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Cardiovascular outcomes of SGLT-2 inhibitors and GLP-1 agonist based on race, ethnicity, and gender: A systematic review and meta-analysis of randomized trials

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Abstract

The ethnic differences in cardiovascular outcomes with sodium-glucose cotransporter-2 inhibitors (SGLT2i) and glucagon-like peptide-1 (GLP-1) receptor agonists in patients with type 2 diabetes and heart failure are not well established. We conducted the current study to evaluate the effects of both drugs on the major adverse cardiovascular effects (MACE) stratified by race, ethnicity, and gender.

We searched Medline (via PubMed), Embase, and the Cochrane Library for randomized controlled trials (RCTs) investigating the effects of SGLT2 inhibitors and GLP-1 receptor agonists on the MACE risk. The data of MACE were pooled as risk ratios (RRs), with 95% confidence intervals, using R software (meta-package 4.9-0) for windows and a subgroup analysis was conducted.

Sixteen RCTs were finally included in the meta-analysis. In patients with T2DM and high cardiovascular risk, the effect showed that SGLT-2 inhibitors and GLP-1 receptor agonists significantly reduced the MACE risk among the White and Asian populations, and both males and females. Subgroup analysis showed no significant differences between SGLT2 inhibitors and GLP-1 receptor agonists on the MACE outcomes stratified by race, ethnicity, or gender. In patients with known heart failure, the effect showed that SGLT-2 inhibitors significantly reduced MACE risk in all subgroups.

It remains unclear whether the lack of significant reduction in MACE risk and significant heterogenicity observed could be because of inconsistent representation of these ethnic groups across RCTs. Further multicenter RCTs with a larger sample size are recommended to evaluate the effect of these drugs to better understand the ethnic difference in cardiovascular outcomes.

Keywords: GLP-1 receptor agonists; SGLT2 inhibitors; Cardiovascular outcomes; MACE; Type 2 diabetes

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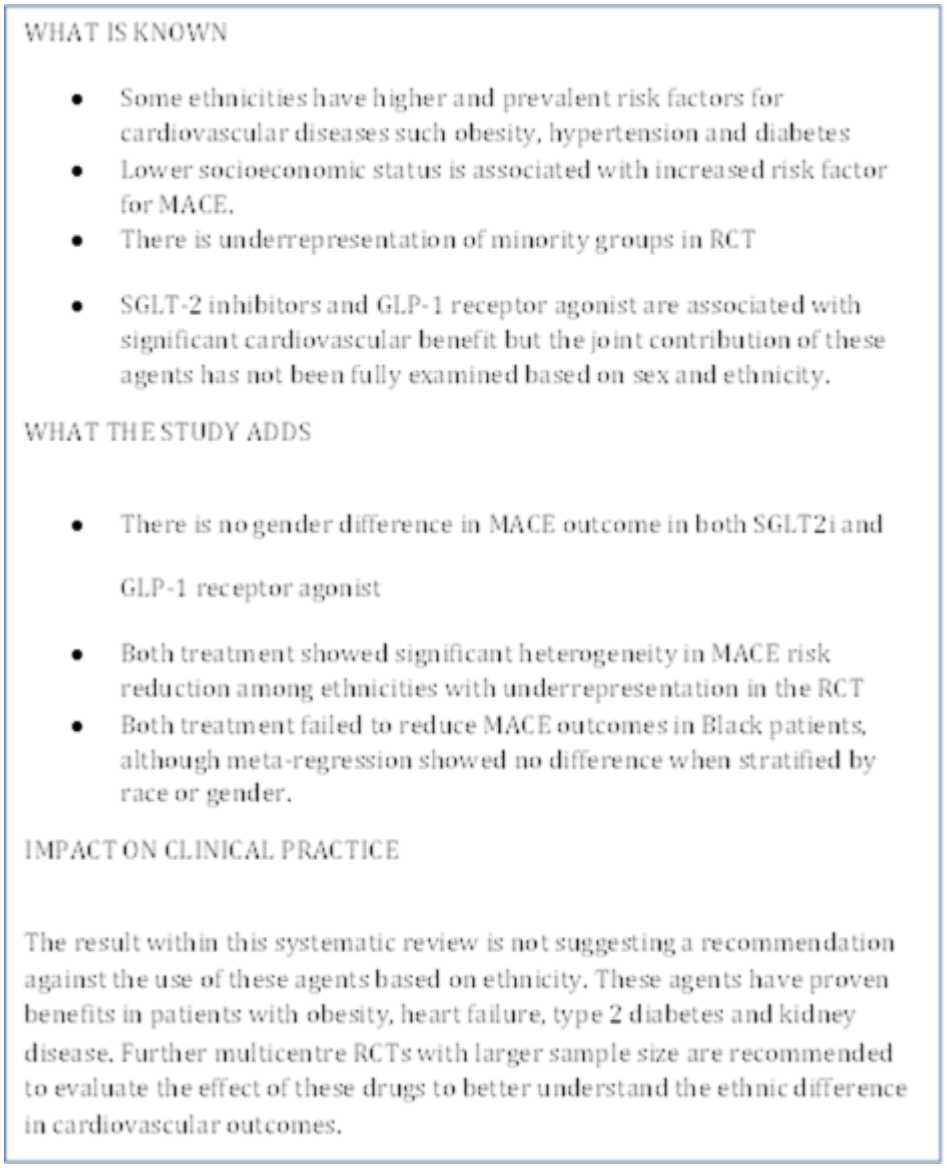
Abstract Figure



1. Introduction

Diabetes is one of the leading risk factors for cardiovascular diseases, such as arrhythmia and congestive heart failure, and kidney disease [1,2]. People with diabetes are more likely to develop heart disease. Cardiovascular disease often leads to morbidity and mortality among diabetic patients. It affects approximately one-third of patients and is responsible for about 50% of deaths in patients with type 2 diabetes (T2DM) [3].

Glucagon-like peptide-1 (GLP-1) receptor agonists and sodium-glucose cotransporter2 inhibitors (SGLT2i) can help reduce the risk of cardiovascular risk in T2DM patients (4). SGLT2 inhibitors considerably reduce the risk of heart failure, frequency of hospitalizations because of heart failure, cardiovascular mortality, all-cause mortality, and nonfatal myocardial infarction. SGLT2 inhibitors also improve cardio-renal outcomes in diabetic patients. In contrast, GLP-1 receptor agonists mainly reduced the risk of atherosclerotic progression and inflammation, and both drugs had variable impacts on cardiovascular death [5].

