SUPPLEMENTARY DATA

Table 1 of the supplementary data. Search strategy

Pubmed			EMBASE			Cochrane Library		
#1	"sglt 2 inhibitor"[Title] OR "sodium glucose co-transporter 2 inhibitor"[Title] OR "dapagliflozin"[Title] OR "empagliflozin"[Title] OR "sotagliflozin"[Title] OR "canagliflozin"[Title] OR "ertugliflozin"[Title]	**4400**	**#1**	'sglt-2 inhibitor' OR 'sodium glucose co-transporter-2 inhibitor' OR dapagliflozin OR empagliflozin OR sotagliflozin OR canagliflozin OR ertugliflozin:ti	**19407**	**#1**	'sglt-2 inhibitor' OR 'sodium glucose co-transporter-2 inhibitor' OR dapagliflozin OR empagliflozin OR sotagliflozin OR canagliflozin OR ertugliflozin [Record Title]	**4293**
#2	"heart failure"[Title]	**92347**	**#2**	'heart failure':ti	**147222**	**#2**	'heart failure' [Record Title]	**17977**
#3	"randomized clinical trial"[Title/Abstract] OR "randomized controlled trial"[Title/Abstract] OR "randomized"[Title/Abstract]	**711793**	**#3**	'randomized clinical trial' OR 'randomized controlled trial' OR 'randomized':ti,ab	**1493489**	**#3**	'randomized clinical trial' OR 'randomized controlled trial' OR 'randomized' [Title Abstract Keyword]	**1166542**
#4	clinicaltrial[Filter] OR randomized controlled trial[Filter]	**997384**	**#4**	([controlled clinical trial]/lim OR [randomized controlled trial]/lim) AND ([article]/lim OR [article in press]/lim) AND [humans]/lim	**702561**	**#4**	#1 AND #2 AND #3	**421**
#5	#1 AND #2 AND #3 AND #4	**119**	**#5**	#1 AND #2 AND #3 AND #4	**227**			

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Table 2 of the supplementary data. Reasons for exclusion after full-text assessment

Acronym	Year published	Study title	Reason for exclusion
DEFINE-HF[1]	2019	Dapagliflozin Effects on Biomarkers, Symptoms, and Functional Status in Patients With Heart Failure With Reduced Ejection Fraction: the DEFINE-HF Trial	Clinical endpoints were not stratified according to eGFR
CANA-HF[2]	2020	The effects of canagliflozin compared to sitagliptin on cardiorespiratory fitness in type 2 diabetes mellitus and heart failure with reduced ejection fraction: the CANA-HF study	Compared against other glucose lower agents
EMPA-RESPONSE-AHF[3]	2020	Randomized, double-blind, placebo-controlled, multicentre pilot study on the effects of empagliflozin on clinical outcomes in patients with acute decompensated heart failure (EMPA-RESPONSE-AHF)	Clinical endpoints were not stratified according to eGFR
Boer et al.[4]	2020	Effects of the dual sodium-glucose linked transporter inhibitor, licogliflozin vs placebo or empagliflozin in patients with type 2 diabetes and heart failure	Clinical endpoints were not stratified according to eGFR
EMPA[5]	2020	Empagliflozin in Heart Failure: Diuretic and Cardiorenal Effects	Did not report clinical endpoints
Empire HF[6]	2020	Twelve weeks of treatment with empagliflozin in patients with heart failure and reduced ejection fraction: A double-blinded, randomized, and placebo-controlled trial	Clinical endpoints were not stratified according to eGFR
RECEDE-CHF[7]	2020	Renal and Cardiovascular Effects of SGLT2 Inhibition in Combination With Loop Diuretics in Patients With Type 2 Diabetes and Chronic Heart Failure: The RECEDE-CHF Trial	Clinical endpoints were not stratified according to eGFR
Omar et al.[8]	2020	Effect of Empagliflozin on Hemodynamics in Patients With Heart Failure and Reduced Ejection Fraction	Clinical endpoints were not stratified according to eGFR
REFORM[9]	2020	Dapagliflozin Versus Placebo on Left Ventricular Remodeling in Patients With Diabetes and Heart Failure: The REFORM Trial	Clinical endpoints were not stratified according to eGFR

