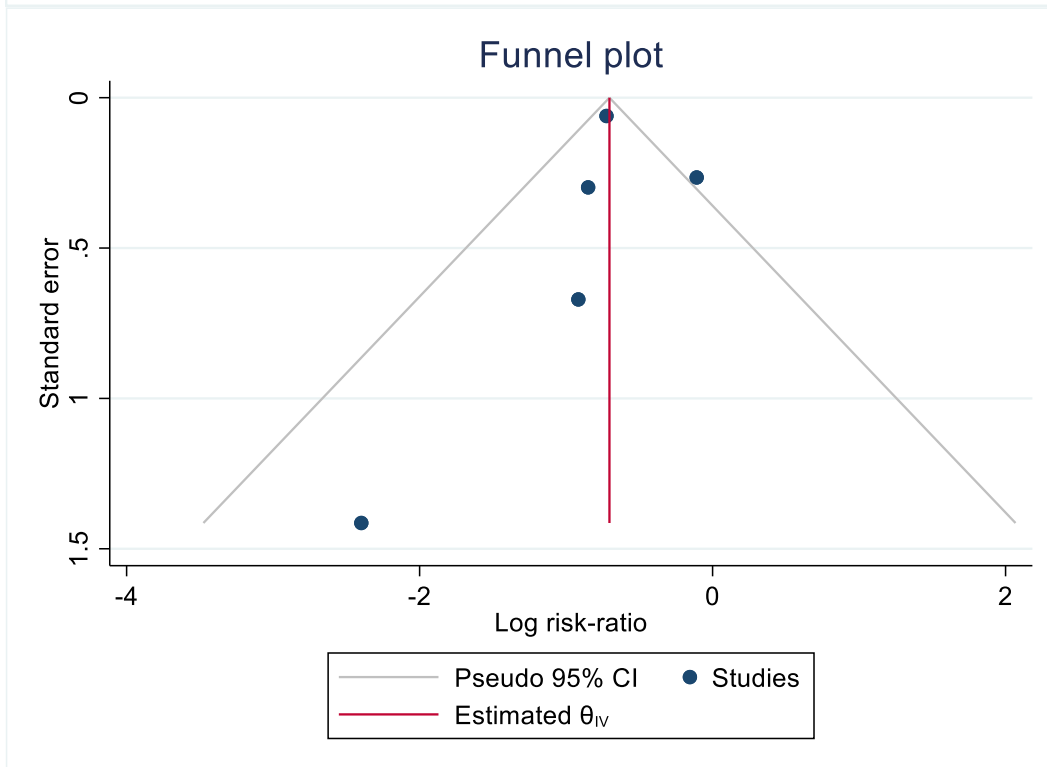
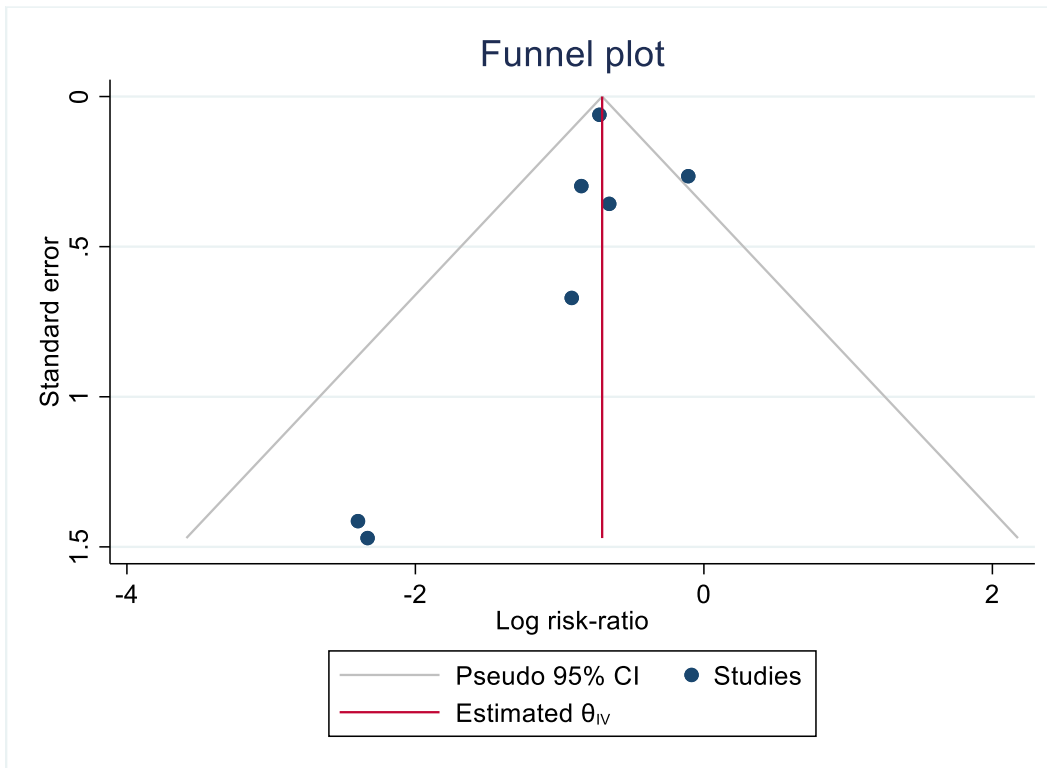