In early 2019, a consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) recommended the use of SGLT2 inhibitors or GLP-1 receptor agonists as a second-line treatment. Metformin is the suggested first-line glucose-lowering agent in patients with T2DM and cardiovascular disease (CVD).

These guidelines are based on the findings from recent cardiovascular outcome trials (CVOTs) [7-10] and meta-analysis [5,11]. However, it is not yet clear whether these newer classes of drugs have a similar impact on the MACE rate in different ethnicity, race, and or gender.

Therefore, we conducted the current systematic review and meta-analysis, including up-to-date cardiovascular outcome trials, investigating the effects of SGLT2 inhibitors and GLP-1 receptor agonists on the major adverse cardiovascular effects (MACE) in patients with T2DM and heart failure. Furthermore, we stratified the MACE risk per race (White, Black, Asian, and others), ethnicity (Hispanic and non-Hispanic), and gender (male and female).

2. Methods

All steps of this study were conducted per the Cochrane handbook of systematic reviews of interventions in addition to PRISMA statement guidelines, Appendix A [12]. The protocol of this meta-analysis was published online at the PROSPERO International Prospective Register of Systematic Reviews under registration number (ID: CRD42021255192).

2.1. Literature search strategy

We searched Medline (via PubMed), Embase, Scopus, Cochrane CENTRAL, Web of science, and EBSCO, up to May 2021, for randomized controlled trials (RCTs) evaluating the cardiovascular outcomes of SGLT2 inhibitors and GLP-1 receptor agonists compared to placebo. We used the possible combinations of the keywords: (("Sodium-Glucose Transporter 2 Inhibitors" OR "Sodium-glucose co-transporter 2" OR "SGLT2 inhibitors" OR Empagliflozin OR Dapagliflozin OR Canagliflozin OR ertugliflozin OR "glucagon-like peptide 1 receptor agonists" OR lixisenatide OR liraglutide OR semaglutide OR exenatide OR albiglutide OR dulaglutide) AND ("Diabetes Mellitus, Type 2" OR "diabetes mellitus type 2" OR "type 2 diabetes mellitus" OR "T2DM") AND ("cardiovascular death" OR "myocardial infarction" OR "Cardiovascular Events" OR "cardiac Events" OR "MACE" OR "major adverse cardiovascular events" OR "major adverse cardiac events")). Additionally, the reference lists of identified articles were checked manually. Detailed search strategies can be seen in Appendix B.

2.2. Eligibility criteria

We included RCTs that assessed the cardiovascular outcomes between SGLT2 inhibitors and GLP-1 receptor agonist versus placebo for the treatment of patients with type 2 diabetes mellitus and heart failure. Studies had to stratify the included population according to race (White, Black, Asian, or others), ethnicity (Hispanic or non-Hispanic), and gender (male or female). Primary outcomes included MACE which is defined as a composite of nonfatal stroke, nonfatal myocardial infarction, and *cardiovascular* death. Other studies defined MACE as *cardiovascular events*, admission for Heart Failure, and ischemic *cardiovascular events*. We excluded observational studies, animal models, reviews, case reports, case series, conference abstracts, and duplicate references.

2.3. Study selection

First, we conducted title/abstract screening for eligibility for the current study. Second, we conducted the full-text screening. Each step was performed by three independent reviewers and disagreements were resolved upon consensus.

2.4. Data Extraction

Requisite data were extracted by three independent authors (CN, KD, and AM) into a data extraction form. The extracted data included the following items: study design, population, number of patients in each group, mean age, female percentage, intervention, control, race percentages, mean observation period in years, and primary outcomes.

2.5. Risk of bias assessment

We used Cochrane collaboration's tool for assessing the risk of bias of included RCTs [11]. Risk of bias assessment included the following domains: 1) sequence generation, 2) allocation sequence concealment, 3) blinding of participants and personnel, 4) blinding of outcome assessment, 5) incomplete outcome data, 6) selective outcome reporting and 7) other potential sources of bias; the authors' judgment is categorized as 'Low risk', 'High risk' or 'Unclear risk' of bias.

2.6. Data Synthesis

Dichotomous data, as MACE outcome, were pooled as risk ratio (RR), with a 95% confidence interval (CI). We used R software (meta-package) for data synthesis. Heterogeneity was assessed by visual inspection of the forest plots and

measured by Q statistic and statistic. Significant statistical heterogeneity was indicated by Q statistic P-value less than 0.1 or by more than 50%. In the case of significant heterogeneity, a random-effects model was employed. Subgroup analysis of studies including patients with heart failure was performed. We conducted sensitivity analyses by excluding one study at a time to assess any sources of heterogeneity. Publication bias was assessed using the funnel plot method.

2.7. Quality of evidence

Two reviewers independently (AD, SD) assessed the strength of recommendations and evidence provided by the pooled results using the Grading of the Recommendations Assessment, Development, and Evaluation (GRADE) Handbook. This looks at risk of bias, inconsistency, indirectness, imprecision, and publication bias with overall levels of quality classified as "high", "moderate", "low", or "very low" [13].

3. Results

3.1. Search strategy results

Our literature search yielded 2701 unique records. After title and abstract screening, 73 were retrieved and screened for eligibility. Of them, 16 studies were included in the final analysis. 57 studies were excluded because they did not report outcomes based on ethnicities, race, or gender. The flow of study selection is shown in the PRISMA flow diagram, Figure 1. A list of excluded studies after full-text screening is shown in Appendix B.