CANDLE[10]	2020	Effects of canagliflozin in patients with type 2 diabetes and chronic heart failure: a randomized trial (CANDLE)	Compared against other glucose lower agents
EMPERIAL[11]	2021	Effect of empagliflozin on exercise ability and symptoms in heart failure patients with reduced and preserved ejection fraction, with and without type 2 diabetes	Clinical endpoints were not stratified according to eGFR
SOLOIST-WHF[12]	2021	Sotagliflozin in Patients with Diabetes and Recent Worsening Heart Failure	Did not report specific event numbers
Empire HF Renal[13]	2021	Effects of empagliflozin on estimated extracellular volume, estimated plasma volume, and measured glomerular filtration rate in patients with heart failure (Empire HF Renal): a prespecified substudy of a double-blind, randomised, placebo-controlled trial	Clinical endpoints were not stratified according to eGFR
SUGAR-DM-HF[14]	2021	Effect of Empagliflozin on Left Ventricular Volumes in Patients With Type 2 Diabetes, or Prediabetes, and Heart Failure With Reduced Ejection Fraction (SUGAR-DM-HF)	Clinical endpoints were not stratified according to eGFR
EMBRACE-HF[15]	2021	Empagliflozin Effects on Pulmonary Artery Pressure in Patients With Heart Failure: Results From the EMBRACE-HF Trial	Clinical endpoints were not stratified according to eGFR
PRESERVED-HF[16]	2021	The SGLT2 inhibitor dapagliflozin in heart failure with preserved ejection fraction: a multicenter randomized trial	Clinical endpoints were not stratified according to eGFR
Ovchinnikov et al.[17]	2021	Effects of empagliflozin on exercise tolerance and left ventricular diastolic function in patients with heart failure with preserved ejection fraction and type 2 diabetes: a prospective single-center study	Not in English; Clinical endpoints were not stratified according to eGFR
Pietschner et al.[18]	2021	Effect of empagliflozin on ketone bodies in patients with stable chronic heart failure	Did not report clinical endpoints
EMPA-TROPISM[19]	2021	Randomized Trial of Empagliflozin in Nondiabetic Patients With Heart Failure and Reduced Ejection Fraction	Did not report clinical endpoints
Tamaki et al.[20]	2021	Effect of Empagliflozin as an Add-On Therapy on Decongestion and Renal Function in Patients With Diabetes Hospitalized for Acute	Did not report clinical endpoints

		Decompensated Heart Failure: A Prospective Randomized Controlled Study	
Charaya et al.[21]	2022	Impact of dapagliflozin treatment on renal function and diuretics use in acute heart failure: a pilot study	Clinical endpoints were not stratified according to eGFR
Hao et al.[22]	2022	Different Doses of Empagliflozin in Patients with Heart Failure with Reduced Ejection Fraction	Compared different dosage of SGLT2 inhibitor
DAPA-VO2[23]	2022	Short-term Effects of Dapagliflozin on Maximal Functional Capacity in Heart Failure with Reduced Ejection Fraction (DAPA-VO2): a Randomized Clinical Trial	Did not report clinical endpoints
Reis et al.[24]	2022	Dapagliflozin Impact on the Exercise Capacity of Non-Diabetic Heart Failure with Reduced Ejection Fraction Patients	Clinical endpoints were not stratified according to eGFR
EMPAG-HF[25]	2022	Effects of Early Empagliflozin Initiation on Diuresis and Kidney Function in Patients With Acute Decompensated Heart Failure (EMPAG-HF)	Clinical endpoints were not stratified according to eGFR
CHIEF-HF[26]	2022	The SGLT2 inhibitor canagliflozin in heart failure: the CHIEF-HF remote, patient-centered randomized trial	Clinical endpoints were not stratified according to eGFR
Thiele et al.[27]	2022	Empagliflozin reduces markers of acute kidney injury in patients with acute decompensated heart failure	Did not report clinical endpoints
EXCEED[28]	2022	Effects of ipragliflozin on left ventricular diastolic function in patients with type 2 diabetes and heart failure with preserved ejection fraction: The EXCEED randomized controlled multicenter study	Did not report clinical endpoints
CAMEO-DAPA[29]	2023	Cardiac and Metabolic Effects of Dapagliflozin in Heart Failure With Preserved Ejection Fraction: The CAMEO-DAPA Trial	Clinical endpoints were not stratified according to eGFR
Charaya et al.[30]	2023	Impact of Dapagliflozin Treatment on Serum Sodium Concentrations in Acute Heart Failure	Did not report clinical endpoints
Charaya et al.[31]	2023	The use of Dapagliflozin in Acute Decompensated Heart Failure: Results of the Randomized Study	Not in English

