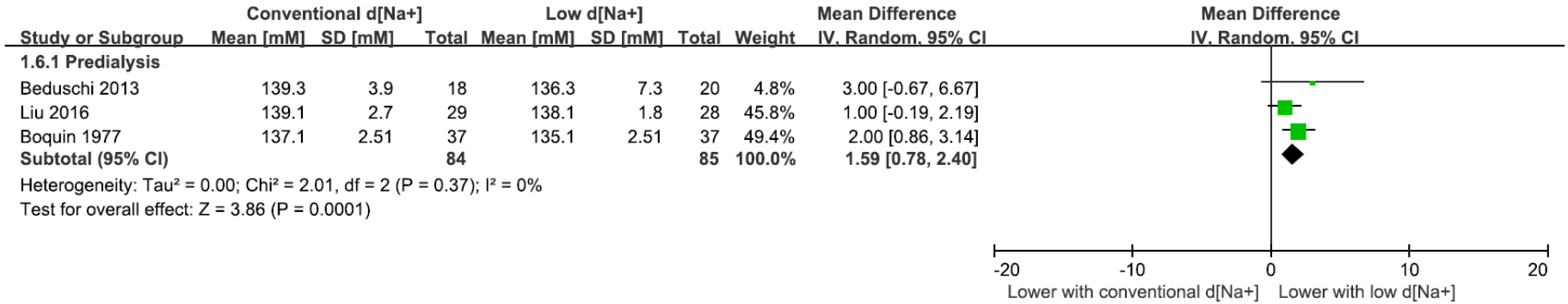
Footnotes
(1) Aggregated equivalent dose units

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

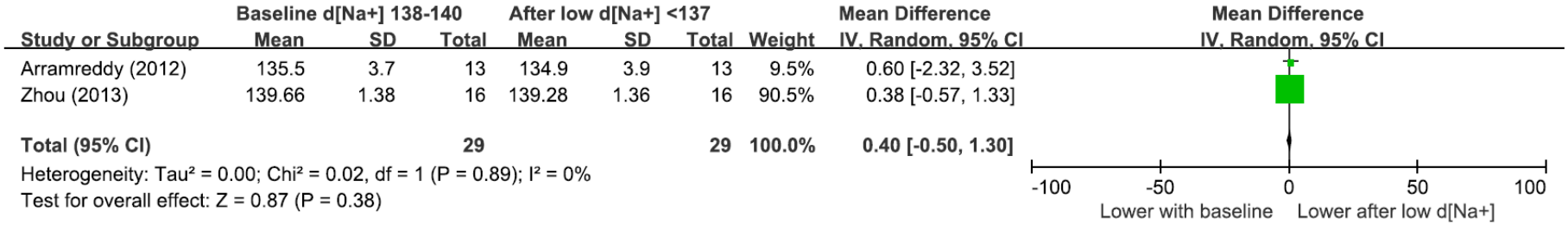


1.5. Serum Na

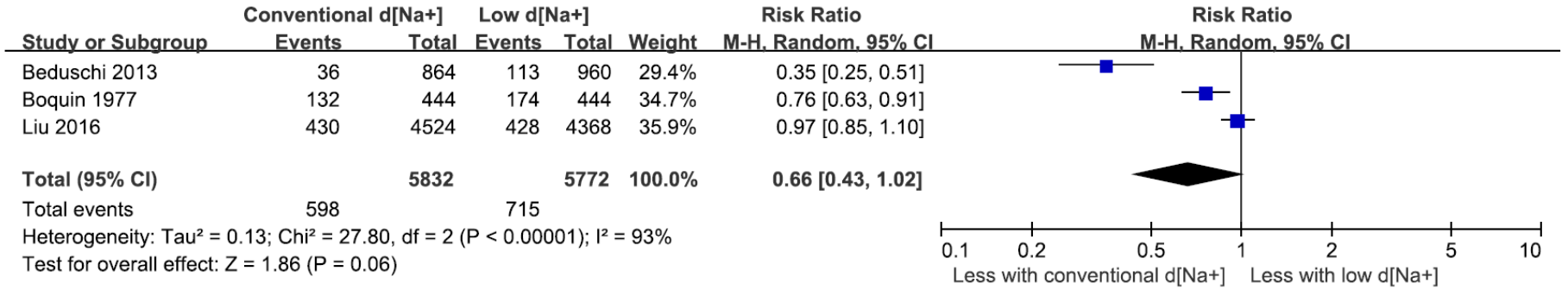
1.5.1. Low dialysate [Na^+] (<138 mEq/L) vs. conventional dialysate [Na^+] (138 -140 mEq/L): RCT



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



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



Key question 6.1.

