
SUPPLEMENTAL MATERIALS

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Supplemental Table 1. Search Strategy

Search date: March 28th 2021

Data source	Search terms
PubMed	(“Sodium-Glucose Transporter 2 Inhibitor*”[MeSH] OR “Sodium Glucose co-transporter*” OR “Sodium-dependent glucose cotransporter*” OR “Sodium Glucose transporter*” OR SGLT2 OR SGLT-2 OR “SGLT 2*” OR empagliflozin OR dapagliflozin OR canagliflozin OR sotagliflozin OR luseogliflozin OR ipragliflozin OR remogliflozin OR sergliflozin OR ertugliflozin OR tofogliflozin OR “Dipeptidyl-Peptidase IV Inhibitors” [MeSH] OR “Dipeptidyl-Peptidase IV Inhibitor*” OR “Dipeptidyl peptidase 4 inhibitor*” OR “DPP-4 inhibitor*” OR Gliptins OR DPP-4i OR sitagliptin OR vildagliptin OR saxagliptin OR linagliptin OR gemigliptin OR teneligliptin OR alogliptin OR trelagliptin OR evogliptin OR gosogliptin OR dutogliptin OR omarigliptin OR “Glucagon-Like Peptide-1 Receptor”[Mesh] OR “Glucagon-like peptide 1 receptor agonist*” OR “GLP-1 receptor agonist*” OR “GLP-1 agonist*” OR “GLP-1RA” OR exenatide OR liraglutide OR lixisenatide OR albiglutide OR dulaglutide OR semaglutide) AND (“Diabetes Mellitus, Type 2”[Mesh] OR “Type 2 diabetes” OR T2DM OR T2D) AND (“Randomized Controlled Trial”[Publication Type] OR random* OR RCT* OR placebo OR trial*) AND (Cardiovascular OR renal OR CVOT*) AND (English and human)/limit
CENTRAL	TITLE-ABSTRACT- KEYWORDS (“Sodium-Glucose Transporter 2 Inhibitor*” OR “Sodium Glucose co-transporter*” OR “Sodium-dependent glucose cotransporter*” OR “Sodium Glucose transporter*” OR SGLT2 OR SGLT-2 OR “SGLT 2*” OR empagliflozin OR dapagliflozin OR canagliflozin OR sotagliflozin OR luseogliflozin OR ipragliflozin OR remogliflozin OR sergliflozin OR ertugliflozin OR tofogliflozin OR “Dipeptidyl-Peptidase IV Inhibitor*” OR “Dipeptidyl peptidase 4 inhibitor*” OR “DPP-4 inhibitor*” OR Gliptins OR DPP-4i OR sitagliptin OR vildagliptin OR saxagliptin OR linagliptin OR gemigliptin OR teneligliptin OR alogliptin OR trelagliptin OR evogliptin OR gosogliptin OR dutogliptin OR omarigliptin OR “Glucagon-like peptide 1 receptor agonist*” OR “GLP-1 receptor agonist*” OR “GLP-1 agonist*” OR “GLP-1RA” OR exenatide OR liraglutide OR lixisenatide OR albiglutide OR dulaglutide OR semaglutide) AND (“Type 2 diabetes” OR T2DM OR T2D) AND (random* OR RCT* OR placebo OR trial*) AND (Cardiovascular OR Renal OR CVOT*))
Embase	TITLE-ABSTRACT-INDEX TERM