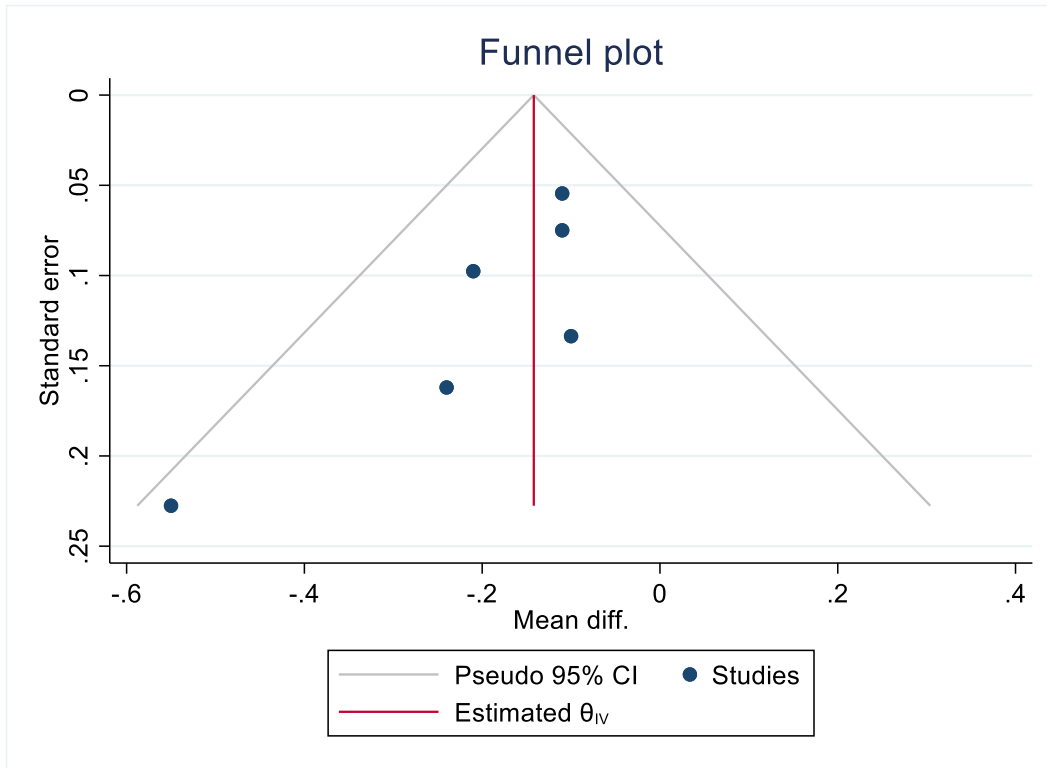


