

**REGIONAL CITRATE ANTICOAGULATION VERSUS SYSTEMIC HEPARIN IN CONTINUOUS KIDNEY REPLACEMENT THERAPY: EXAMINING THE ROLE
OF EVIDENCE IN HEALTH TECHNOLOGY ASSESSMENT**

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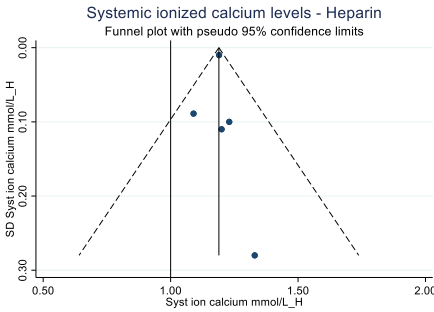
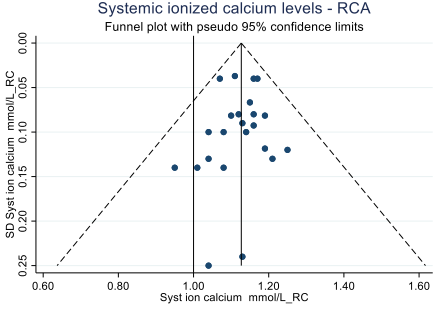
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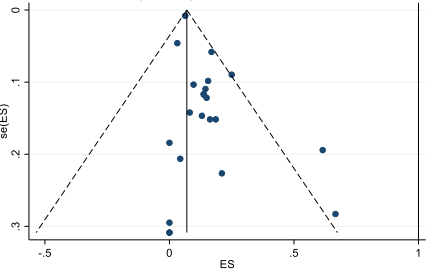
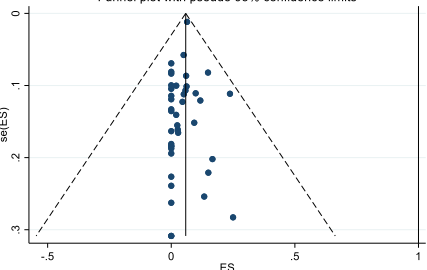
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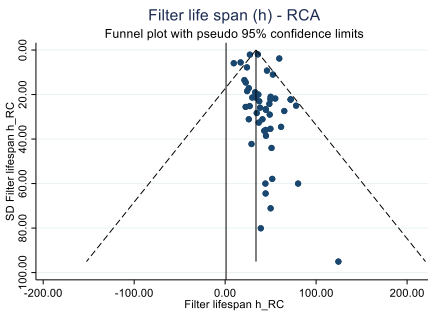
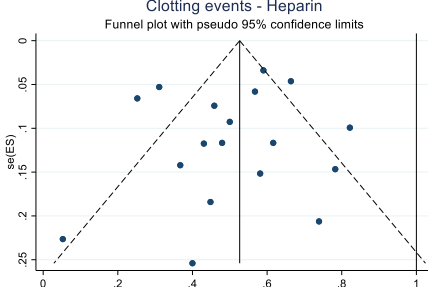
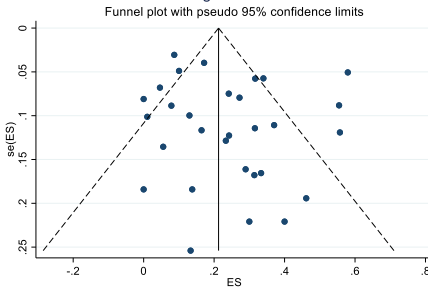
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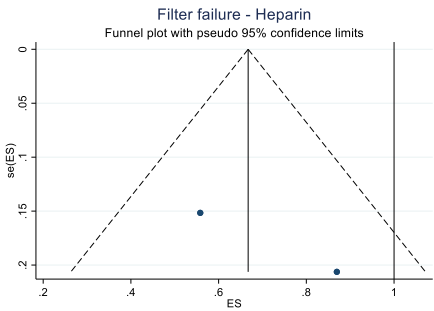
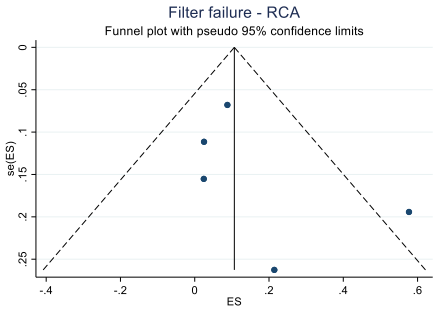
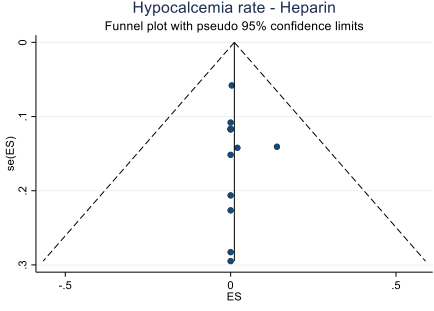
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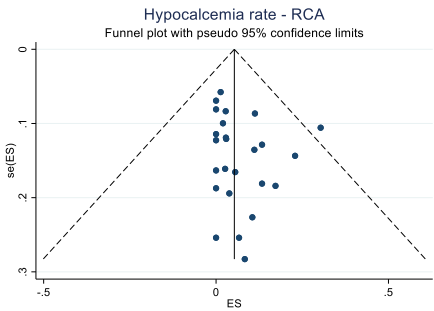
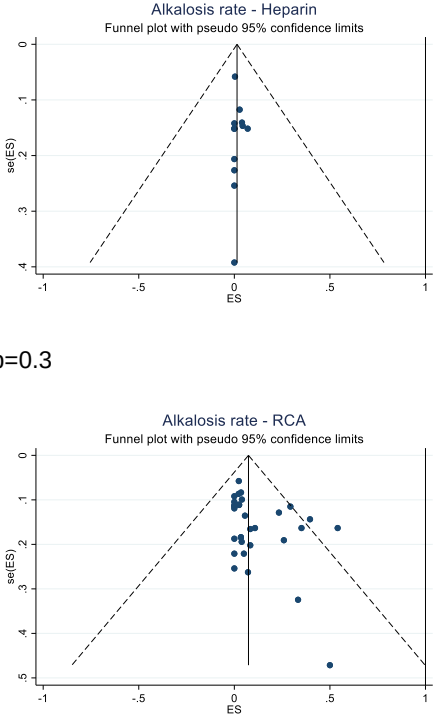
GRADE assessment