((“Sodium-Glucose Transporter 2 Inhibitor*” OR “Sodium Glucose co-transporter*” OR “Sodium-dependent glucose cotransporter*” OR “Sodium Glucose transporter*” OR SGLT2 OR SGLT-2 OR “SGLT 2*” OR empagliflozin OR dapagliflozin OR canagliflozin OR sotagliflozin OR luseogliflozin OR ipragliflozin OR remogliflozin OR sergliflozin OR ertugliflozin OR tofogliflozin OR “Dipeptidyl-Peptidase IV Inhibitor*” OR “Dipeptidyl peptidase 4 inhibitor*” OR “DPP-4 inhibitor*” OR Gliptins OR DPP-4i OR sitagliptin OR vildagliptin OR saxagliptin OR linagliptin OR gemigliptin OR teneligliptin OR alogliptin OR trelagliptin OR evogliptin OR gosogliptin OR dutogliptin OR omarigliptin OR “Glucagon-like peptide 1 receptor agonist*” OR “GLP-1 receptor agonist*” OR “GLP-1 agonist*” OR “GLP-1RA” OR exenatide OR liraglutide OR lixisenatide OR albiglutide OR dulaglutide OR semaglutide)

AND (“Type 2 diabetes” OR T2DM OR T2D)

AND (random* OR RCT* OR placebo OR trial*)

AND (Cardiovascular OR Renal OR CVOT*))

AND (English and human)/limit

Supplemental Table 2. The definition of the outcome from each trial

Study	Trial name	Definition
MACE		
Pfeffer 2015 ¹	ELIXA	composite of death from cardiovascular causes, nonfatal myocardial infarction, nonfatal stroke, or hospitalization for unstable angina
Marso 2016 ²	LEADER	composite of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke
Marso 2016 ³	SUSTAIN-6	composite of cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke
Holman 2017 ⁴	EXSCEL	composite of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke
Hernandez 2018 ⁵	HARMONY	composite of death from cardiovascular causes, myocardial infarction, and stroke
Gerstein 2019 ⁶	REWIND	composite of nonfatal myocardial infarction, nonfatal stroke, and death from cardiovascular causes or unknown causes
Husain 2019 ⁷	PIONEER-6	composite of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke
Zinman 2015 ⁸	EMPA-REG	composite of death from cardiovascular causes, nonfatal myocardial infarction (excluding silent myocardial infarction), or nonfatal stroke.
Neal 2017 ⁹	CANVAS	composite of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke
Wiviott 2019 ¹⁰	DECLARE–TIMI 58	composite of cardiovascular death, myocardial infarction, or ischemic stroke
Cannon 2020 ¹¹	VERTIS CV	composite of cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke
Composite renal outcomes		
Heerspink 2020 ¹²	DAPA-CKD	composite of a sustained decline in the estimated GFR of $\geq 50\%$, end-stage kidney disease, or death from renal or cardiovascular causes
Perkovic 2019 ¹³	CREDENCE	composite of end-stage kidney disease (dialysis, transplantation, or a sustained estimated GFR of <15 ml per minute per 1.73 m ²), a doubling of the serum creatinine level, or death from renal or cardiovascular causes.
Composite endpoint of heart failure hospitalization or cardiovascular death		
Wiviott	DECLARE–	composite of cardiovascular death or hospitalization for heart failure