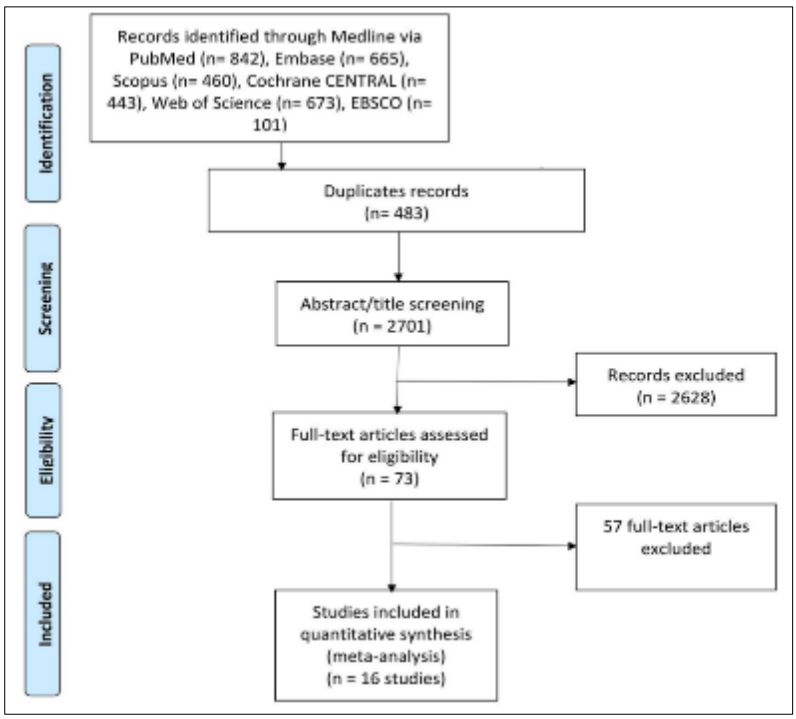


Figure 1 The PRISMA flow diagram of study selection

3.2. Characteristic of included studies

Sixteen RCTs were finally included in the meta-analysis, with a total of 123,253 patients. Nine studies assessed SGLT2 inhibitors, and seven studies assessed GLP-1 receptor agonists. The number of White patients was 73101 (59%), Asian 10432 (8%), Black 4591 (3.7%), Other race 4304 (3.4%), Hispanic 10697 (8.6%), and non-Hispanic 40054 (32%). Summary of the design and baseline characteristics of enrolled patients are presented in table 1. All included RCTs achieved a low risk of bias in all domains of the Cochrane collaboration's tool for assessing the risk of bias. The summary of the risk of bias assessment is shown in Appendix B.

Table 1 Summary of the design and baseline characteristics of enrolled patients

Study	Year	Study design	Population	Number of patients in the drug group	Age	Female	Intervention	Control	Black race (drug/placebo)	Mean observation period in years	Primary outcome
SGLT2 inhibitors											
EMPA-REG OUTCOME	2015	RCT	T2DM and high CV risk	4687/2333	63.1	2004 (28.5%)	Empagliflozi, 10 or 25 m	Placebo	237/120	3.1	Composite of CV death, nonfatal MI, nonfatal stroke
CANVAS Program	2017	RCT	T2DM and high CV risk	5795/4347	63.3	3633 (36%)	Canagliflozin, 100 or 300 mg	Placebo	176/160	2.4	Composite of CV death, nonfatal MI, nonfatal stroke
VERTIS CV	2020	RCT	T2DM and ASCVD	8246	64	2477 (30%)	Ertugliflozin, 5 or 15 mg	Placebo	166	3	MACE (Composite of CV death / nonfatal MI / nonfatal stroke)
DAPA-HF	2020	RCT	HF with reduced ejection fraction, with and without T2DM	4744	66.2	1109 (23%)	Dapagliflozin	Placebo	122	2	Composite of worsening HF (hospitalization or urgent visit resulting in IV therapy for HF) / CV death
EMPEROR-Reduced	2020	RCT	HF with reduced ejection fraction, with and without T2DM	3730	67.2	437 (23.5%)	Empagliflozin	Placebo	123	1.3	Composite of CV death / hospitalization for worsening HF
DECLARE-TIMI		RCT	T2DM and high CV risk	17160	63.9	6422 (37%)	Dapagliflozin, 10 mg	Placebo	295	4.2	MACE (Composite of CV death / nonfatal MI / nonfatal stroke)
CREDENCE	2019	RCT	T2DM, chronic kidney disease and risk for CV disease	4401	63	1494 (33.9%)	Canagliflozin, 100 mg	Placebo	112	2.6	Cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke
SCORED †	2020	RCT	T2DM, chronic kidney disease	10584	69	4754 (44.9%)	Sotagliflozin, 200–400 mg	Placebo	176	1.3	Composite of total number of CV death / HFH / urgent visits for HF (original coprimary endpoints: first occurrence

			and risk for CV disease								of CV death / nonfatal MI / nonfatal stroke and first occurrence of CV death / HFH)
SOLOIS trial	2020	RCT	T2DM and high CV risk	1222	70	412 (33.7%)	Sotagliflozin, 200–400 mg	Placebo	-	0.8	Total CV Death, HHF, and Urgent HF Visit
GLP-1 receptor agonist											
LEADER	2016	RCT	T2DM and high CV risk	4668/4672	64.2/64.4	3337	LiraGlutide, 1.8 mg	Placebo	370/407	3.8	MACE (death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke)
SUSTAIN-6	2016	RCT	T2DM and high CV risk	1648/1649	64.6	1295	Semaglutide, 0.5, 1 mg	Placebo	108/113	2.1	MACE (cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke)
EXSCEL	2017	RCT	T2DM and high CV risk	7356/7396	62.7	5604	Exenatide, 2mg injection	Placebo	442/436	3.2	Death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke
Harmony	2018	RCT	T2DM and CV disease	4731/4732	64.1/64.2	1427/1467	Albiglutide (30-50 mg)	Placebo	111/114	1.6	Cardiovascular death, myocardial infarction, or stroke
ELIXA	2015	RCT	T2DM and acute coronary syndrome	3034/3034	59.9/60.6	923/938	Lixisenatide, 10 µg	Placebo	118/103	2.1	MACE (cardiovascular death, myocardial infarction, stroke, or hospitalization for unstable angina)
REWIND	2019	RCT	T2DM and high CV risk	4949/4952	66.2/66.2	2306/2283	Dulaglutide 1.5 mg	Placebo	-	5.4	MACE (non-fatal myocardial infarction, non-fatal stroke, or death from cardiovascular causes)
PIONEER6	2019	RCT	T2DM and high CV risk	1591/1592	66/66	507/500	Semaglutide, 14 mg	Placebo	89/103	1.3	MACE (death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke

*CANVAS Program comprises of two trials, CANVAS and CANVAS-R. † Sotagliflozin is a dual inhibitor of SGLT2 and SGLT1. T2DM; type 2 diabetes mellitus; ASCVD, atherosclerotic cardiovascular disease; CV, cardiovascular; HF, heart failure; HFH, heart failure hospitalization, MACE, major adverse cardiovascular event; MI, myocardial infarction; SGLT2i, sodium-glucose co-transporter 2 inhibitors; GLP-1, glucagon like peptide; RCT, randomized controlled trials