DAPA-RESPONSE-AHF[32]	2023	The clinical outcomes of dapagliflozin in patients with acute heart failure: A randomized controlled trial (DAPA-RESPONSE-AHF)	Clinical endpoints were not stratified according to eGFR
Golubovskaya et al.[33]	2023	Clinical Efficacy and Safety of Empagliflozin in Patients with Acute Heart Failure from the First Day of Hospitalization	Not in English
EMPA-VISION[34]	2023	Assessment of Cardiac Energy Metabolism, Function, and Physiology in Patients With Heart Failure Taking Empagliflozin: The Randomized, Controlled EMPA-VISION Trial	Did not report clinical endpoints
Kolwelter et al.[35]	2023	The SGLT2 inhibitor empagliflozin reduces tissue sodium content in patients with chronic heart failure: results from a placebo-controlled randomised trial	Did not report clinical endpoints
Mustapic et al.[36]	2023	Impact of SGLT2 Inhibitor Therapy on Right Ventricular Function in Patients with Heart Failure and Reduced Ejection Fraction	Did not report clinical endpoints
DAPPER[37]	2023	DAPagliflozin for the attenuation of albuminuria in Patients with hEaRt failure and type 2 diabetes (DAPPER study): a multicentre, randomised, open-label, parallel-group, standard treatment-controlled trial	Clinical endpoints were not stratified according to eGFR
EmDia[38]	2023	Effects of empagliflozin on left ventricular diastolic function in addition to usual care in individuals with type 2 diabetes mellitus—results from the randomized, double-blind, placebo-controlled EmDia trial	Did not report clinical endpoints
Afshani et al.[39]	2024	Effect of empagliflozin on left ventricular volumes in type 2 diabetes or prediabetes heart failure patients with reduced ejection fraction	Clinical endpoints were not stratified according to eGFR
Asif et al.[40]	2024	Effectiveness of Dapagliflozin in Reducing Incidence of Worsening Heart Failure Events among patients with Reduced Ejection Fraction	Clinical endpoints were not stratified according to eGFR
DICTATE-AHF[41]	2024	Efficacy and Safety of Dapagliflozin in Patients With Acute Heart Failure	Clinical endpoints were not stratified according to eGFR
Gilani et al.[42]	2024	Early initiation of Dapagliflozin and its effect on health related quality of life in acute heart failure: a randomised controlled trial	Did not report clinical endpoints

EFFORT[43]	2024	Ertugliflozin for Functional Mitral Regurgitation Associated With Heart Failure: EFFORT Trial	Did not report clinical endpoints
DAPA-Shuttle1[44]	2024	Water Conservation Overrides Osmotic Diuresis During SGLT2 Inhibition in Patients With Heart Failure	Did not report clinical endpoints
DETERMINE[45]	2024	Effect of Dapagliflozin Versus Placebo on Symptoms and 6-Minute Walk Distance in Patients With Heart Failure: The DETERMINE Randomized Clinical Trials	Clinical endpoints were not stratified according to eGFR
DAHOS[46]	2024	DAHOS Study: Efficacy of dapagliflozin in treating heart failure with reduced ejection fraction and obstructive sleep apnea syndrome - A 3-month, multicenter, randomized controlled clinical trial	Did not report clinical endpoints

eGFR, estimated glomerular filtration rate.