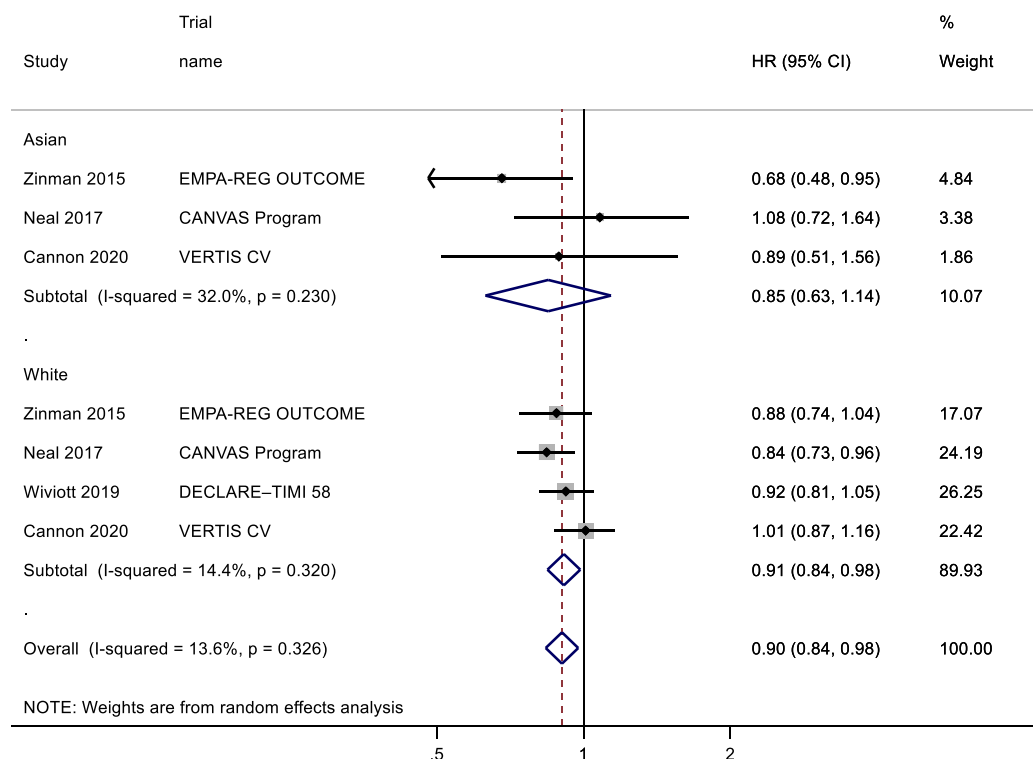
2019 ¹⁰	TIMI 58	
McMurray 2019 ¹⁴	DAPA-HF	composite of hospitalization for heart failure, an urgent visit resulting in intravenous therapy for heart failure, or death from cardiovascular causes
Cannon 2020 ¹¹	VERTIS CV	composite of cardiovascular death or heart failure hospitalization
Packer 2020 ¹⁵	EMPEROR-Reduced	composite outcome of death from cardiovascular causes or hospitalization for heart failure
Bhatt 2021 ¹⁶	SOLOIST-WHF	composite of deaths from cardiovascular causes and hospitalizations and urgent visits for heart failure
Bhatt 2021 ¹⁷	SCORED	composite of deaths from cardiovascular causes, hospitalizations for heart failure, and urgent visits for heart failure

MACE, major adverse cardiovascular events; GFR, glomerular filtration rate; ESRD, end-stage renal disease.

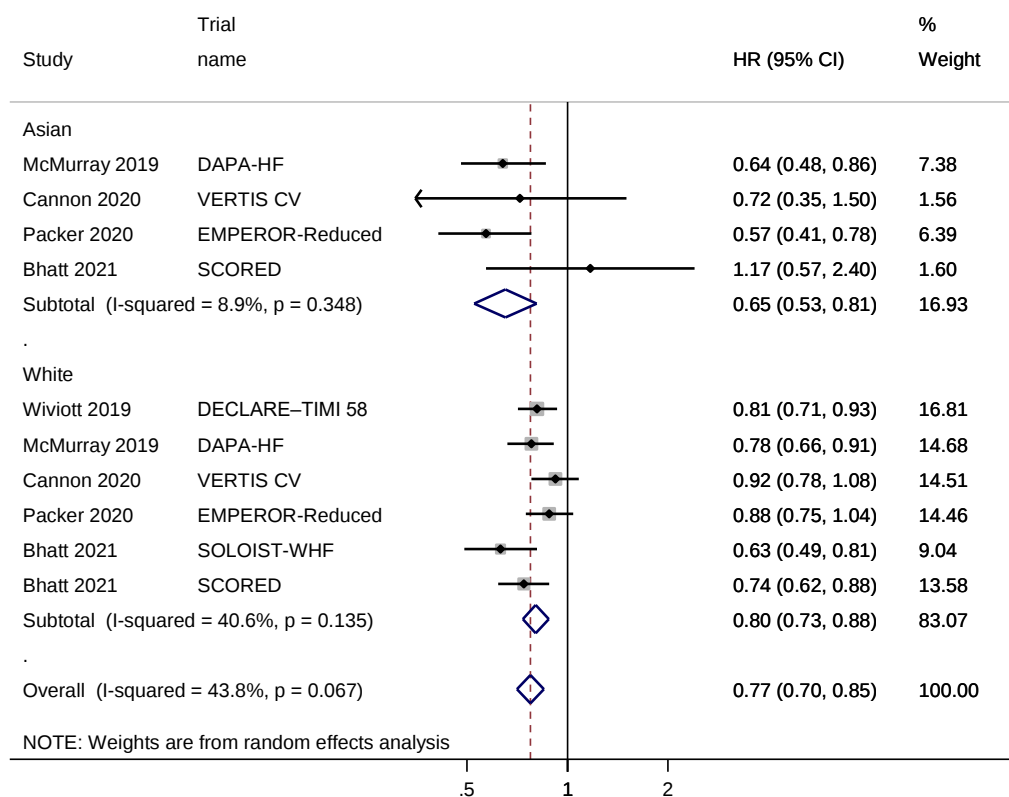
Supplemental Figure 1. Pairwise meta-analysis of the effects of SGLT2 inhibitors on MACE outcome (p-interaction=0.55).

