Timing of Renal Replacement Therapy for patients with Acute Kidney Injury: A Systematic Review and Meta-Analysis - Supplementary Material 1

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# ▲	Searches
1	exp Renal Replacement Therapy/
2	exp Renal Dialysis/
3	exp Dialysis/
4	exp Hemofiltration/
5	exp Hemodiafiltration/
6	1 or 2 or 3 or 4 or 5
7	exp Randomized Controlled Trials as Topic/
8	exp Controlled Clinical Trial/
9	7 or 8
10	(time or timing or early or earlier or late or later or delayed or initiation or start).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]
11	6 and 9 and 10
12	limit 11 to english language

Figure s1.1: MEDLINE/CENTRAL search strategy

▼ **Search History** (12)

# ▲	Searches
1	exp renal replacement therapy/
2	exp hemodialysis/
3	exp dialysis/
4	exp hemofiltration/
5	exp hemodiafiltration/
6	1 or 2 or 3 or 4 or 5
7	(time or timing or early or earlier or late or later or delayed or initiation or start).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]
8	exp randomized controlled trial/
9	exp controlled clinical trial/
10	8 or 9
11	6 and 7 and 10
12	limit 11 to english language

Save Remove Combine with: AND OR

Figure s1.2: EMBASE search strategy

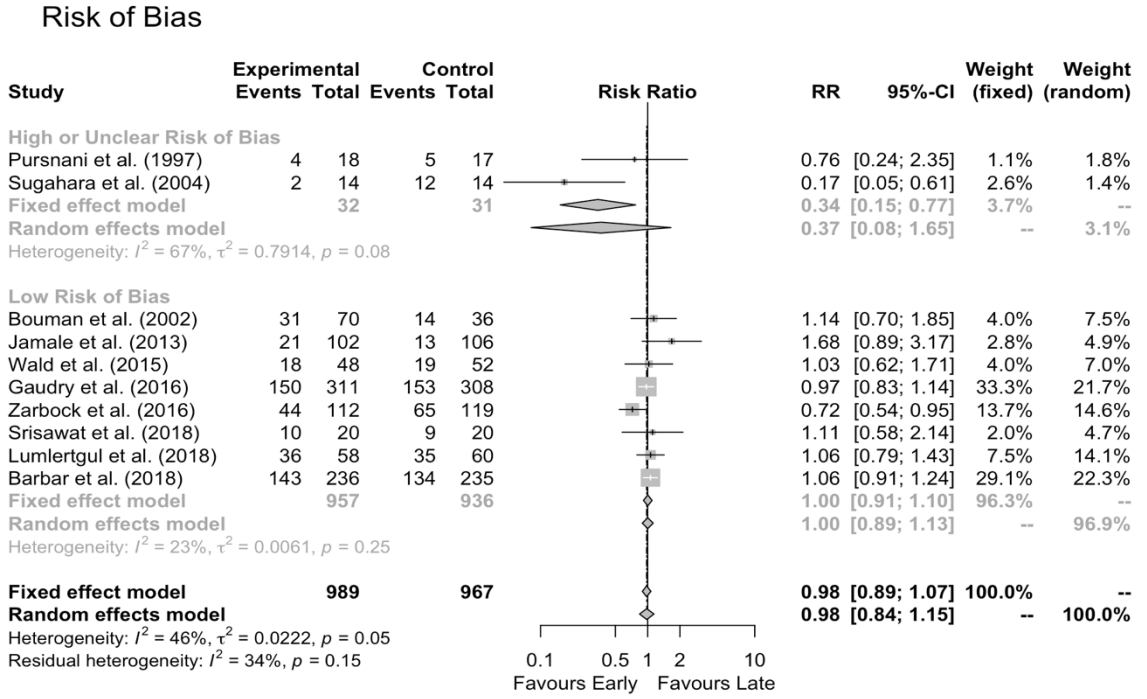

Figure s1.3: Subgroup analysis of low vs high/unclear risk of bias