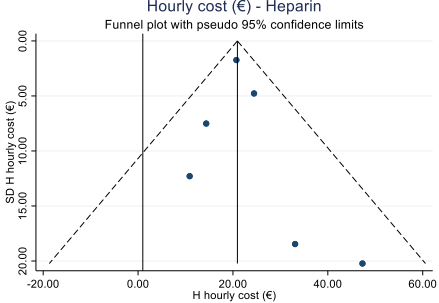
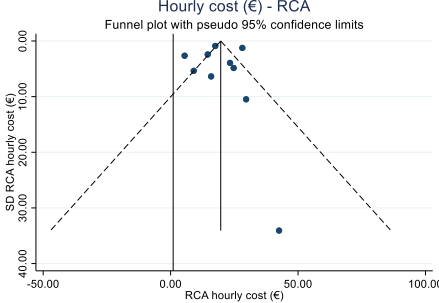
Outcome	Number of studies	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias (Begg's test p-values)	Impact	Quality of evidence
<i>Whole population</i>								
Ionized calcium levels	Heparin: 3 RCTs, 2 observational studies RCA: 4 RCTs, 19 observational studies	Not serious (most observational studies)	Not serious	Not serious	Not serious	Not serious  p=0.33  p=0.23	Risk of bias is balanced between RCTs and observational studies	⊕⊕⊕○ Moderate
Bleeding episodes	Heparin: 12 RCTs, 15 observational studies RCA: 10 RCTs, 26	Not serious (most observational studies)	Not serious	Not serious	Not serious	Not serious	Heterogeneity in the studies likely due to different definitions of bleeding	⊕⊕⊕○ Moderate

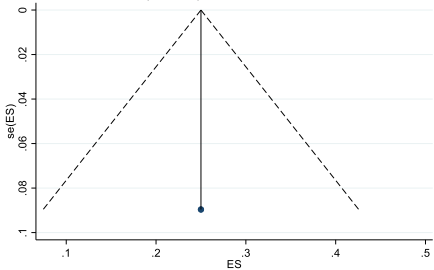
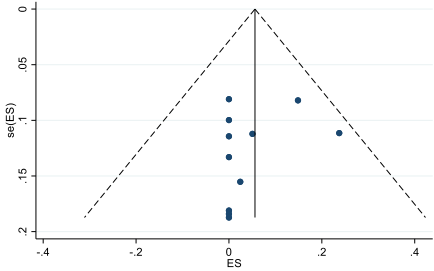
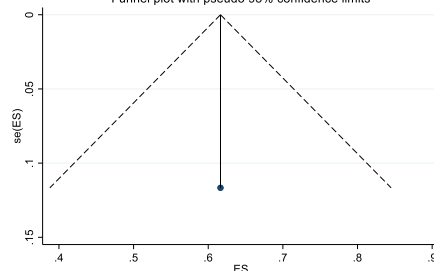
		observational studies					Bleeding episodes - Heparin Funnel plot with pseudo 95% confidence limits  p=0.14 Bleeding episodes - RCA Funnel plot with pseudo 95% confidence limits  p=0.16		
Filter span	life	Heparin: 8 RCTs, 12 observational studies RCA: 17 RCTs, 38 observational studies	Not serious (most observational studies)	Not serious	Not serious	Not serious	Not serious	Heterogeneity across studies was higher for RCA compared to heparin, probably due to the differences in protocols used	⊕⊕⊕○ Moderate