3.3. Outcomes

3.3.1. The MACE risk in patients with type 2 diabetes and high cardiovascular risk

Compared with placebo, meta-analysis showed that SGLT2 inhibitors and GLP-1 receptor agonists significantly reduced the risk of MACE outcome among the White population (RR= 0.87, 95% CI [0.82, 0.92]; I2=0%, p=0.51 and RR= 0.90, 95% CI [0.85, 0.95]; I2=36%, p=0.16, respectively, Figure 2), the Asian population (RR= 0.70, 95% CI [0.60, 0.81]; I2=0%, p=0.56, and RR= 0.71, 95% CI [0.58, 0.87]; I2= 0%, p=0.82, respectively, Figure 3), males (RR= 0.80, 95% CI [0.74, 0.86]; I2=0%, p=0.71 and RR= 0.89, 95% CI [0.83, 0.94]; I2= 23%, p=0.26, respectively, Figure 4), and females (RR= 0.82, 95% CI [0.74, 0.91]; I2=0%, p=0.67 and RR= 0.86, 95% CI [0.78, 0.94]; I2= 0%, p=0.58, respectively, Figure 5).

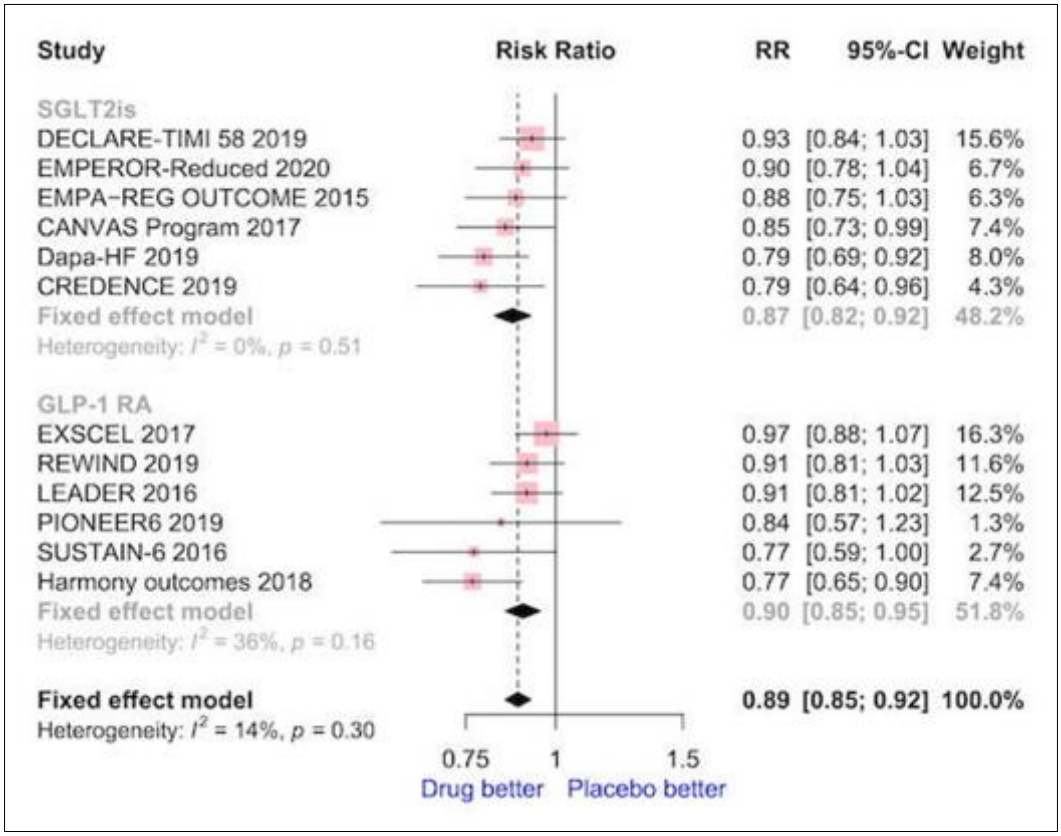


Figure 2 Forest plot comparing MACE rate between SGLT2 inhibitors and GLP-1 receptor vs placebo in the White population

While, both treatments failed to reduce the MACE risk in the Black population (RR= 0.77, 95% CI [0.55, 1.08]; I2=46%, p=0.11 and RR= 0.93, 95% [0.69, 1.25]; I2=49%, p=0.07, respectively, Figure 6) and the other race (RR= 0.90, 95% CI [0.60, 1.37]; I2=29%, p=0.24 and RR= 0.83, 95% CI [0.68, 1.01]; I2= 0.68, 1.01, respectively, Figure 7).

Further, no significant difference between SGLT2 inhibitors and placebo was found among the Hispanic and non-Hispanic population ((RR= 0.84, 95% CI [0.71, 1.00]; I2=58%, p=0.12 and RR= 0.91, 95% CI [0.81, 1.03]; I2=0%, p=0.98, respectively). On the other hand, GLP-1 receptor agonists significantly reduced the MACE risk in both Hispanic and non-Hispanic population (RR= 0.79, 95% CI [0.66, 0.96]; I2=0%, p=0.81 and RR= 0.89, 95% CI [0.83, 0.94]; I2=33%, p=0.22, respectively), Figures 8 and 9.