SGLT2 inhibitors, sodium-glucose cotransporter-2 inhibitors; MACE, major adverse cardiovascular events; HR, hazard ratio.

DECLARE-TIMI 58 reported the outcomes by Caucasian and non-caucasian, thus DECLARE-TIMI 58 was included in the White population only.

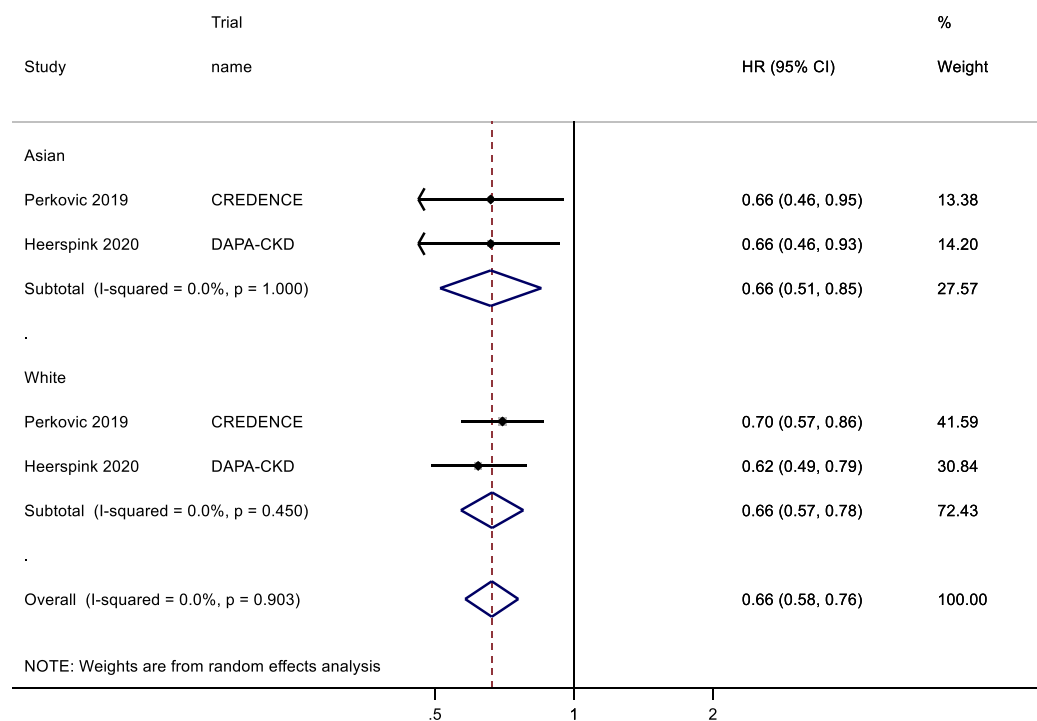


Supplemental Figure 2. Pairwise meta-analysis of the effects of SGLT2 inhibitors on CV death/HHF (p-interaction=0.13).
SGLT2 inhibitors, sodium-glucose cotransporter-2 inhibitors; CV death/HHF, cardiovascular death and/or heart failure hospitalization; HR, hazard ratio.
SOLOIST-WHF and SCORED reported the results for the White population only



