Supplementary Table 1: Detailed search strategy

Database	Search Strategy	Results
PubMed	(("finerenone"[Supplementary Concept] OR "finerenone"[All Fields] OR ("Non-steroidal"[All Fields] AND ("mineralocorticoid receptor antagonists"[Pharmacological Action] OR "mineralocorticoid receptor antagonists"[MeSH Terms] OR ("mineralocorticoid"[All Fields] AND "receptor"[All Fields] AND "antagonists"[All Fields]) OR "mineralocorticoid receptor antagonists"[All Fields] OR ("mineralocorticoid"[All Fields] AND "receptor"[All Fields] AND "antagonist"[All Fields]) OR "mineralocorticoid receptor antagonist"[All Fields])) OR ("Non-steroidal"[All Fields] AND ("microbiol resour announc"[Journal] OR "med res arch"[Journal] OR "mra"[All Fields]))) AND ((("cardiacs"[All Fields] OR "heart"[MeSH Terms] OR "heart"[All Fields] OR "cardiac"[All Fields]) AND ("outcome"[All Fields] OR "outcomes"[All Fields])) OR ("Cardio-renal"[All Fields] AND ("outcome"[All Fields] OR "outcomes"[All Fields]))) AND ("diabetes mellitus, type 2"[MeSH Terms] OR "type 2 diabetes mellitus"[All Fields] OR "type 2 diabetes"[All Fields] OR ("diabetes mellitus"[MeSH Terms] OR ("diabetes"[All Fields] AND "mellitus"[All Fields]) OR "diabetes mellitus"[All Fields]))))	47
Google Scholar	((((Finerenone) OR (Non-steroidal mineralocorticoid receptor antagonist)) OR (Non-steroidal MRA)) AND ((Cardiac outcomes) OR (Cardio-renal outcomes))) AND ((Type 2 diabetes) OR (Diabetes mellitus))	30
Embase	((((Finerenone) OR (Non-steroidal mineralocorticoid receptor antagonist)) OR (Non-steroidal MRA)) AND ((Cardiac outcomes) OR (Cardio-renal outcomes))) AND ((Type 2 diabetes) OR (Diabetes mellitus))	25

Supplementary Table 2: Characteristics of included studies

Characteristics	Bakris 2015 [13]	Bakris 2020 [14]	Betram 2021 [10]	Gerasimos 2021 [15]	Gerasimos 2022 [16]	Agarwal 2022 [5]	Katayama 2017 [17]
Study name	Effect of Finerenone on Albuminuria in Patients with Diabetic Nephropathy a Randomized Clinical Trial	Effect of Finerenone on Chronic Kidney Disease Outcomes in Type 2 Diabetes	Cardiovascular Events with Finerenone in Kidney Disease and Type 2 Diabetes	Finerenone and Cardiovascular Outcomes in Patients with Chronic Kidney Disease and Type 2 Diabetes	Finerenone Reduces Risk of Incident Heart Failure in Patients with Chronic Kidney Disease and Type 2 Diabetes: Analyses From the FIGARO-DKD Trial	Cardiovascular and kidney outcomes with finerenone in patients with type 2 diabetes and chronic kidney disease: the FIDELITY pooled analysis	A randomized controlled study of finerenone versus placebo in Japanese patients with type 2 diabetes mellitus and diabetic nephropathy
Patients, n	812	5674	7352	5674	7352	13,026	2013
Enrolment initiation	2013	2015	2015	2015	2015	2015	2014
Enrolment completion	2014	2020	2021	2018	2018	2021	2015
Year of completion	2015	2020	2021	2020	2022	2021	2017
Follow up duration	90	2.6 years	3.4 years	2.57 years	3.4	3 years	90 days
Population	Patients with diabetes and high or very high	Patients with CKD and type 2 diabetes	patients with CKD and type 2 diabetes	Patients with chronic kidney disease and type 2 diabetes	patients with albuminuric chronic kidney	Patients with CKD and type 2 diabetes	Japanese patients with T2DM and albuminuria ≥