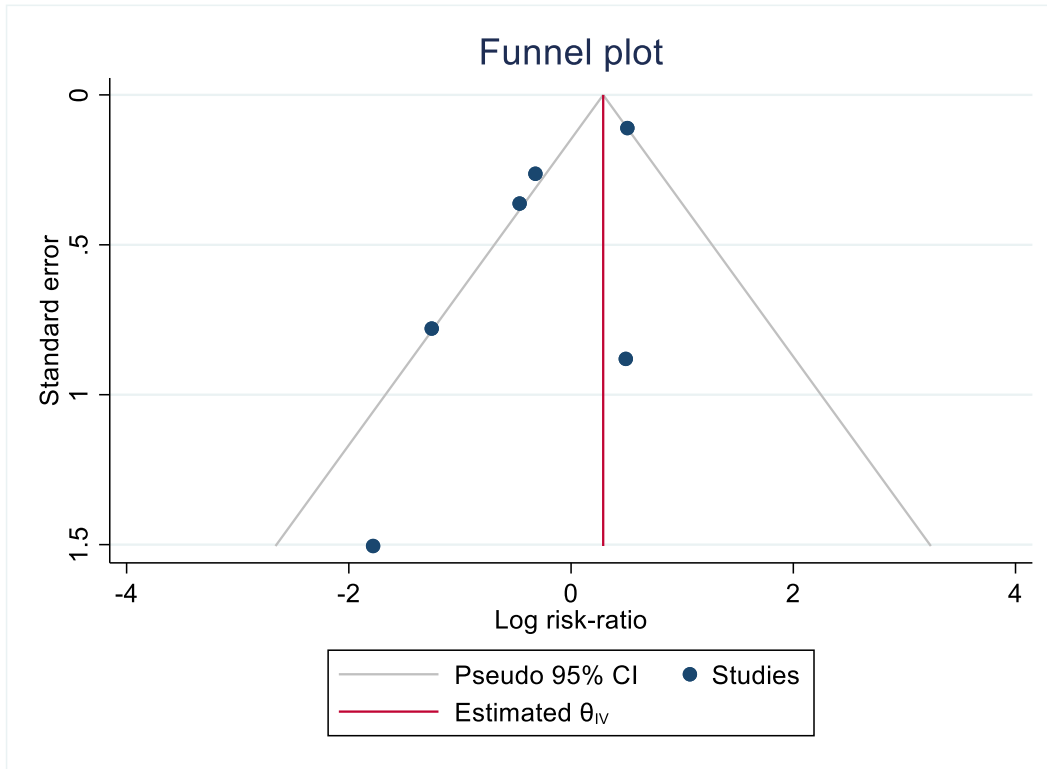
**Figure S1.** Forest plot demonstrating pooled effect of imipenem-cilastatin on acute kidney injury from all studies and stratified by treatment type. Note: The study by Hornik et al included 223 infants who received imipenem-cilastatin and the comparator carbapenem antibiotics at different times. Abbreviations: CI, confidence interval; DL, DerSimonian and Laird; n, number of acute kidney injury events; N, total number of study participants;