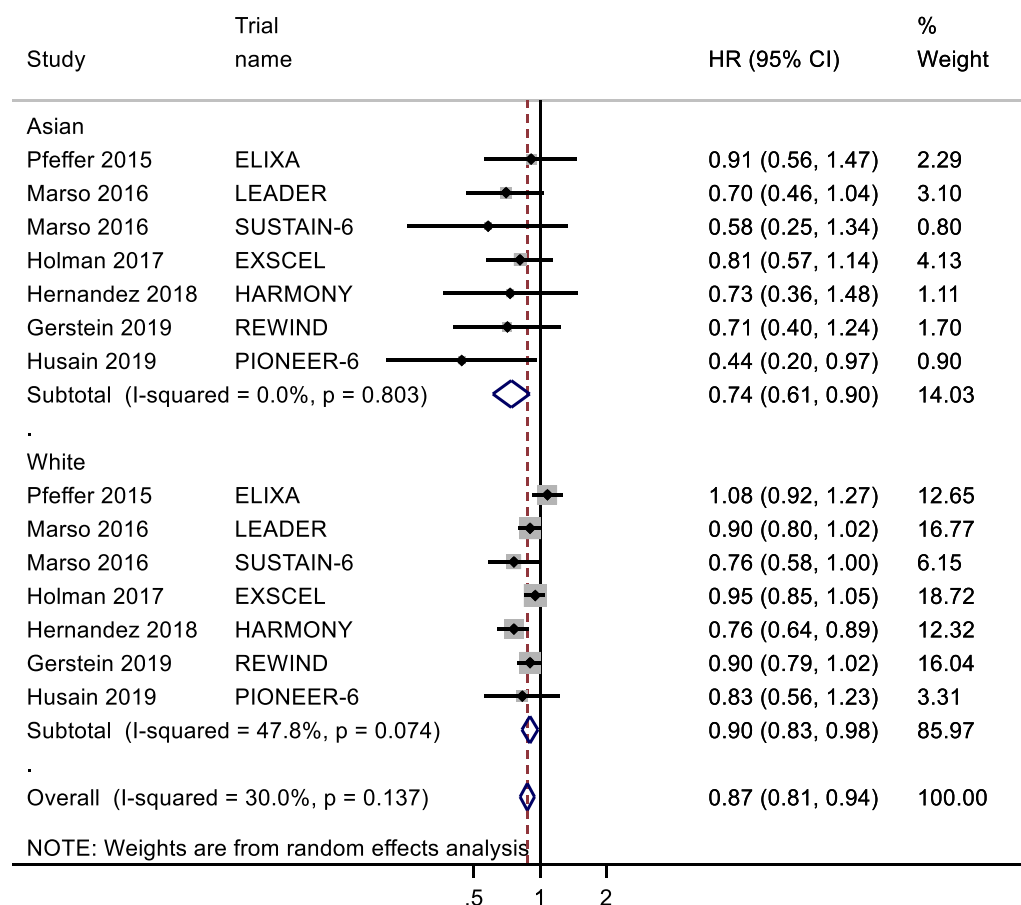
Supplemental Figure 3. Pairwise meta-analysis of the effects of SGLT2 inhibitors on composite renal outcomes (p-interaction=0.97).

SGLT2 inhibitors, sodium-glucose cotransporter-2 inhibitors; HR, hazard ratio.



Supplemental Figure 4. Pairwise meta-analysis of the effects of GLP-1RAs on MACE outcome (p-interaction=0.1).

GLP-1RAs, glucagon-like peptide-1 receptor agonists; MACE, major adverse cardiovascular events; HR, hazard ratio.



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