	albuminuria who are receiving an angiotensin-converting enzyme inhibitor or an angiotensin receptor blocker.				disease and type 2 diabetes.		30 mg/g and receiving therapy with a RAS blocker
Trial type	Multicentre, randomized, double-blind, placebo-controlled, parallel-group, phase 2B	Phase 3, randomized, double-blind, placebo-controlled, multicentre clinical trail	Phase 3, multicentre, randomized, double-blind, placebo-controlled, event-driven clinical trial.	Phase III randomized, double-blind, placebo-controlled, parallel-group, event-driven trial	Randomized, double-blind, placebo-controlled, multicentre, phase III trial	Two phase III, multicentre, double-blind trials	Multicentre, randomized, double-blind, placebo-controlled, phase 2b study.
Inclusion criteria	-Type 2 Diabetes - UACRs in two of three first morning samples, with both being ≥300 mg/g (≥34 mg/mmol; very high albuminuria) or both being ≥30– <300 mg/g (≥3.4– <34 mg/mmol; high albuminuria) plus an estimated	-Adults (≥18 years of age) with type 2 diabetes and CKD treated with an ACE inhibitor or ARB at the maximum dose on the manufacturer's label that did not cause unacceptable side effects.	-Male or female patient aged ≥18 years. - Patient with type 2 diabetes (T2D) as defined by the American Diabetes Association in the 2010 Standards of Medical Care in Diabetes. - Patient with a diagnosis of chronic kidney disease.\	- Patients aged ≥18 years with a clinical diagnosis of T2D and moderately elevated albuminuria - eGFR (calculated using the Chronic Kidney Disease Epidemiology Collaboration formula) ≥25 to <60 mL per min per 1.73 m2	- Patients aged ≥18 years with a clinical diagnosis of T2D and moderately elevated albuminuria - eGFR (calculated using the Chronic Kidney Disease Epidemiology Collaboration formula) ≥25 to <60 mL per min per 1.73 m2	-Age ≥18 years -T2D and CKD defined as UACR 30– <300 mg/g, eGFR 25– <60 mL/min/1.73 m2, and diabetic retinopathy, or UACR 300– 5000 mg/g and eGFR 25– <75 mL/min/1.73 m2 -Maximum tolerated dose	- Japanese subjects with type 2 diabetes mellitus and a clinical diagnosis of DN (Diabetic Nephropathy) treated with at least the minimal recommended dose of an Angiotensin Converting Enzyme Inhibitor (ACEI) and/or

	glomerular filtration rate eGFR ≥30 mL/min/1.73 m2.	- Patient with prior treatment with an angiotensin-converting enzyme inhibitor (ACEi) or angiotensin receptor blocker (ARB). - Patient with serum potassium ≤4.8 mmol/L at both the run-in visit and the screening visit - For women of child-bearing potential, a negative pregnancy test at screening visit and agreeing to use adequate contraception. - Patient with ability to understand and follow study-related instructions. - Patient providing written	- history of diabetic retinopathy, or severely elevated albuminuria - on stable treatment with a maximum tolerated labelled dose of an angiotensin-converting enzyme inhibitor or angiotensin receptor blocker for at least 4 weeks before the screening visit. - A serum potassium ≤4.8 mEq/L	- history of diabetic retinopathy, or severely elevated albuminuria - on stable treatment with a maximum tolerated labelled dose of an angiotensin-converting enzyme inhibitor or angiotensin receptor blocker for at least 4 weeks before the screening visit. - A serum potassium ≤4.8 mEq/L	of an RAS inhibitor -Serum potassium ≤4.8 mmol/L	Angiotensin Receptor Blocker (ARB) - Subjects with a clinical diagnosis of Diabetic Nephropathy. - Serum potassium </=4.8 mmol/L at both the run-in visit and the screening visit