**A. Funnel Plot for AKI**



### B. Funnel Plot for Serum Creatinine



### C. Funnel Plot for All-cause Mortality

Figure S2. Funnel plots for small study effects suggesting publication bias.

**Table S1 Literature search strategy applied to electronic bibliographic databases**

<b>Databases</b>	<b>Search number</b>	<b>Search Query</b>	<b>Number of Results as of (1946 to November 21, 2023) (A)</b>	<b>Number of Results as of (1946 to May 28, 2024) (B)</b>
<b>Ovid MEDLINE(R)</b>	1	exp Acute Kidney Injury/	56,927	58,347
	2	("acute kidney injuries" or "kidney injur*or renal injur*" or "renal insufficienc*" or "kidney insufficienc*" or "kidney failure*").tw,kf.	38,245	39297
	3	exp Kidney Failure, Chronic/	101,630	102586
	4	("end-stage kidney disease*" or "end stage kidney disease*" or "chronic kidney failure" or "end-stage renal disease*" or "end stage renal disease*" or "end-stage renal failure" or "end stage renal failure" or "chronic renal failure" or "kidney dysfunction" or esrd).tw,kf.	83,827	85726
	5	(nephroprotection or nephroprotective* or prevention* or protection* or nephrotoxicity or "preventive measure*" or "all cause mortality" or mortality or death or "cardiovascular event*" or "kidney	2,953,944	3049140

		function*" or "kidney dysfunction" or creatinine or "cystatin c" or "glomerular filtration rate" or "urine output" or "allograft function" or proteinuria or albuminuria or NGAL or KIM-1 or Il-18 or L-FABP or IGFBP7 or TIMP-2).tw,kf.		
	6	1 or 2 or 3 or 4 or 5	3,084,479	3181515
	7	exp Cilastatin/ or exp Cilastatin, Imipenem Drug Combination/	1,055	1062
	8	(141a6amn38 or 5428wxz74m or 81129-83-1 or "monona salt" or "82009-34-5 cilastatin monosodium salt" or "cilastatin sodium" or "mk 0791" or mk 791 or "monosodium salt, cilastatin" or "salt, cilastatin monosodium" or "sodium, cilastatin").tw,kf.	209	212
	9	7 or 8	1,103	1113
	10	6 and 9	194	200
	11	animals/ not human/	5,139,807	5191962
	12	10 not 11	161	166
	13	limit 12 to yr="2023 - 2024" (9)	-	9
<b>Total =</b>			<b>170</b>	
<b>Embase</b>			<b>1974 to 2023 November 21 (A)</b>	<b>1974 to 2024 May 28 (B)</b>
	1	exp acute kidney failure/	125,050	129,619
	2	("acute kidney injuries" or "kidney injur*or renal injur*" or "renal	55,319	57,279

		insufficienc*" or "kidney insufficienc*" or "kidney failure*").tw,kf.		
	3	exp chronic kidney failure/	155,047	165,951
	4	("end-stage kidney disease*" or "end stage kidney disease*" or "chronic kidney failure" or "end-stage renal disease*" or "end stage renal disease*" or "end-stage renal failure" or "end stage renal failure" or "chronic renal failure" or "kidney dysfunction" or esrd).tw,kf.	130,552	134,320
	5	(nephroprotection or nephroprotective* or prevention* or protection* or nephrotoxicity or "preventive measure*" or "all cause mortality" or mortality or death or "cardiovascular event*" or "kidney function*" or "kidney dysfunction" or creatinine or "cystatin c" or "glomerular filtration rate" or "urine output" or "allograft function" or proteinuria or albuminuria or NGAL or KIM-1 or Il-18 or L-FABP or IGFBP7 or TIMP-2).tw,kf.	4,076,741	4,229,222
	6	exp cilastatin/ or exp cilastatin, imipenem drug combination/	8,053	8,255
	7	(141a6amn38 or	457	461

		5428wxz74m or 81129-83-1 or "mono-na salt" or "82009-34-5 cilastatin monosodium salt" or "cilastatin sodium" or "mk 0791" or mk 791 or "monosodium salt, cilastatin" or "salt, cilastatin monosodium" or "sodium, cilastatin").tw,kf.		
	8	1 or 2 or 3 or 4 or 5	4,278,218	4,439,057
	9	6 or 7	8,075	8,277
	10	8 and 9	1,864	1,930
	11	animals/ not human/	1,043,676	1,059,243
	12	10 not 11	1,861	1,927
	13	limit 12 to (full text and abstracts and human)	324	326
	14.	limit 13 to yr="2023 - 2024"	-	15
<b>Total=</b>			<b>339</b>	
<b>Cochrane Controlled Trials Registry</b>			<b>2023-11-21 (A)</b>	<b>2024-05-28 (B)</b>
	1	[mh "acute kidney injury"]	2,056	2,387
	2	("acute kidney injuries" or "kidney injury or renal injury" or "renal insufficiency" or "kidney insufficiency" or "kidney failure"):ti,ab,kw	21,152	2,387
	3	[mh "Kidney Failure, Chronic"]	5,555	6,065
	4	((("end-stage kidney disease" or "end stage kidney disease" or "chronic kidney failure" or "end-stage	13,078	13,876