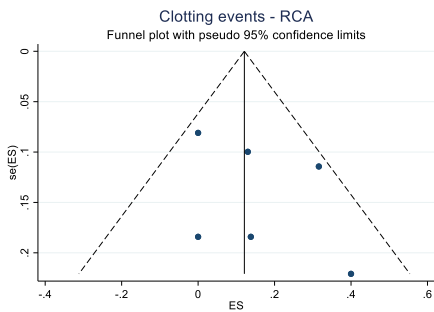
						Filter life span (h) - RCA Funnel plot with pseudo 95% confidence limits  p=0.12		
Clotting issues	Heparin: 7 RCTs, 9 observational studies RCA: 11 RCTs, 21 observational studies	Not serious (most observational studies)	Serious	Not serious	Not serious	Clotting events - Heparin Funnel plot with pseudo 95% confidence limits  p=0.49 Clotting events - RCA Funnel plot with pseudo 95% confidence limits  p=0.49	Large variability across studies for both RCA and heparin	⊕⊕○○ Low

Filter failure	Heparin: 1 RCTs, 1 observational studies RCA: 1 RCTs, 4 observational studies	Not serious (most observational studies)	Not serious	Not serious	Serious	Not serious  p=0.32  p=0.33	Broad definition of failure	⊕⊕○○ Low
Hypocalcemia rate	Heparin: 8 RCTs, 10 observational studies RCA: 4 RCTs, 15 observational studies	Not serious (balanced types of studies)	Not serious	Not serious	Not serious	Serious 	Heterogeneity across studies was higher for RCA compared to heparin, likely due to differences in the protocols applied. Possible publication bias for both	⊕⊕○○ Low

						p=0.003  Hypocalcemia rate - RCA Funnel plot with pseudo 95% confidence limits p=0.034	RCA and heparin.	
Alkalosis rate	Heparin: 6 RCTs, 7 observational studies RCA: 6 RCTs, 24 observational studies	Not serious (most observational studies)	Not serious	Not serious	Not serious	Serious  Alkalosis rate - Heparin Funnel plot with pseudo 95% confidence limits Alkalosis rate - RCA Funnel plot with pseudo 95% confidence limits p=0.3	Heterogeneity was particularly high for RCA, likely due to variations in RCA protocols, including differences in citrate dosing, calcium supplementation, and patient management strategies.	⊕⊕○○ Low

						p=0.003		
Hourly cost	Heparin: 2 RCTs, 2 observational studies RCA: 4 RCTs, 8 observational studies	Not serious (most observational studies)	Not serious	Not serious	Not serious	Not serious  Hourly cost (€) - Heparin Funnel plot with pseudo 95% confidence limits p=0.35  Hourly cost (€) - RCA Funnel plot with pseudo 95% confidence limits p=0.42	Risk of bias is balanced between RCTs and observational studies	⊕⊕⊕○ Moderate
<i>High risk of bleeding population</i>								
Bleeding episodes	Heparin: 1 RCT RCA: 1 RCT, 10 observational studies	Serious (mainly observational studies)	Not serious	Not serious	Not serious	Not serious	Risk of bias mainly due to the presence of observational studies	⊕⊕○○ Low

						Bleeding episodes - Heparin Funnel plot with pseudo 95% confidence limits  p=not measurable Bleeding episodes - RCA Funnel plot with pseudo 95% confidence limits  p=0.59		
Clotting events	Heparin: 1 observational study RCA: 6 observational studies	Serious (only observational studies)	Not serious	Not serious	Not serious	Not serious Clotting events - Heparin Funnel plot with pseudo 95% confidence limits 	Risk of bias mainly due to the presence of observational studies	⊕⊕○○ Low

						p=not measurable Clotting events - RCA Funnel plot with pseudo 95% confidence limits  <table><tr><th>ES</th><th>se(ES)</th></tr><tr><td>0.0</td><td>0.07</td></tr><tr><td>0.0</td><td>0.18</td></tr><tr><td>0.1</td><td>0.10</td></tr><tr><td>0.1</td><td>0.18</td></tr><tr><td>0.3</td><td>0.12</td></tr><tr><td>0.4</td><td>0.22</td></tr><tr><td>0.4</td><td>0.20</td></tr></table> p=0.44	ES	se(ES)	0.0	0.07	0.0	0.18	0.1	0.10	0.1	0.18	0.3	0.12	0.4	0.22	0.4	0.20		
ES	se(ES)																							
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