			informed consent before any study-specific criteria				
Exclusion criteria	-If they received concomitant therapy with eplerenone, spironolactone, any renin inhibitor, or a potassium-sparing diuretic that could not be discontinued for the run-in and treatment periods	- Known significant non-diabetic kidney disease, including clinically relevant renal artery stenosis - Concomitant therapy with eplerenone, spironolactone, any renin inhibitor, or potassium-sparing diuretic which cannot be discontinued ≥4 weeks prior to the screening visit - Concomitant therapy with both ACEi and ARBs which cannot be discontinued for the purpose of the study - Concomitant therapy with potent	- Known significant non-diabetic kidney disease, including clinically relevant renal artery stenosis. - Concomitant therapy with eplerenone, spironolactone, any renin inhibitor, or potassium-sparing diuretic which cannot be discontinued ≥4 weeks prior to the screening visit. - Concomitant therapy with both ACEi and ARBs which cannot be discontinued for the purpose of the study - Concomitant therapy with potent	Patients were excluded if they had: -Known nondiabetic kidney disease. -Chronic symptomatic heart failure with reduced ejection fraction (New York Heart Association Class II–IV). -A recent history of dialysis for acute kidney failure. - A kidney transplant. - Uncontrolled hypertension.	Patients were excluded if they had: -Known nondiabetic kidney disease. -Chronic symptomatic heart failure with reduced ejection fraction (New York Heart Association Class II–IV). -A recent history of dialysis for acute kidney failure. - A kidney transplant. - Uncontrolled hypertension.	-Non-diabetic kidney disease -Uncontrolled hypertension -HbA1c >12% -SBP <90 mmHg -Chronic symptomatic HFrEF	Patients were excluded if they had: -Known nondiabetic kidney disease. -Chronic symptomatic heart failure with reduced ejection fraction (New York Heart Association Class II–IV). -A recent history of dialysis for acute kidney failure. - A kidney transplant. - Uncontrolled hypertension.

		cytochrome P450 isoenzyme 3A4. - Any other condition or therapy, which would make the patient unsuitable for this study and will not allow participation for the full planned study period (e.g., active malignancy or other condition limiting life expectancy to <12 months)	cytochrome P450 isoenzyme 3A4. - Any other condition or therapy, which would make the patient unsuitable for this study and will not allow participation for the full planned study period (e.g., active malignancy or other condition limiting life expectancy to <12 months)				
Treatment	Finerenone, 1.25 to 20 mg once daily	Patients with an eGFR of 25 to less than 60 ml per minute per 1.73 m2 at the screening visit received an initial dose of 10 mg once daily, and those with an eGFR of 60 ml per minute per 1.73 m2 or more at the screening	patients with an eGFR at the screening visit of 25 to less than 60 ml per minute per 1.73 m2 received an initial dose of 10 mg once daily, and those with an eGFR of at least 60 ml per minute per 1.73 m2 received an	Initial dose of study drug was either 10 or 20 mg OD based on an eGFR at the screening visit of 25 to <60 or ≥60 mL per min per 1.73 m2, respectively. Study drug up titration from 10 to 20 mg OD was encouraged	Initial dose of study drug was either 10 or 20 mg OD based on an eGFR at the screening visit of 25 to <60 or ≥60 mL per min per 1.73 m2, respectively. Study drug up titration from 10 to 20 mg OD was encouraged	Oral finerenone (10 or 20 mg)	Finerenone (1.25 mg, 2.5 mg, 5 mg, 7.5 mg or 10 mg)

		visit received an initial dose of 20 mg once daily. An increase in the dose from 10 to 20 mg once daily was encouraged after 1 month.	initial dose of 20 mg once daily.	from month 1 onwards, provided the serum potassium was ≤4.8 mEq/L and eGFR was stable.	from month 1 onwards, provided the serum potassium was ≤4.8 mEq/L and eGFR was stable.		
Primary outcomes	ratio of the urinary albumin-creatinine ratio (UACR) at day 90 vs at baseline	Composite of kidney failure.	- Composite of death from cardiovascular causes, nonfatal myocardial infarction, nonfatal stroke, or hospitalization for heart failure.	- Composite of death from cardiovascular causes, nonfatal myocardial infarction, nonfatal stroke, or hospitalization for heart failure.	- Composite of death from cardiovascular causes, nonfatal myocardial infarction, nonfatal stroke, or hospitalization for heart failure.	-Time to kidney failure -Sustained ≥40% decrease in eGFR from baseline - Renal death	Change of urinary albumin-to creatinine ratio
Secondary outcomes	-Proportion of patients with adverse and serious adverse events. -Change in serum potassium levels. - The incidence of serum potassium levels of 5.6 mmol/L or higher and	- Composite of death from cardiovascular causes, nonfatal myocardial infarction, nonfatal stroke, or hospitalization for heart failure. - Death from any cause. - Hospitalization for any cause. - Change in the	- composite of the first occurrence of kidney failure, a sustained decrease from baseline of at least 40% in the eGFR for a period of at least 4 weeks, or death from renal causes. - Hospitalization	- composite of the first occurrence of kidney failure, a sustained decrease from baseline of at least 40% in the eGFR for a period of at least 4 weeks, or death from renal causes. - Hospitalization	- composite of the first occurrence of kidney failure, a sustained decrease from baseline of at least 40% in the eGFR for a period of at least 4 weeks, or death from renal causes. - Hospitalization	Time to CV death - non-fatal MI, -non-fatal stroke -HHF	Change in serum potassium concentration