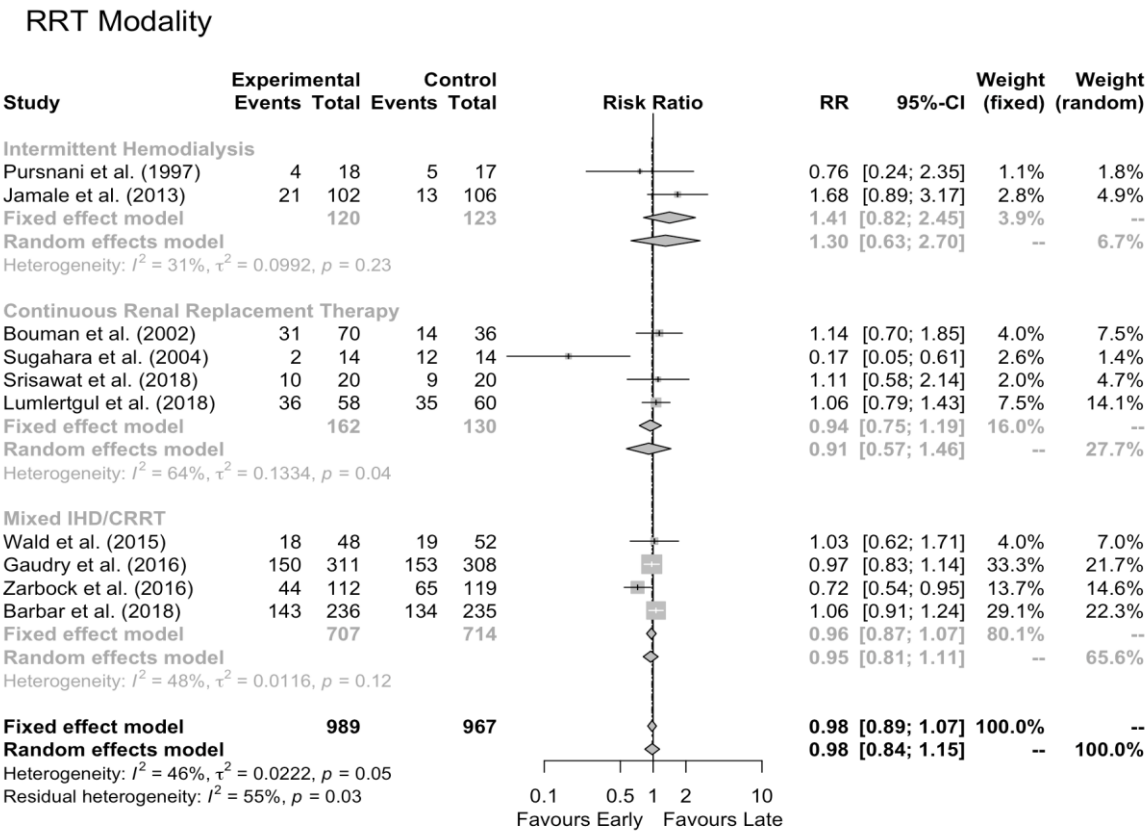

Figure s1.4: Subgroup analysis of RRT modality

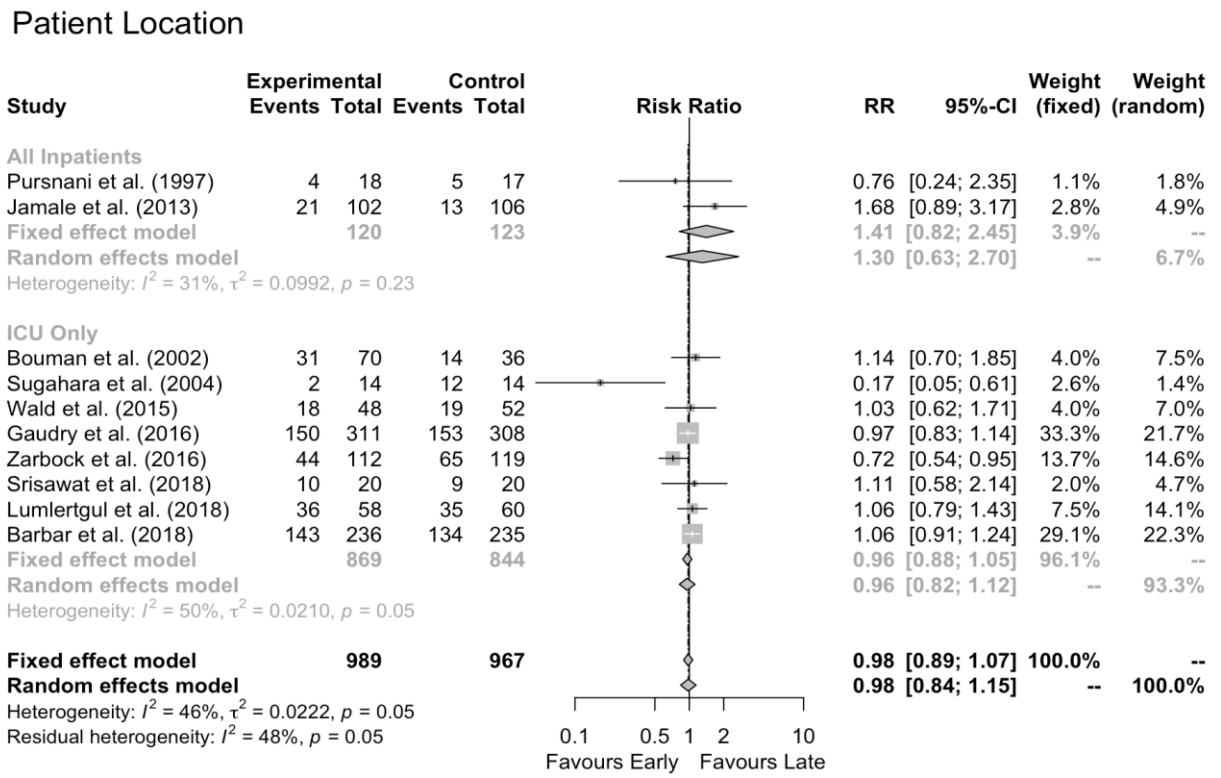

Figure s1.5: Subgroup analysis of inpatients vs ICU only patients

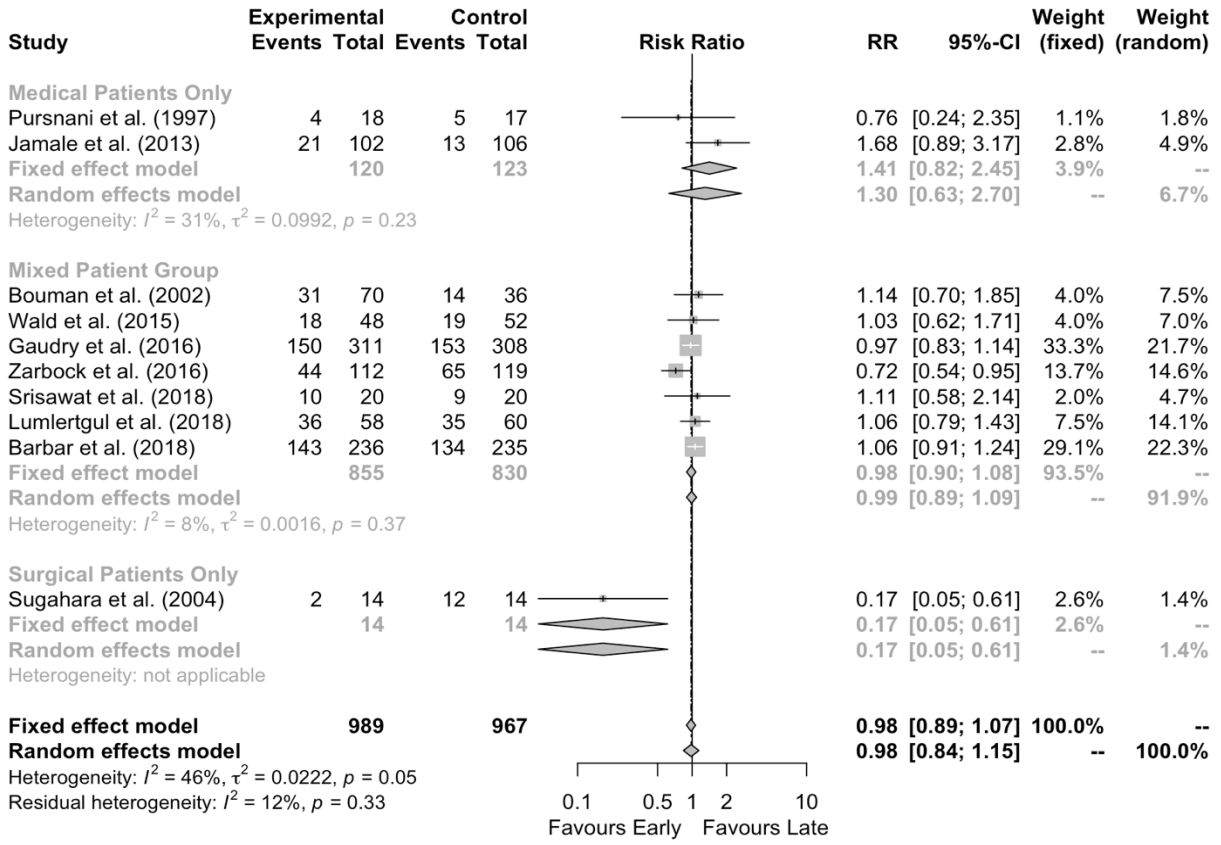

Figure s1.6: Subgroup analysis of medical, surgical and mixed patient population

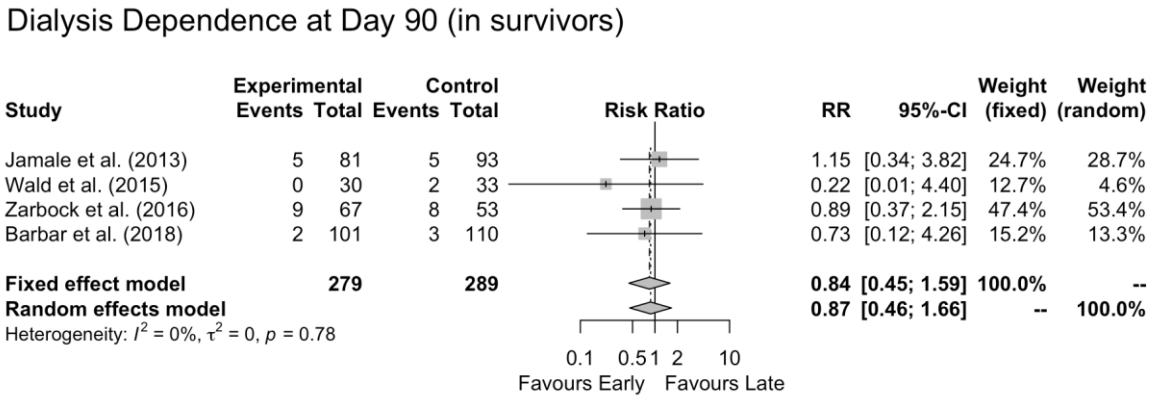

Figure s1.7: Dialysis dependence in survivors at 90 days

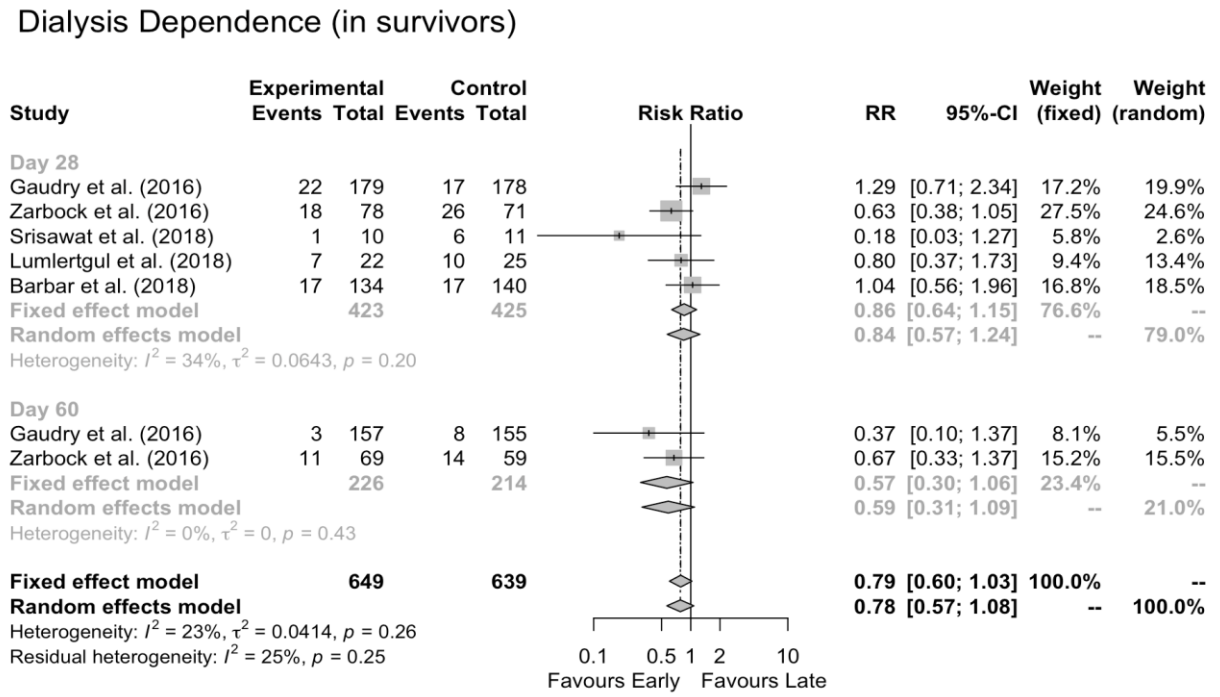

Figure s1.8: Dialysis dependence in survivors at 28 and 60 days

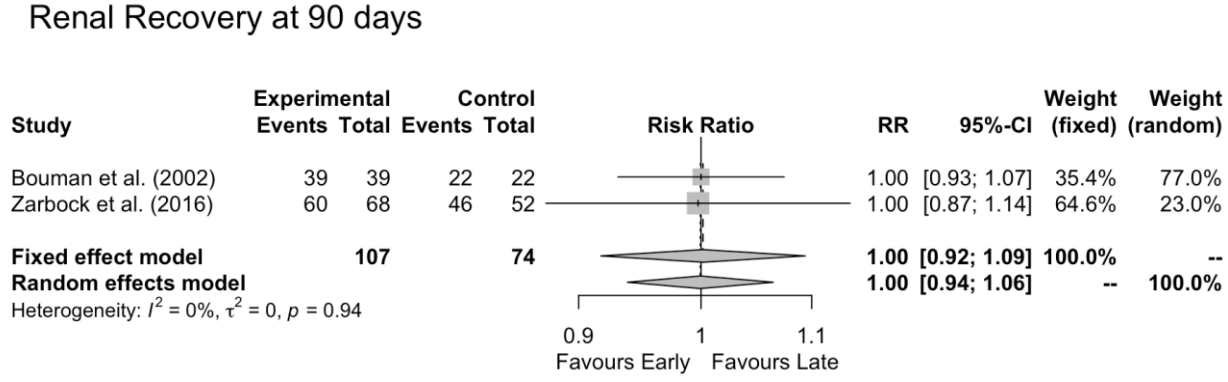

Figure s1.9: Renal recovery in survivors at 90 days