Not applicable

Key question 6.2.

Not applicable

Key question 7.1.

Not applicable

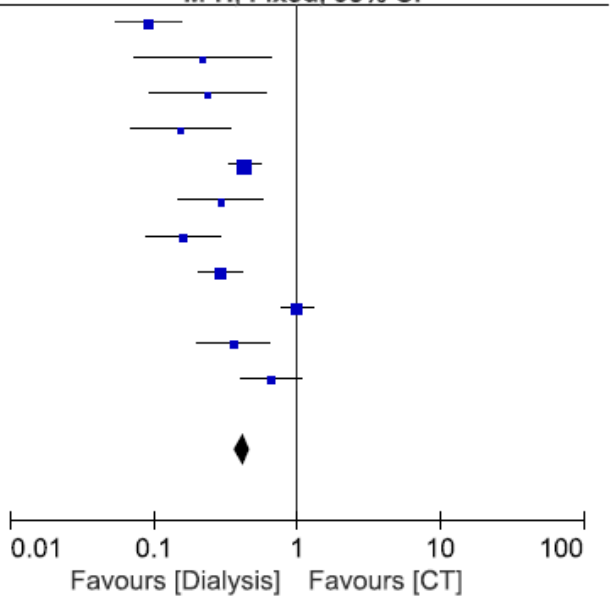
Key question 8.1.

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

	Dialysis		Conservative treatment			Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
Brown 2015	28	273	68	122	11.4%	0.09 [0.05, 0.15]	
Carson 2009	100	173	25	29	2.4%	0.22 [0.07, 0.66]	
Joly 2003	60	101	37	43	2.9%	0.24 [0.09, 0.61]	
Murtagh 2007	12	52	51	77	4.3%	0.15 [0.07, 0.34]	
Pyart 2020	420	841	262	375	24.6%	0.43 [0.33, 0.56]	
Raman 2017	72	123	67	81	4.5%	0.29 [0.15, 0.58]	
Smith 2003	41	258	34	63	6.2%	0.16 [0.09, 0.29]	
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]	
van Loon 2019	31	192	31	89	4.8%	0.36 [0.20, 0.64]	
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: Chi² = 102.60, df = 10 (P < 0.00001); I² = 90%

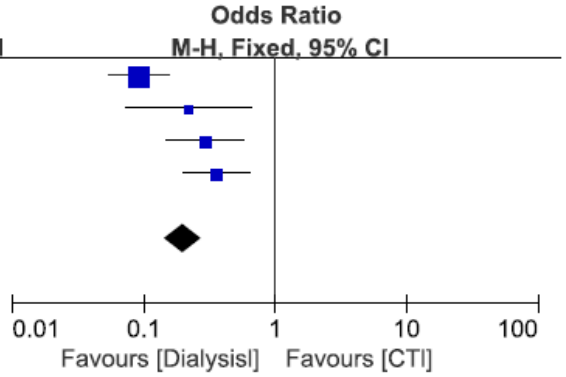
Test for overall effect: Z = 13.34 (P < 0.00001)



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

Study or Subgroup	Dialysis Events	Dialysis Total	Conservative treatment Events	Conservative treatment Total	Weight	Odds Ratio M-H, Fixed, 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			

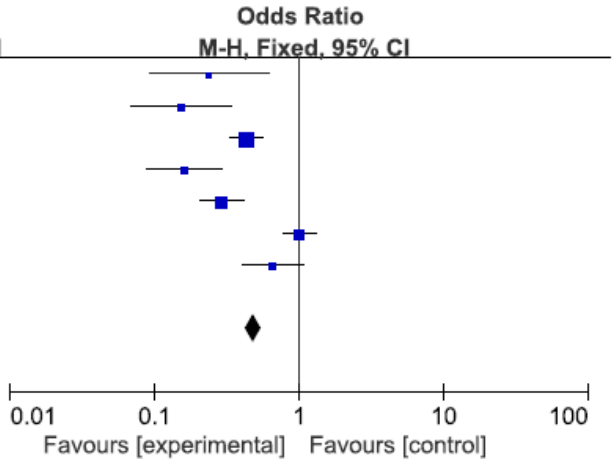
Heterogeneity: Chi² = 13.77, df = 3 (P = 0.003); I² = 78%
Test for overall effect: Z = 9.83 (P < 0.00001)



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

Study or Subgroup	Dialysis Events	Dialysis Total	Conservative treatment Events	Conservative treatment Total	Weight	Odds Ratio 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]**
Total events	1170		901			

Heterogeneity: Chi² = 63.79, df = 6 (P < 0.00001); I² = 91%
Test for overall effect: Z = 10.10 (P < 0.00001)



Key question 8.2.

Not applicable