	higher than 6.0 mmol/L -The incidence of a decrease in eGFR of 30% or more, 40% or more, and 57%. -The change in UACR at day 30 and day 60 relative to baseline.	urinary albumin-to-creatinine ratio from baseline to month 4, -composite of kidney failure.	for any cause. -death from any cause. - The change in the urinary albumin-to-creatinine ratio from baseline to month 4. - A kidney composite outcome, the first onset of kidney failure. - A sustained decrease from baseline of at least 57% in the eGFR for a period of at least 4 weeks	for any cause. -death from any cause. - The change in the urinary albumin-to-creatinine ratio from baseline to month 4. - A kidney composite outcome, the first onset of kidney failure. - A sustained decrease from baseline of at least 57% in the eGFR for a period of at least 4 weeks	for any cause. -death from any cause. - The change in the urinary albumin-to-creatinine ratio from baseline to month 4. - A kidney composite outcome, the first onset of kidney failure. - A sustained decrease from baseline of at least 57% in the eGFR for a period of at least 4 weeks

N= number of patients

Supplementary Table 3: Co-morbidities of patients included in the study

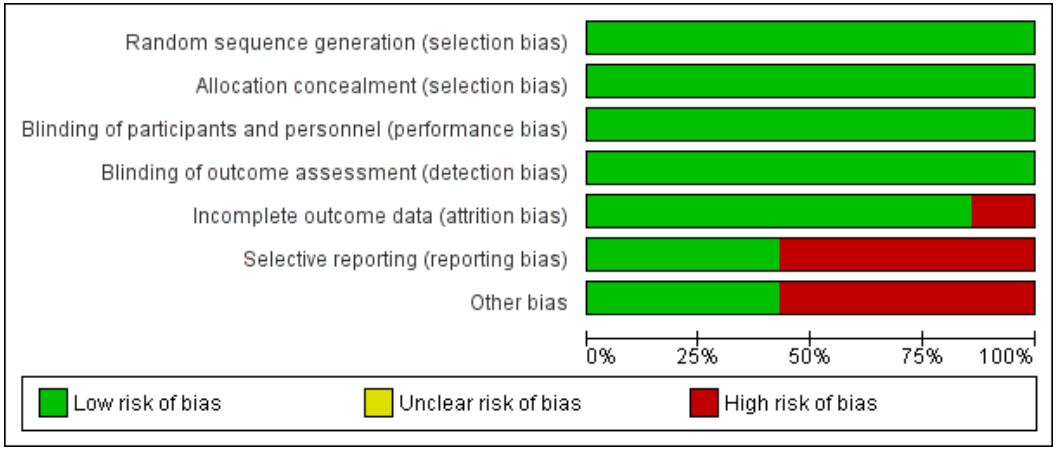
Study	Hypertension No. (%)		Diabetic retinopathy No. (%)		Diabetic neuropathy No. (%)		History of cardiovascular diseases No. (%)		Heart failure No. (%)		Peripheral arterial occlusive disease No. (%)		Ischemic stroke No. (%)	
	Finerenone	Placebo	Finerenone	Placebo	Finerenone	Placebo	Finerenone	Placebo	Finerenone	Placebo	Finerenone	Placebo	Finerenone	Placebo
Bakris (2015)[13]	685(94.2)	89 (94.7)	149(20.4)	19 (20.2)	139(19.1)	27(28.7)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Katayama (2017)[17]	84 (100)	12 (100)	40 (47.6)	5 (41.7)	30 (35.7)	6 (50)	15(17.8)	3(25)	N/A	N/A	N/A	N/A	N/A	N/A
Bakris (2020)[14]	2737 (96.6)	2768 (97.4)	1312 (46.3)	1351 (47.6)	738 (26.1)	716 (25.2)	1303 (46.0)	1302 (45.8)	195 (6.9)	241 (8.5)	470 (16.6)	453 (15.9)	329 (11.6)	360 (12.7)
Bertram (2021)[10]	3544 (96.1)	3517 (95.9)	1193 (32.4)	1098 (30.0)	1046 (28.4)	990 (27.0)	1676 (45.5)	1654 (45.1)	290 (7.9)	281 (7.7)	587 (15.9)	575 (15.7)	442 (12.0)	425 (11.6)
Gerasimos (2021)[15]	2737(96.6)	2768(97.3)	1312(46.3)	1351(47.5)	742(26.1)	722(25.4)	1303(45.9)	1302(45.8)	195 (6.8)	241(8.4)	N/A	N/A	N/A	N/A
Agarwal (2022)[5]	6281 (96.3)	6285 (96.6)	2505 (38.4)	2449 (37.6)	1788 (27.4)	1712(26.3)	2979 (45.7)	2956 (45.4)	485 (7.4)	522 (8.0)	1057 (16.2)	1028 (15.8)	771 (11.8)	785 (12.1)
Gerasimos (2022)[16]	3436(93.2)	3398(92.6)	N/A	N/A	N/A	N/A	1676(45.4)	1654(45.1)	290 (7.8)	281 (7.6)	N/A	N/A	N/A	N/A