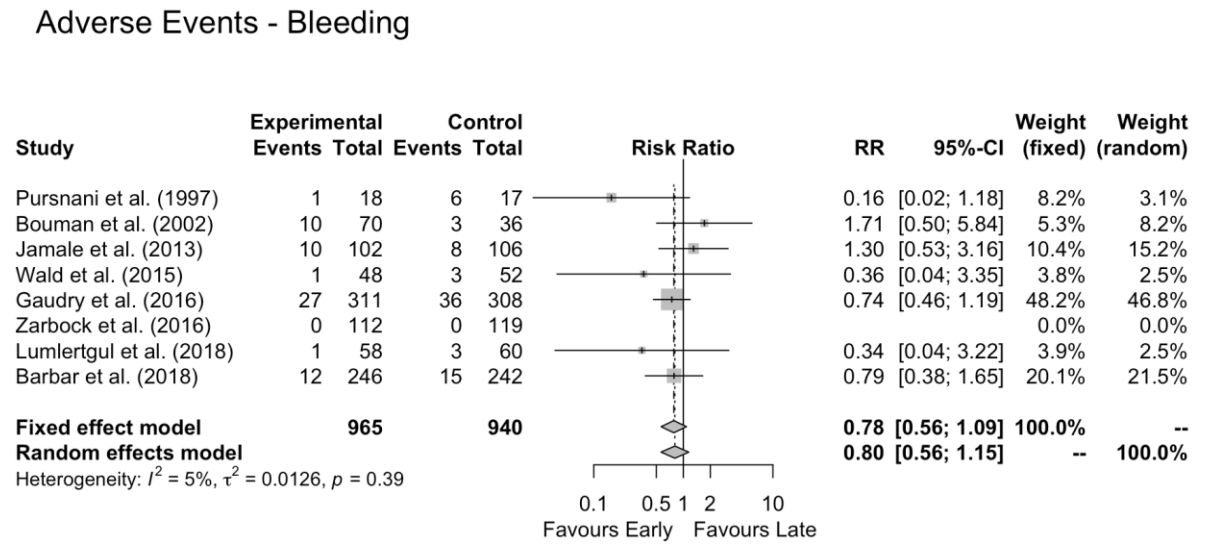

Figure s1.10: Adverse Events - Bleeding

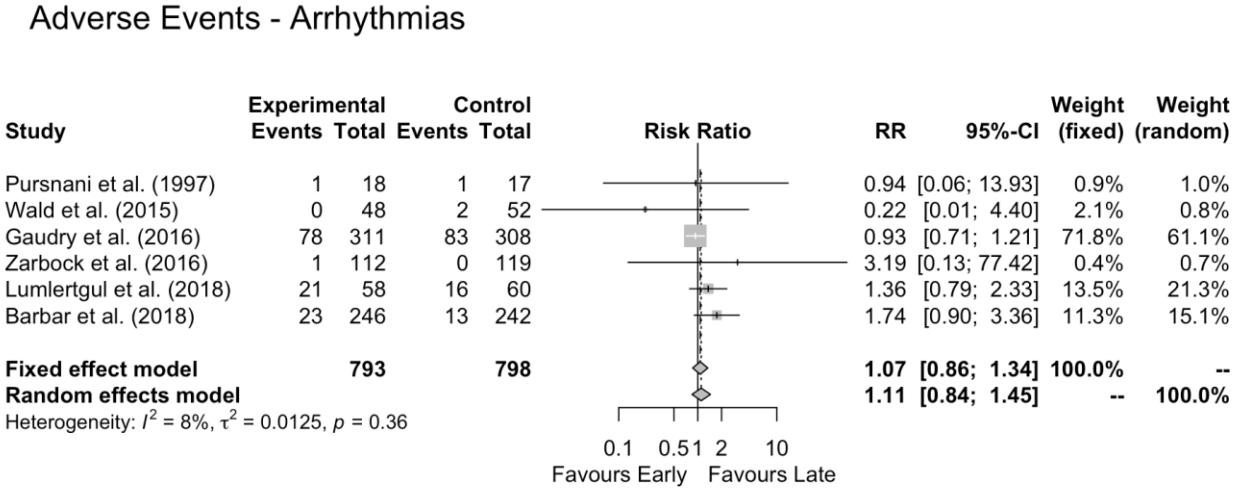

Figure s1.11: Adverse Events – Arrhythmias

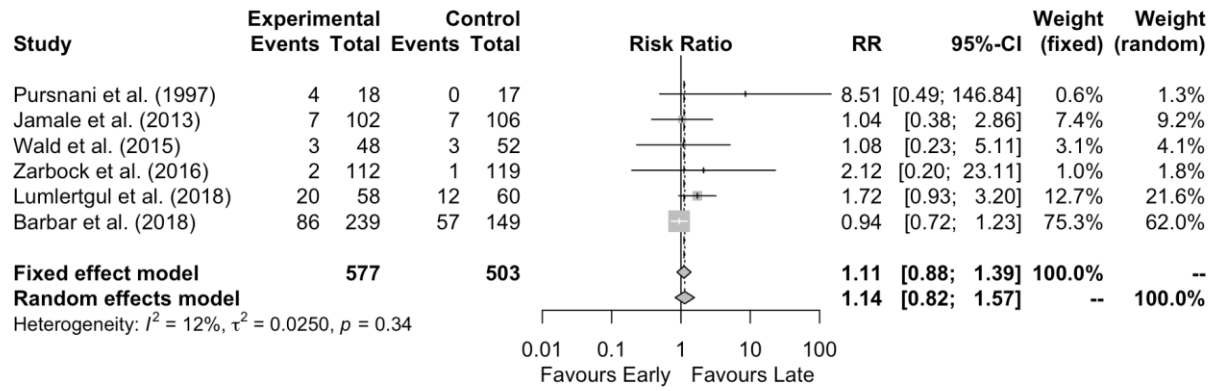

Figure s1.12: Adverse Events – Hypotension

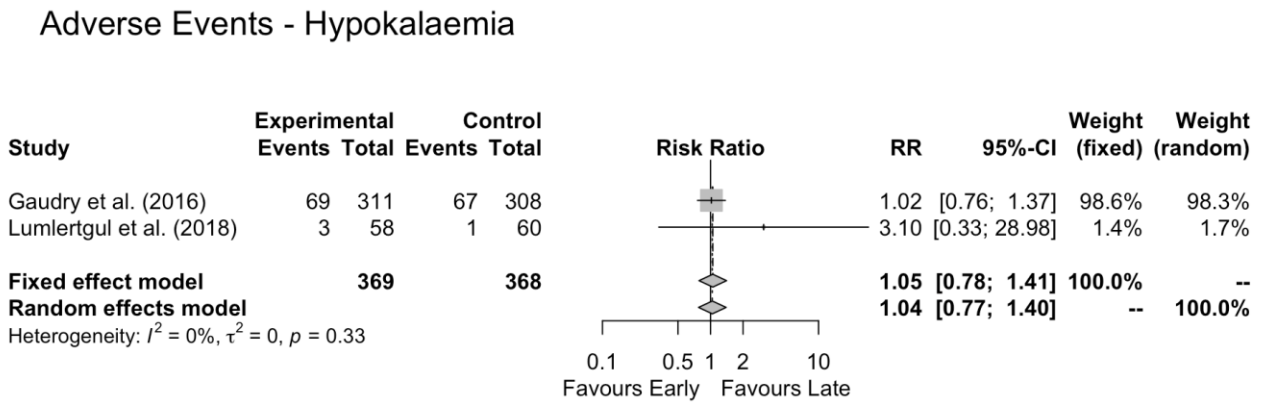

Figure s1.13: Adverse Events - Hypokalaemia

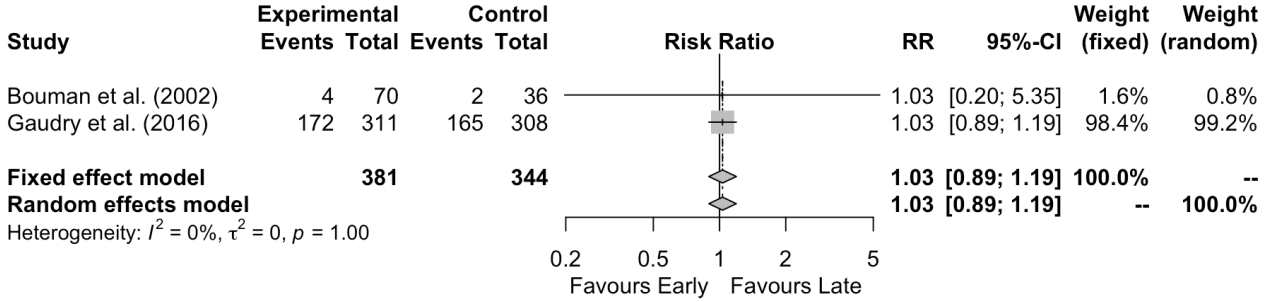

Figure s1.14: Adverse Events – Thrombocytopenia

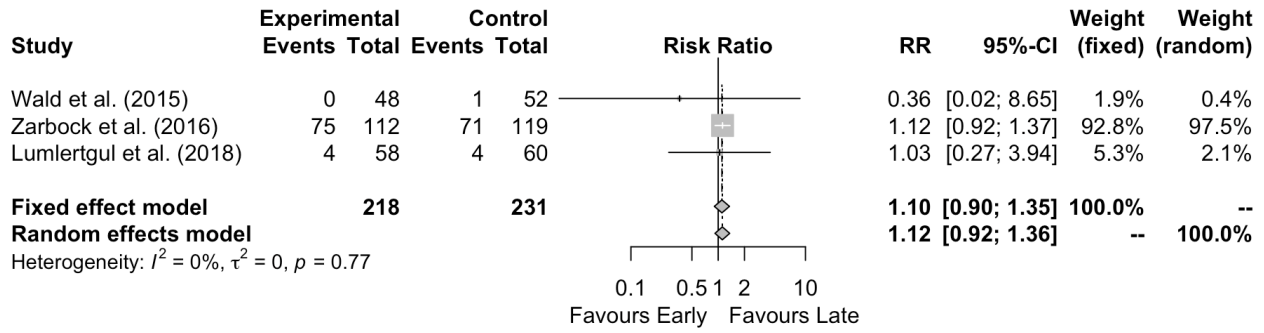

Figure s1.15: Adverse Events – Hypocalcaemia

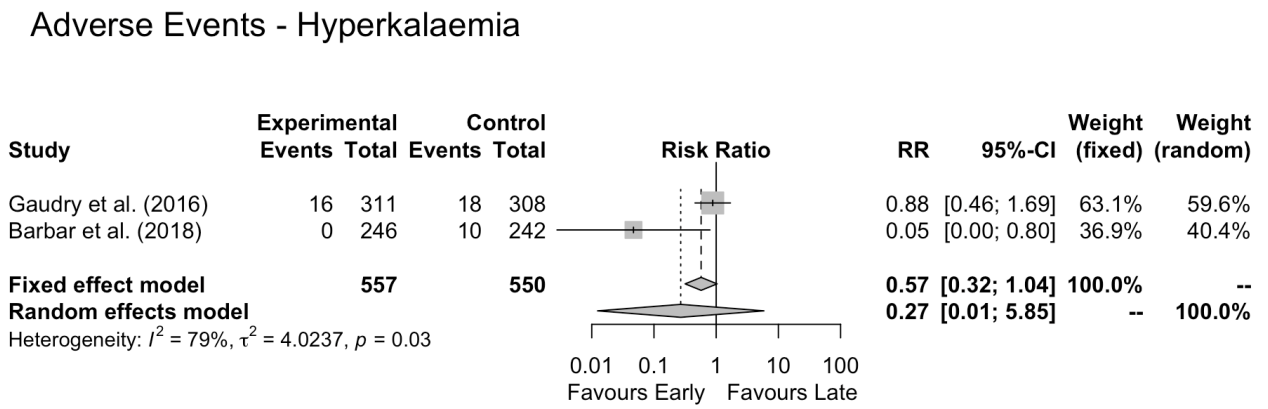

Figure s1.16: Adverse Events - Hyperkalaemia

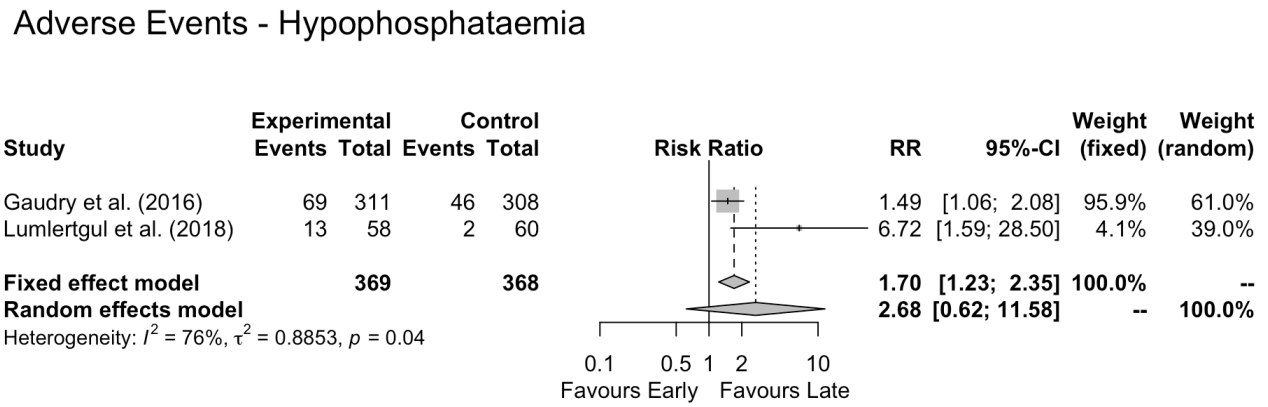