Table 3 of the supplementary data. Definitions of heart failure events, composite kidney outcome, and early decrease in estimated glomerular filtration rate

Heart failure events	
Trial	
DAPA-HF[47]	Heart failure hospitalization or urgent visit for heart failure requiring intravenous therapy
EMPEROR- Reduced[48]	Heart failure hospitalization
EMPEROR- Preserved[49]	Heart failure hospitalization
EMPULSE[50]	HF events included heart failure hospitalizations, urgent heart failure visits and unplanned outpatient heart failure visits. An event was considered a HF events only if worsening signs and symptoms of heart failure were present and an intensification of therapy (defined as an increase of oral or i.v. diuretics, augmentation of a vasoactive agent, or starting a mechanical or surgical intervention) was performed.
DELIVER[51]	Heart failure hospitalization or urgent heart failure visit
Composite kidney outcomes	
Trial	*Definition*
DAPA-HF[47]	A composite of ≥50% sustained decline eGFR or end-stage renal disease or renal death.
EMPEROR-Reduced[48]	First occurrence of chronic dialysis, kidney transplant, sustained reduction of ≥40% eGFR, or sustained eGFR <15 mL/min/1.73 m^2 if eGFR was >30 mL/min/1.73 m^2 or <10 mL/min/1.73 m^2 for patients with baseline eGFR ≤30 mL/min/1.73 m^2
EMPEROR-Preserved[49]	First occurrence of chronic dialysis, kidney transplant, sustained reduction of ≥40% eGFR or sustained eGFR <15 mL/min/1.73 m^2 if baseline eGFR was >30 mL/min/1.73 m^2 or <10 mL/min/1.73 m^2 for patients with baseline eGFR <30 mL/min/1.73 m^2.
EMPULSE[50]	-
DELIVER[52]	First occurrence of *(a)* sustained 50% or greater decline in eGFR relative to baseline; *(b)* development of end-stage kidney disease (from adverse event reporting or sustained decline in eGFR to <15 mL/min/1.73 m^2); or *(c)* death due to kidney causes.
Early decrease in estimated glomerular filtration rate	
Trial	*Definition*
DAPA-HF[53]	>10% decrease in eGFR at 14 d

EMPEROR-Reduced[54]	>20% decrease in eGFR at 4 wk
EMPEROR-Preserved[55]	>8.8% decrease in eGFR at 4 wk
EMPULSE[50]	-
DELIVER[52]	>10% decrease in eGFR at 1 mo

eGFR, estimated glomerular filtration rate.

Table 4 of the supplementary data. Definitions of adverse events

	DAPA-HF[47]	EMPEROR-Reduced[48]	EMPEROR-Preserved[49]	EMPULSE[50]	DELIVER[51]
Serious adverse events	An adverse event that fulfils one or more of the following criteria: - Results in death - Is immediately life-threatening - Requires in-patient hospitalization or prolongation of existing hospitalization - Results in persistent or significant disability/incapacity or substantial disruption of the ability to conduct normal life functions - Is a congenital abnormality or birth defect - Is an important medical event that may jeopardize the patient or may require medical intervention to prevent one of the	Any adverse events which: - Results in death - Is life-threatening, this refers to an event in which the patient was at risk of death at the time of the event; it does not refer to an event that hypothetically might have caused death if more severe - Requires inpatient hospitalization or prolongation of existing hospitalization - Results in persistent or significant disability or incapacity - Is a congenital anomaly/birth defect - Is to be deemed serious for any other reason if it is an important medical event when based upon appropriate medical judgment which may jeopardize the patient and may require medical or surgical intervention to prevent one of the other outcomes listed in the above definitions	Any adverse events that which: - Results in death - Is life-threatening, this refers to an event in which the patient was at risk of death at the time of the event; it does not refer to an event that hypothetically might have caused death if more severe - Requires inpatient hospitalization or prolongation of existing hospitalization - Results in persistent or significant disability or incapacity - Is a congenital anomaly/birth defect - Is to be deemed serious for any other reason if it is an important medical event when based upon appropriate medical judgment which may jeopardize the patient and may require medical or	Any adverse event fulfils at least one of the following criteria: - results in death, - is life-threatening, which refers to an event in which the patient was at risk of death at the time of the event; it does not refer to an event that hypothetically might have caused death if more severe, - requires inpatient hospitalization or prolongation of existing hospitalization, - results in persistent or	An adverse event that fulfils one or more of the following criteria: - Results in death - Is immediately life-threatening - Requires in-subject hospitalization or prolongation of existing hospitalization - Results in persistent or significant disability or incapacity - Is a congenital abnormality or birth defect - Is an important medical event that may

	outcomes listed above		surgical intervention to prevent one of the other outcomes listed in the above definitions	significant disability or incapacity, - is a congenital anomaly / birth defect, - is deemed serious for any other reason if it is an important medical event when based on appropriate medical judgment which may jeopardize the patient and may require medical or surgical intervention to prevent one of the other outcomes listed in the above definitions. Examples of such events are intensive treatment in an emergency room or at	jeopardize the subject or may require medical treatment to prevent one of the outcomes listed above.