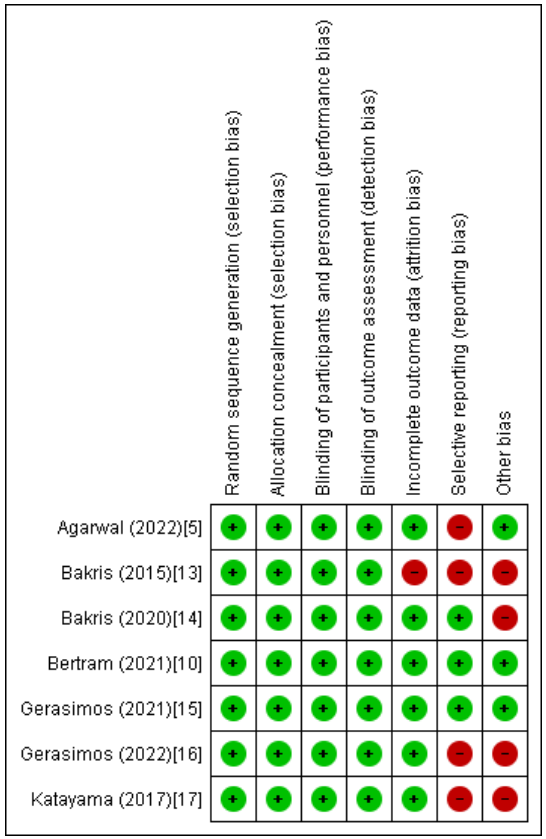
N/A= not applicable

Supplementary Table 4: Medication history of patients included in the history

Study	ACE inhibitor No. (%)		Angiotensin receptor blocker No. (%)		Diuretic No. (%)		Statin No. (%)		Potassium lowering agent No. (%)		Platelet aggregation inhibitors No. (%)		Insulin No. (%)		GLP-1 receptor Agonist No. (%)		SGLT-2 inhibitor No. (%)		Metformin No. (%)		Sulfonylurea No. (%)		Alpha-glucosidase inhibitor No. (%)		DPP-4 inhibitors No. (%)	
	Finerenone	Placebo	Finerenone	Placebo	Finerenone	Placebo	Finerenone	Placebo	Finerenone	Placebo	Finerenone	Placebo	Finerenone	Placebo	Finerenone	Placebo	Finerenone	Placebo	Finerenone	Placebo	Finerenone	Placebo	Finerenone	Placebo	Finerenone	Placebo
Bakris (2015)[xx]	334 (45.9)	41 (43.6)	397 (54.6)	55 (58.5)	543 (74.6)	76 (80.8)	558 (76.7)	67 (71.3)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Katayama (2017)[xx]	9 (10.7)	0	75 (89.2)	12 (100)	19 (22.6)	3 (25)	9 (75)	48 (57.1)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Bakris (2020)[xx]	950 (33.5)	992 (34.9)	1879 (66.3)	1846 (65.0)	1577 (55.7)	1637 (57.6)	2105 (74.3)	2110 (74.3)	70 (2.5)	66 (2.3)	1633 (57.6)	1595 (56.1)	1843 (65.1)	1794 (63.1)	189 (6.7)	205 (7.2)	124 (4.4)	135 (4.8)	1251 (44.2)	1239 (43.6)	654 (23.1)	673 (23.7)	163 (5.8)	161 (5.7)	764 (27.0)	758 (26.7)