Figure s1.17: Adverse Events – Hypophosphataemia

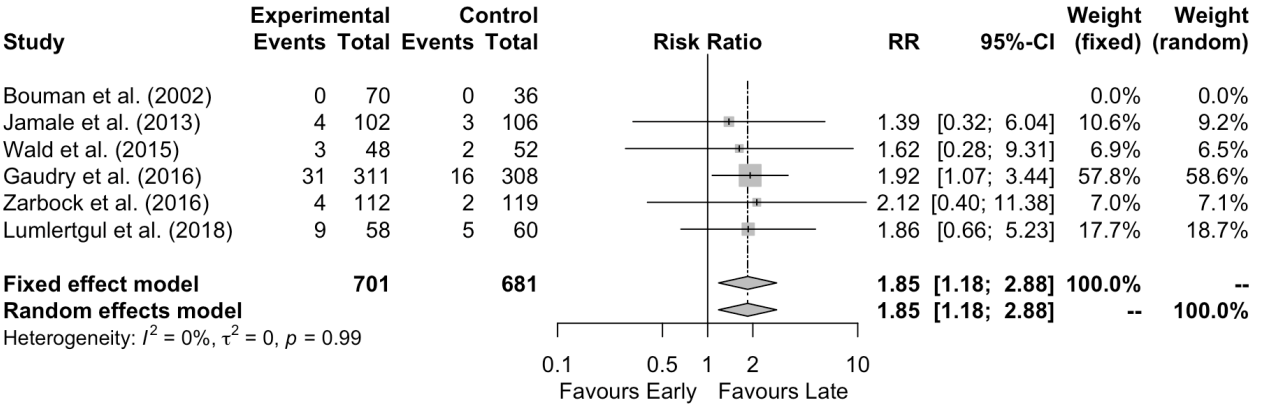

Figure s1.18: Adverse Events - Catheter Related Complications

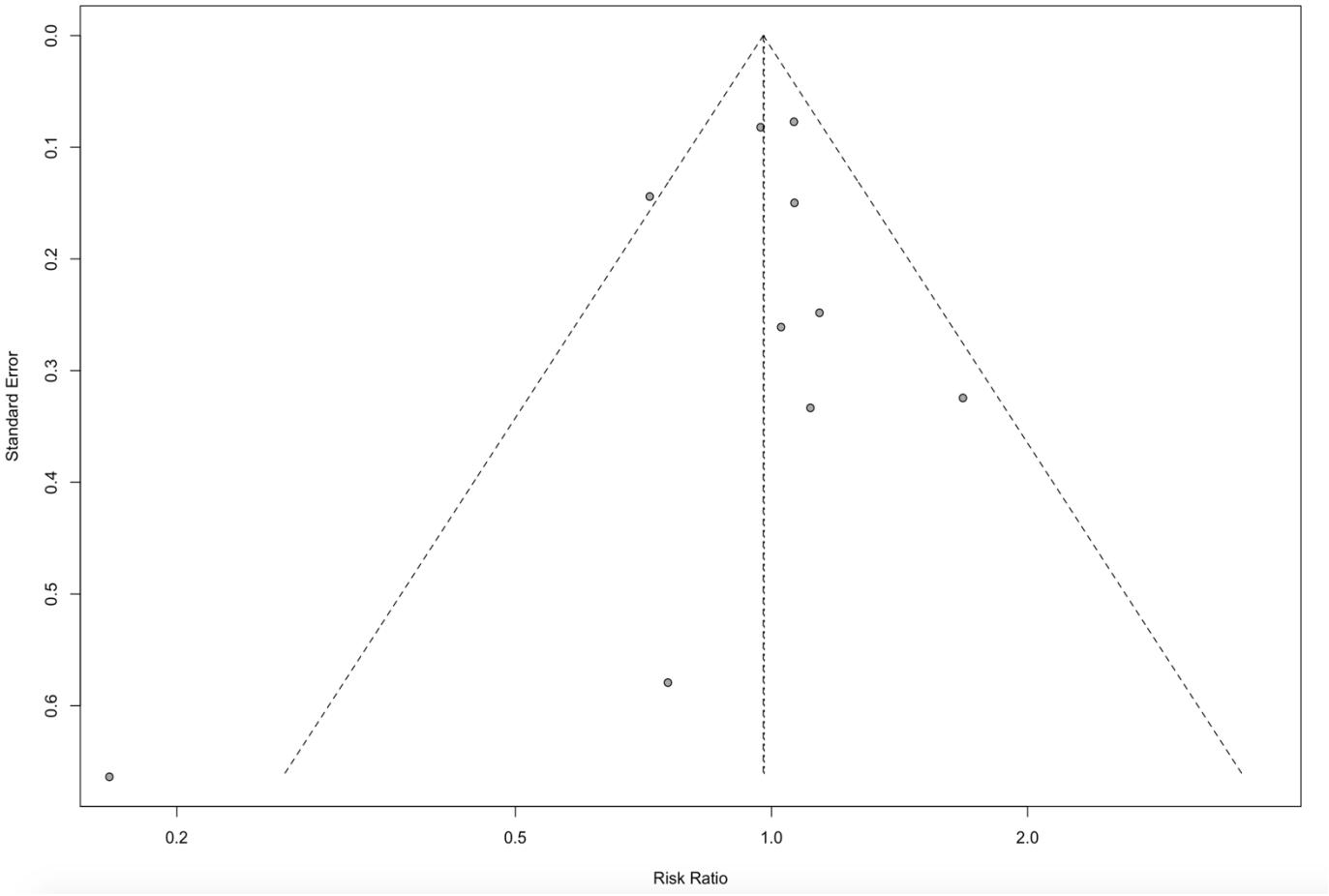

Figure s1.19: Inverted funnel plot using overall mortality outcome

Paper	Random Sequence Generation	Allocation Concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective Reporting	Other Bias	OVERALL
Pursnani (1997)	Unclear	Unclear	Low	Low	Low	Low	Unclear	**Unclear**
Bouman (2002)	Unclear	Low	Low	Low	Low	Low	Low	**Low**
Sugahara (2004)	Unclear	Unclear	Low	Low	High	Low	Unclear	**Unclear**
Jamale (2013)	Low	Low	Low	Low	Low	Low	Low	**Low**