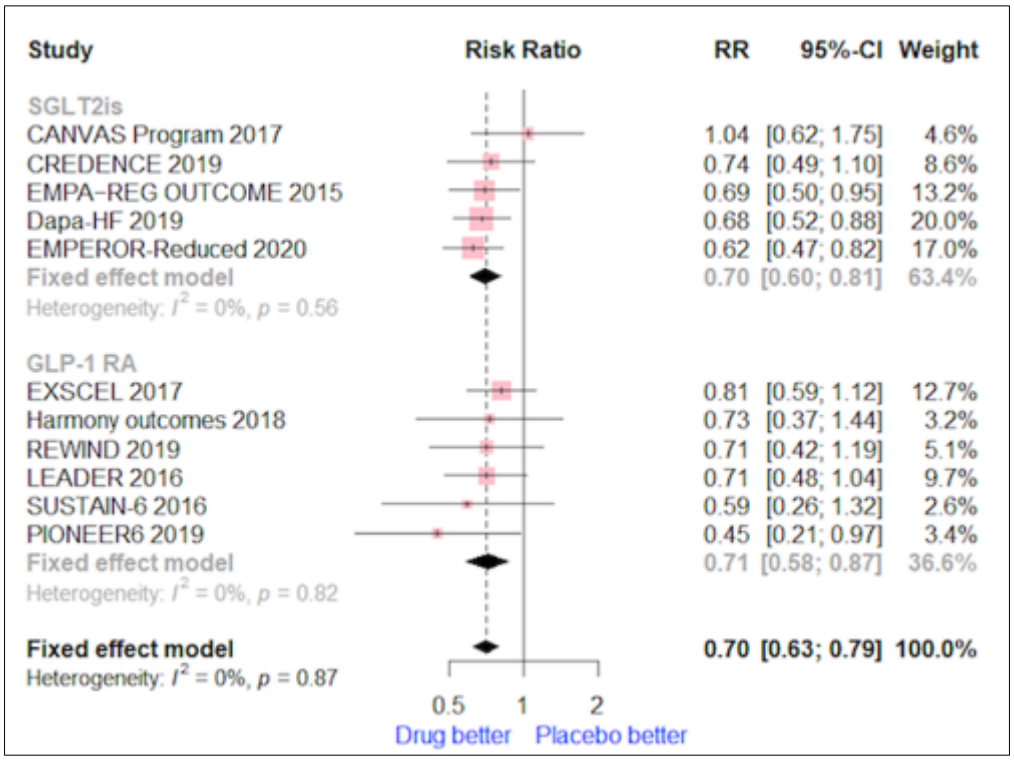


Figure 3 Forest plot comparing MACE rate between SGLT2 inhibitors and GLP-1 receptor vs placebo in the Asian population

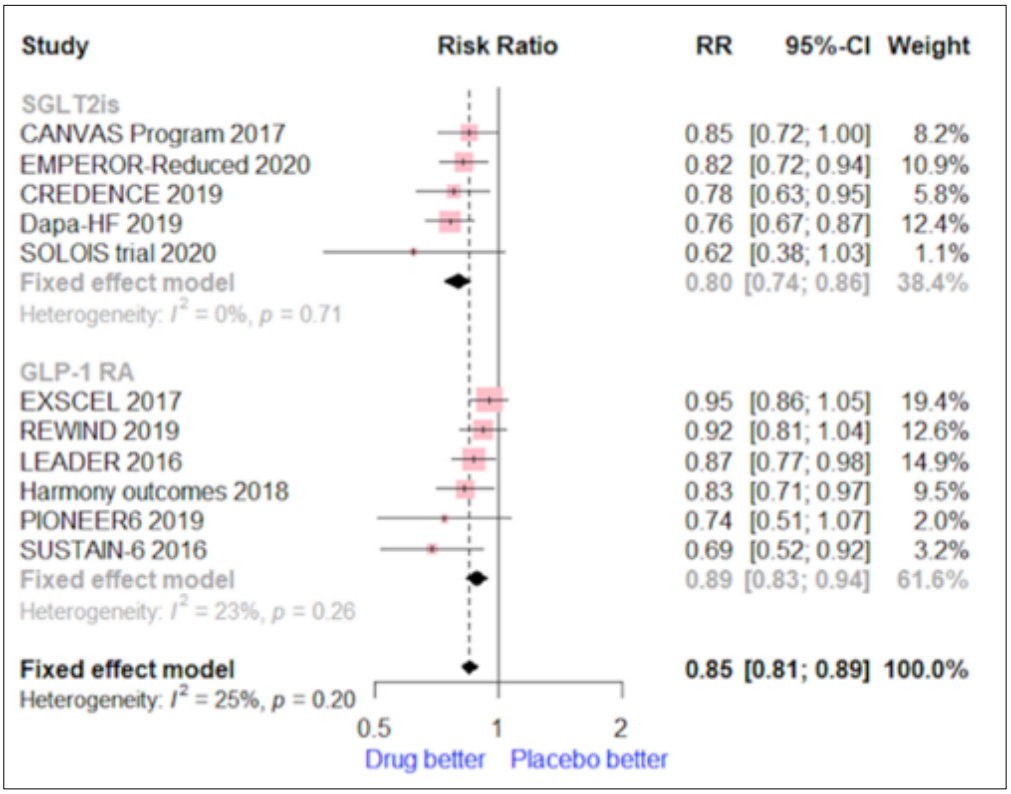


Figure 4 Forest plot comparing MACE rate between SGLT2 inhibitors and GLP-1 receptor vs placebo in males

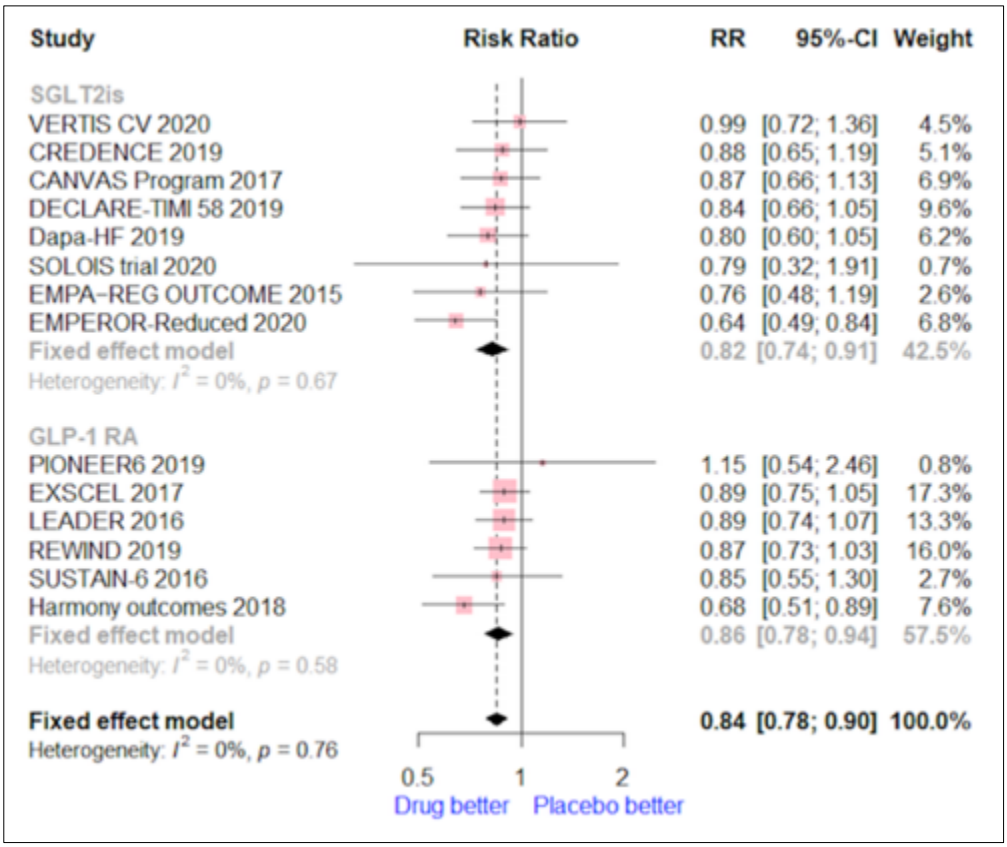


Figure 5 Forest plot comparing MACE rate between SGLT2 inhibitors and GLP-1 receptor vs placebo in females