Bertram (2021)[xx]	1576 (42.8)	1561 (42.6)	2108 (57.2)	2104 (57.4)	1748 (47.4)	1748 (47.7)	2552 (69.2)	2632 (71.8)	24 (0.7)	22 (0.6)	2044 (55.5)	2029 (55.3)	2023 (54.9)	1970 (53.7)	308 (8.4)	242 (6.6)	314 (8.5)	304 (8.3)	2561 (69.5)	2506 (68.4)	1037 (28.1)	1025 (28.0)	160 (4.3)	172 (4.7)	896 (24.3)	860 (23.5)
Gerasimos (2021)[xx]	995 (33.5)	992 (34.9)	1886 (66.5)	1846 (64.9)	1576 (55.6)	1637 (57.6)	2105 (74.3)	2110 (74.2)	80 (2.8)	82 (2.8)	1633 (57.6)	1595 (56.1)	1843 (65)	1794 (63.1)	189 (6.6)	205 (7.2)	124 (4.3)	135 (4.7)	1251 (44.1)	1239 (43.5)	654 (23)	673 (23.6)	N/A	N/A	764 (26.9)	758 (26.6)
Agarwal (2022)[xx]	2526 (38.7)	2553 (39.2)	3987 (61.2)	3950 (60.7)	3325 (51.0)	3385 (52.0)	4657 (71.4)	4742 (72.9)	94 (1.4)	88 (1.4)	3677 (56.4)	3624 (55.7)	3866 (59.3)	3764 (57.8)	497 (7.6)	447 (6.9)	438 (6.7)	439 (6.7)	3812 (58.5)	3745 (57.6)	1691(25.9)	16968 (26.1)	323 (5)	333 (5.1)	1660 (25.5)	1618 (24.9)
Gerasimos (2022)[xx]	1576 (42.7)	1561 (42.5)	2108 (57.1)	2104 (57.3)	1748 (47.4)	1748 (47.6)	2552 (69.2)	2632 (71.7)	24 (0.6)	22 (0.6)	N/A	N/A	2023 (54.8)	1970 (53.7)	308 (8.3)	242 (6.6)	314 (8.5)	304 (8.2)	2561 (69.4)	2506 (68.3)	1037 (28.1)	1025 (27.9)	N/A	N/A	896 (24.3)	860 (23.4)

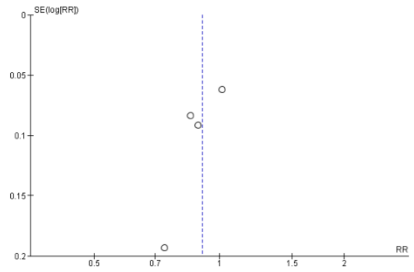
Supplementary Table 5: Quality assessment of included RCTs