				home for allergic bronchospasm, blood dyscrasias or convulsions that do not result in hospitalization or development of dependency or abuse.	
Discontinuation	-	-	-		-
Volume depletion	eg, dehydration, hypovolemia, or hypotension	-	-		-
Urinary traction infection	-	-	-		-
Genital infection	-	-	-		-
Hypoglycemia	An event that requires assistance of another person to actively administer carbohydrates, glucagon, or take other corrective actions	Plasma glucose value of ≤ 70 mg/dL or that required assistance	Plasma glucose value of ≤ 70 mg/dL or that required assistance		A major hypoglycemic event is defined as an event that is characterized by altered mental and/or physical status, any symptoms of

					severe impairment in consciousness or behavior, that require external assistance of another person for treatment of hypoglycemia and recovery, to actively administer carbohydrates, glucagon, or take other corrective actions.
Bone fracture	-	-	-		-

Table 5 of the supplementary data. Baseline characteristics of patients by chronic kidney disease status at baseline

	DAPA-HF[56]	EMPEROR-Reduced[57]	EMPEROR-Preserved[58]	EMPULSE[59]	DELIVER[60]
Mean age, y	70.9/63.2	70.2/63.0	74.2/69.2	72.3/62.2	74.5/69.0
Male sex, %	72.3/79.6	74.5/77.8	51.4/59.7	61.4/73.7	50.7/61.0
NYHA functional class, %					
Ⅲ-Ⅳ	34.2/31.3	27.1/22.4	21.8/14.3	63.1/60.3	28.1/21.5
Ⅳ	0.7/1.0	0.7/0.4	0.4/0.1	9.1/10.8	0.5/0.2
Hypertension, %	81.0/69.6	78.0/66.0	92.6/88.3	85.3/71.1	91.4/86.0
Diabetes mellitus, %	51.0/41.1	53.9/45.0	52.3/45.3	49.7/37.6	49.6/41.0
Primary ischemic cardiomyopathy, %	61.0/53.2	54.4/48.7	-	-	-
History of previous heart failure hospitalization, %	49.4/46.1	31.2/30.5	24.9/20.5	100/100	44.3/37.0
Mean LVEF, %	31.3/30.9	27.7/27.1	54.9/53.7	-	54.5/54.0
Median NT-pro-BNP, pg/mL	1823.8/1261.1	2334.0/1526.4	1789.0/1085.0[a]	4121.0/2378.0[†]	1237.0/889.0[b]
Mean eGFR, mL/min/1.73 m²	47.0/78.7	47.0/79.0	46.3/77.1	-	44.6/77.0
Medical therapy					
ACE inhibitor, %	80.1/85.5[c]	41.2/50.8	37.3/43.6	28.8/39.7	70.6/74.0[c]
ARB, %	80.1/85.5[c]	25.6/23.0	40.1/37.1	25.5/16.5	70.6/74.0[c]
ARNI, %	11.5/10.2	20.1/18.8	2.1/2.3	11.8/22.2	5.0/5.0
Beta-blocker, %	95.4/96.5	94.8/94.8	85.9/86.7	79.7/78.9	81.1/84.0

MRA, %	67.3/73.7	67.9/75.2	38.2/36.6	46.4/61.9	41.2/44.0
Device therapy					
ICD, %	29.5/23.9	35.7/26.6	3.9/3.4	-	-
CRT, %	9.7/6.0	16.0/7.1	-	-	-

ACE, angiotensin converting-enzyme; ARB, angiotensin receptor blockers; ARNI, angiotensin receptor neprilysin inhibitor; CRT, cardiac resynchronisation therapy; eGFR, estimated glomerular filtration rate; ICD, implantable cardioverter defibrillator; LVEF, left ventricular ejection fraction; MRA, mineralocorticoid receptor antagonist; NT-proBNP, N-terminal prohormone of B-type natriuretic peptide; NYHA, New York Heart Association.