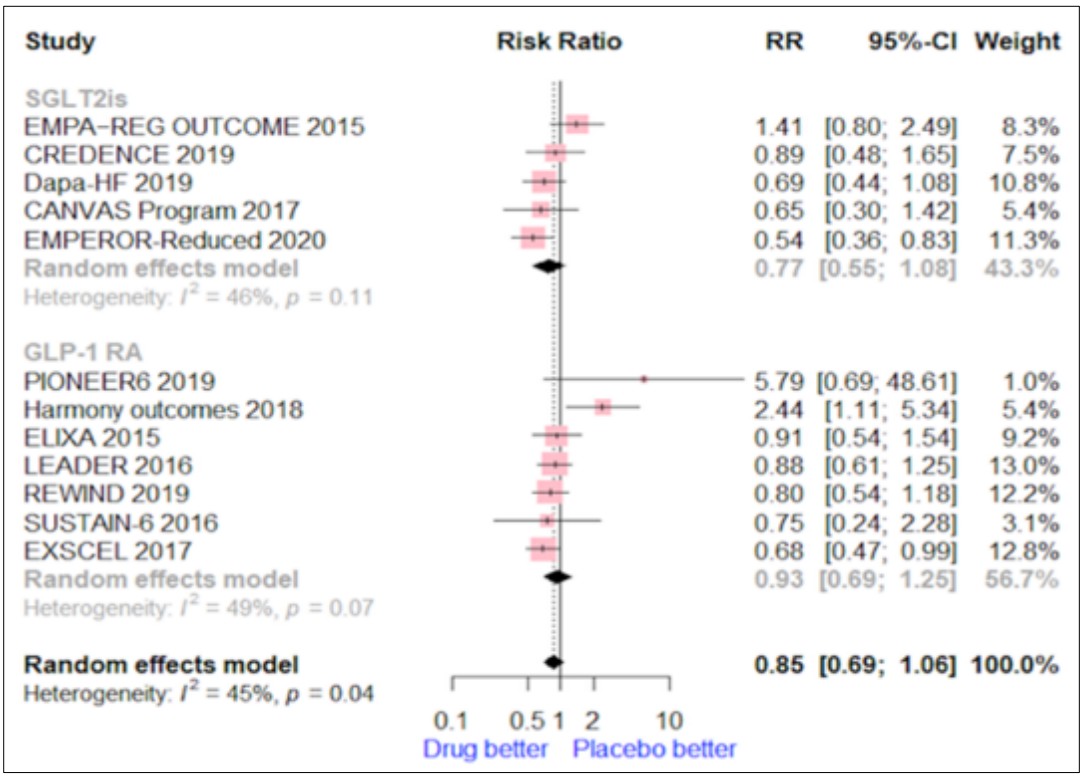


Figure 6 Forest plot comparing MACE rate between SGLT2 inhibitors and GLP-1 receptor vs placebo in the Black population

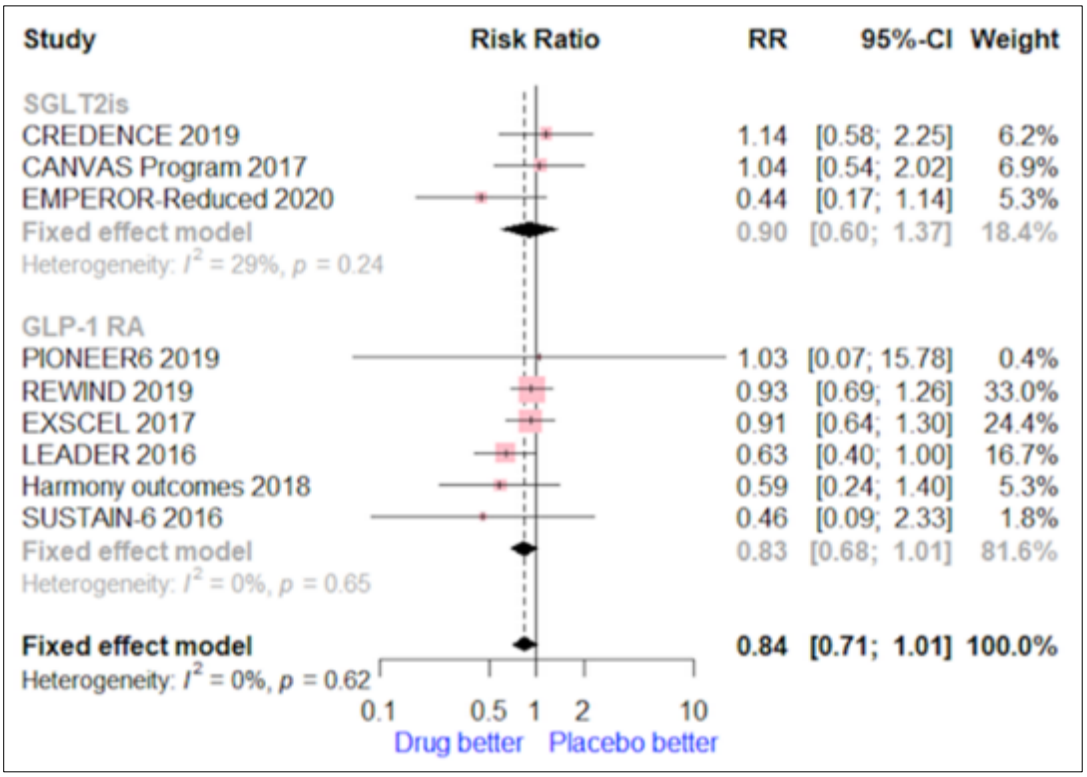


Figure 7 Forest plot comparing MACE rate between SGLT2 inhibitors and GLP-1 receptor vs placebo in other Race