		renal disease" or "end stage renal disease" or "end-stage renal failure" or "end stage renal failure" or "chronic renal failure" or "kidney dysfunction")):ti,ab,kw		
	5	((nephroprotection or nephroprotective or prevention or protection or nephrotoxicity or "preventive measure" or "all cause mortality" or mortality or death or "cardiovascular event" or "kidney function" or "kidney dysfunction" or creatinine or "cystatin c" or "glomerular filtration rate" or "urine output" or "allograft function" or proteinuria or albuminuria or NGAL or KIM-1 or Il-18 or L-FABP or IGFBP7 or TIMP-2)):ti,ab,kw	396,102	418,816
	6	[mh Cilastatin] or [mh "Cilastatin, Imipenem Drug Combination"]	229	244
	7	("141a6amn38" or "5428wxz74m" or "81129-83-1" or "mono-na salt" or "82009-34-5 cilastatin monosodium salt" or "cilastatin sodium" or "mk 0791" or "mk 791" or "monosodium salt, cilastatin" or "salt, cilastatin monosodium" or	37	37

		"sodium, cilastatin"):ti,ab,kw		
	8	#1 or #2 or #3 or #4 or #5	406,304	429,478
	9	#6 or #7	250	262
	10	#8 AND #9	67	73
	11	limit 13 to yr="2023 - 2024"	-	6
<b>Web of Science</b>			<b>2023-11-22 (A)</b>	<b>2024-05-28 (B)</b>
	1	("acute kidney injuries" or "kidney injur*" or "renal injur*" or "renal insufficienc*" or "kidney insufficienc*" or "kidney failure*"). (Topic)	101,950	101,985
	2	TS=((“end-stage kidney disease*” or “end stage kidney disease*” or “chronic kidney failure” or “end-stage renal disease*” or “end stage renal disease*” or “end-stage renal failure” or “end stage renal failure” or “chronic renal failure” or “kidney dysfunction” or esrd))	86,380	89,557
	3	TS=((nephroprotection or nephroprotective* or prevention* or protection* or nephrotoxicity or “preventive measure*” or “all cause mortality” or mortality or death or “cardiovascular event*” or “kidney function*” or “kidney	407,882	409,886

		dysfunction” or creatinine or “cystatin c” or “glomerular filtration rate” or “urine output” or “allograft function” or proteinuria or albuminuria or NGAL or KIM-1 or Il-18 or L-FABP or IGFBP7 or TIMP-2))		
	4	#1 OR #2 OR #3	4,094,231	4,183,501
	5	TS=((Cilastatin or "Cilastatin, imipenem drug combination") or (141a6amn38 or 5428wxz74m or 81129-83-1 or “monona salt” or 82009-34-5 “Cilastatin monosodium salt” or “Cilastatin sodium” or mk 0791 or mk 791 or “monosodium salt, Cilastatin” or “salt, Cilastatin monosodium” or “sodium, Cilastatin”))	1,802	1,962
	6	#4 AND #5	463	483
	7	limit 13 to yr="2023 - 2024"	-	20
<b>Totals</b>			<b>A=1,015</b>	<b>B=50</b>
<b>Total number of articles retrieved as of 2024-05-28 = (A+B) =1065</b>				

## **List of studies included in systematic review and meta-analysis**

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