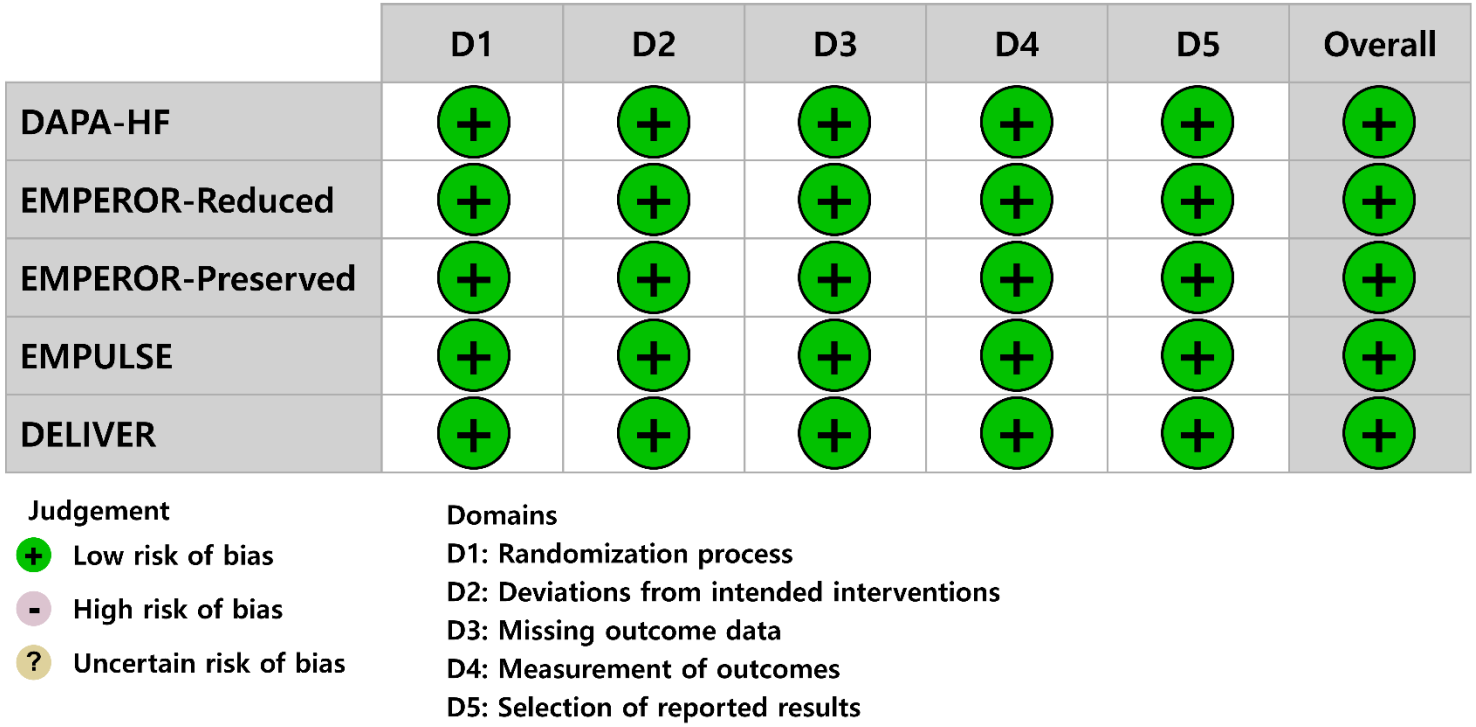
Data are presented as chronic kidney disease/nonchronic kidney disease groups.

[a]Reported as the mean, not the median.

[b]For patients with chronic kidney disease, eGFR was calculated using the weighted median for 2 subgroups: those with eGFR < 45 mL/min/1.73 m^2 and those with eGFR between 45 and 60 mL/min/1.73 m^2.

[c]Either ACE inhibitors or ARB.

Figure 1 of the supplementary data. Risk of bias of individual trials by the Cochrane Risk Assessment Tool



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