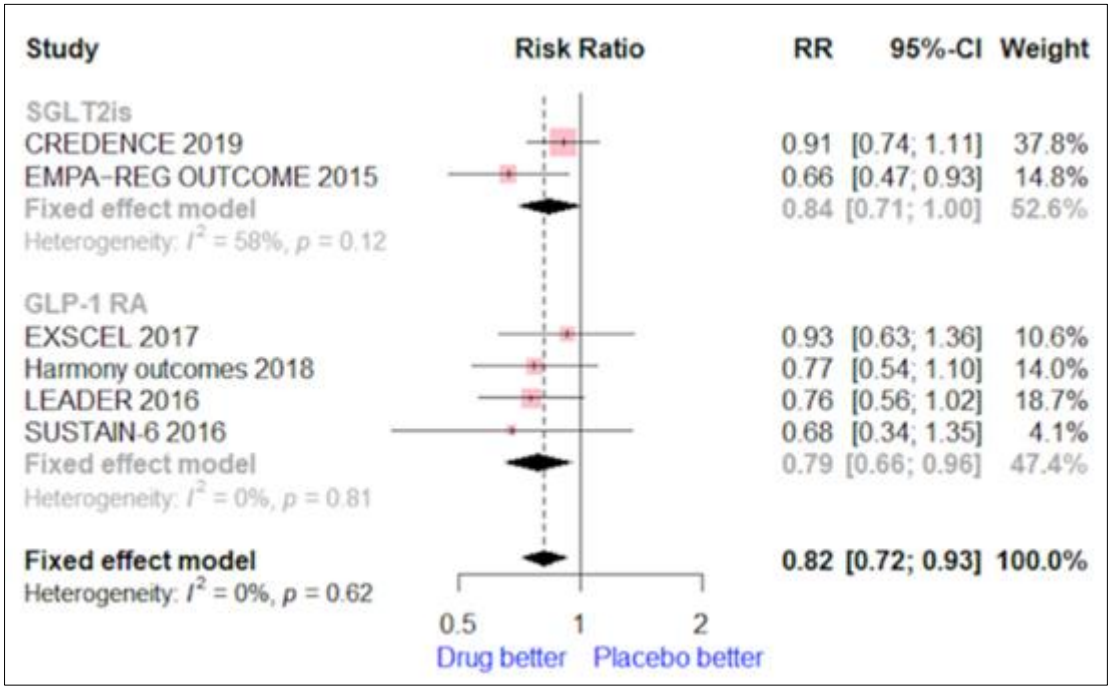


Figure 8 Forest plot comparing MACE rate between SGLT2 inhibitors and GLP-1 receptor vs placebo in the Hispanic population

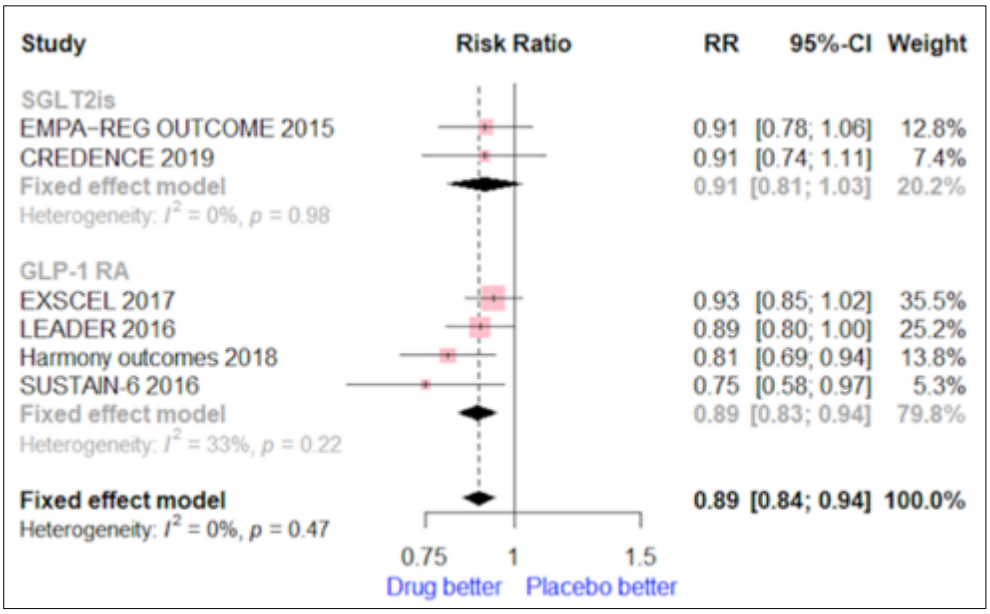


Figure 9 Forest plot comparing MACE rate between SGLT2 inhibitors and GLP-1 receptor vs placebo in the non-Hispanic population

3.3.2. Subgroup analysis of studies including patients with known heart failure

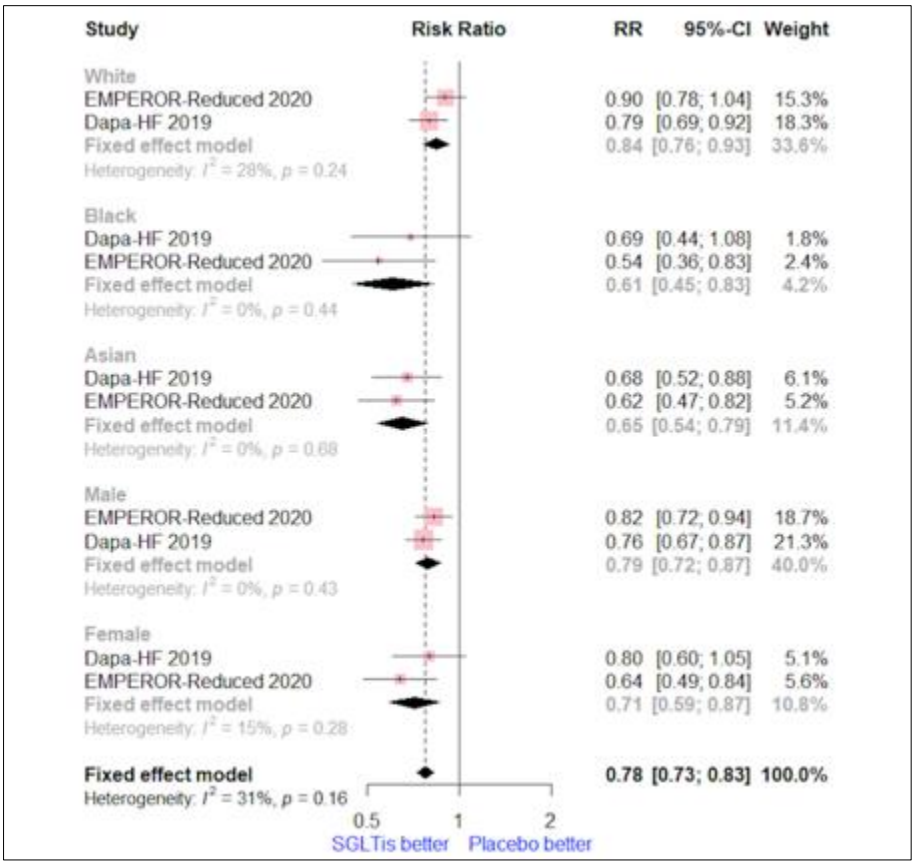


Figure 10 Forest Plot analysis comparing SGLT2 inhibitors and GLP-1 receptor in all subgroup population with heart failure reduced ejection fraction