Supplementary Figure 1: Funnel plots of efficacy and safety outcomes

A



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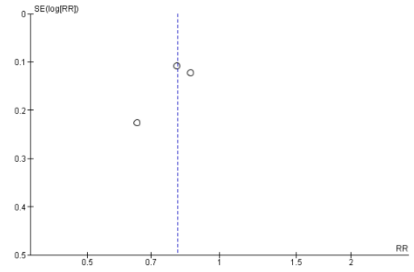

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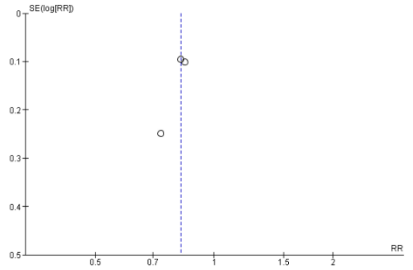

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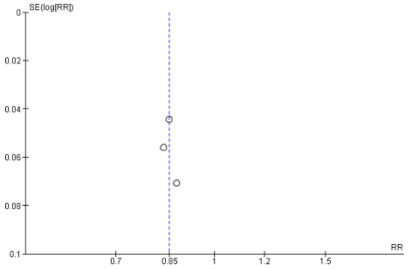

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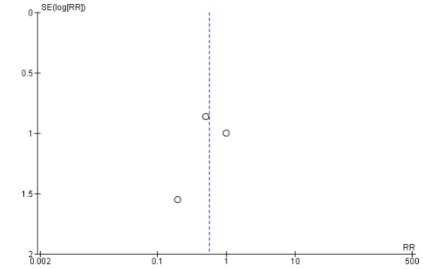
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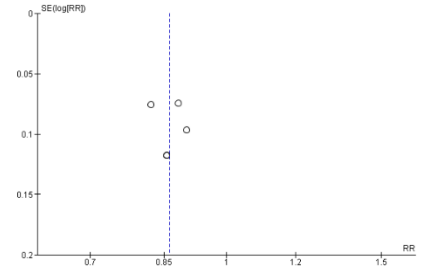
1
1.5
2
RR
0.002
0.1
1
10
500

F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0.2
RR
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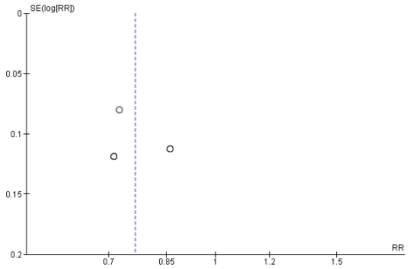
1.2
1.5

I



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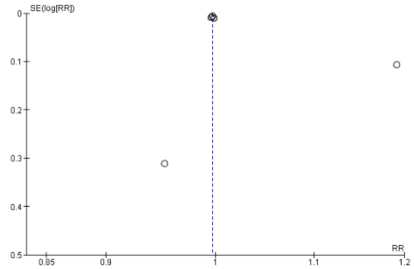

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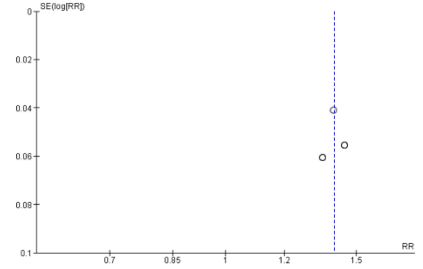

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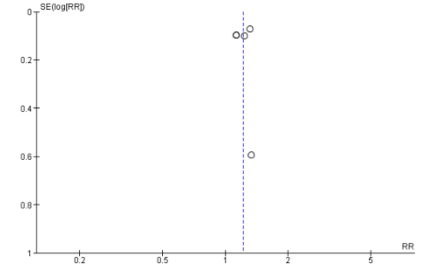

A= Kidney failure, B= End-stage kidney disease, C= Sustained decrease to < 15 ml/min/1.73m2, D= Sustained decrease to eGFR > 40% from baseline, E= Death from renal causes, F= Death from cardiovascular causes, G= Non-fatal MI, H= Non-fatal Stroke, I= Hospitalization for heart failure, J= Death from any cause, K= Hospitalization for any cause, L= Any adverse event.