Wald (2015)	Low	Low	Low	Low	Low	Low	Low	**Low**
Gaudry (2016)	Low	Low	Low	Low	Low	Low	Low	**Low**
Zarbock (2016)	Low	Low	Low	Low	Low	Low	Low	**Low**
Srisawat (2018)	Low	Low	Low	Low	Low	Low	Low	**Low**
Lumlertgul (2018)	Low	Low	Low	Low	Low	Low	Low	**Low**
Barbar (2018)	Low	Low	Low	Low	Low	Low	Low	**Low**

Table s1.1: Risk of bias assessment

Outcomes	Number of participants (studies)	Anticipated absolute effects (95% CI) *		Relative effect (95% CI)	Certainty of evidence (GRADE)
		Control group risk (Late initiation)	Intervention group risk (Early initiation)		
Overall mortality	1956 (10 studies)	473 per 1000	464 per 1000 (397 – 544)	RR = 0.98 (0.84 – 1.15)	⊕⊕⊖⊖ LOW[1,2]
In ICU mortality	206 (2 studies)	293 per 1000	299 per 1000 (193 – 463)	RR = 1.02 (0.66 – 1.58)	⊕⊕⊕⊖ LOW[3]
In hospital mortality	414 (3 studies)	365 per 1000	423 per 1000 (307 – 584)	RR = 1.16 (0.84 – 1.60)	⊕⊕⊕⊖ LOW[3]
28-day mortality	1602 (6 studies)	428 per 1000	424 per 1000 (377 – 475)	RR = 0.99 (0.88 – 1.11)	⊕⊕⊕⊖ MODERATE[1]
60-day mortality	850 (2 studies)	500 per 1000	445 per 1000 (355 – 560)	RR = 0.89 (0.71 – 1.12)	⊕⊕⊖⊖ LOW[1,2]
90-day mortality	808 (3 studies)	538 per 1000	500 per 1000 (371 – 662)	RR = 0.93 (0.69 – 1.23)	⊕⊕⊖⊖ LOW[1,2]
Dialysis dependence at 90 days	568 (4 studies)	57 per 1000	50 per 1000 (26 – 95)	RR = 0.87 (0.46 – 1.66)	⊕⊕⊕⊖ LOW[3]

Table s1.2: GRADE assessment of evidence

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect
* The basis for the baseline risk is calculated using the median control group risk across studies. The anticipated absolute effect is expressed as risk difference (and 95% CI) and is based on baseline risk in comparison group and relative effect of intervention
[1]Imprecision – CIs cross threshold for clinically meaningful effect
[2]Inconsistency – Moderate/high heterogeneity
[3]Serious imprecision – CIs significantly wide and crossing threshold for clinically meaningful effect