Two RCTs included patients with previously known heart failure reduced ejection fraction (HFrEF): DAPA-HF (assessing dapagliflozin) and EMPEROR-Reduced (assessing empagliflozin), with a total of 8474 patients. The pooled estimate showed that SGLT2 inhibitors significantly reduced the MACE risk in all included subgroups: male (RR= 0.79, 95% CI [0.72, 0.87]), female (RR= 0.71, 95% CI [0.59; 0.87]), White (RR= 0.81, 95% CI [0.76, 0.93]), Black (RR= 0.61, 95% CI [0.45, 0.83]), and Asian (RR= 0.65, [0.54, 0.79]), Figure 10. Pooled subgroups are homogenous (I2<50%, p>0.1).

3.4. Differences between the 2 classes on different subgroups

Random-effects subgroup analysis was performed to assess the differences among the included subgroups. The results showed no significant differences between SGLT2 inhibitors and GLP-1 receptor agonists on the MACE outcomes according to race (White, Black, Asian, or others), ethnicity (Hispanic or non-Hispanic), or gender (male or female), p-value > 0.05.

3.5. Heterogeneity

All included comparisons were homogenous (I2<50%, p>0.1), Except for the subgroup of the Black population where a significant heterogeneity was observed (p=0.04) where the random effects model was observed.

3.6. Publication bias

Publication bias was assessed using a funnel plot for the included subgroups. The funnel plot showed no significant evidence of publication bias in any of the included subgroups, Appendix B.

3.7. Quality of evidence

Overall, based on the GRADE approach of assessment, the study outcomes were associated with moderate to a high quality of evidence. None of the outcomes was associated with a low or very low level of quality. As indicated above, details of the GRADE quality of evidence can be seen in Appendix B.

4. Discussion

We conducted this systematic review and meta-analysis to investigate the effect of SGLT-2 inhibitors and GLP-1 receptor agonists on MACE outcomes in patients with T2DM and heart failure. Further, we stratified the MACE outcome based on variables, such as race, ethnicity, and gender.

In patients with T2DM and high cardiovascular risk, our results revealed that SGLT-2 inhibitors and GLP-1 receptor agonists significantly reduced the MACE risk in White, Asians, males, and females. However, we found no significant difference in the Black patients. In patients with known HFrEF, the results showed that SGLT2 inhibitors significantly reduced the MACE risk in all subgroups, including the Black population.

The Asian community develops T2DM and CVD at a relatively younger age than the White population. This was associated with a higher risk of mortality from CVD, especially coronary artery disease and stroke [14, 15]. South Asians have a greater susceptibility to CKD and MACE even at lower BMI levels

Similarly, studies from The Health Improvement Network database showed that T2DM was associated with a significantly higher risk of chronic kidney disease (CKD) and MACE in South Asians [16].

The results of the current meta-analysis showed that SGLT-2 inhibitors and GLP-1 receptor agonists significantly reduced the risk of MACE outcome among the White and Asian population compared with placebo. Our results are consistent with the previous meta-analysis by Ghosal et al. that analyzed CV outcomes with only SGLT-2 inhibitors in 4997 Asian patients. They found that Asian patients treated with SGLT-2 inhibitors showed a significant reduction in MACE outcome, especially hypertensive heart failure and CV death [17].

Intriguingly, our results contradict a meta-analysis by Singh et al. that included 9285 Asian patients and analyzed CV outcomes with SGLT-2 inhibitors and GLP-1 receptor agonists in these patients.

The study showed a substantial reduction in MACE outcome in Asian patients with T2DM and CVD treated with GLP-1 receptor agonists; however, there was no significant reduction in MACE outcome in the group treated with SGLT-2 inhibitors [18]. According to this study, there was no substantial reduction in HHF or CV-death with SGLT-2Is in Asians.

As there was no difference in benefit ethnicity-wise, the results from the individual CVOTs such as (EMPAREG, CANVAS Program, DECLARE-TIMI58, and REWIND investigating SGLT-2Is) and (LEADER, HARMONY, and SUSTAIN-6 investigating GLP-1 receptor agonist) found a significant reduction in MACE outcome and benefits in hospitalization because of heart failure (HHF) or cardiovascular death.

Compared to the White population, Blacks are at a higher risk of cardiovascular death [18]. Further, the risk of obesity, T2DM, CVD, and CKD is higher in Black patients than White patients [20, 21]. Ethnicities with such a high risk need to consider various therapeutic options that will help alleviate these complications and health risks.

Our results showed that both treatments failed to reduce the MACE risk in the Black population. Further subgroup analysis of patients with HFrEF showed that SGLT2 inhibitors were associated with significant reductions in the MACE risk in the Black population. SGLT2 inhibitor agents are effective, especially given the high risk of obesity, T2DM, CVD, and CKD in Black patients. Our results are consistent with the previous meta-analysis conducted by Mishriky et al., who included 4601 Black patients. In that meta-analysis, there was no substantial difference between GLP-1 receptor agonists or SGLT-2 inhibitors and placebo in the incidence of MACE outcome in Black patients with T2DM [22].

Many studies have established the differential risk of cardiovascular outcomes in patients with T2DM based on gender. In patients with T2DM, many studies suggested that women have a greater risk for CVD than men because of less well-controlled HbA1c, higher lipid levels, and uncontrolled hypertension [23, 24]. Our analysis showed that compared to placebo, the reduction in MACE outcome was higher in men treated with SGLT-2 inhibitors than GLP-1 receptor agonists (RR=0.80 vs. 0.89, respectively). However, in the group treated with GLP-1 receptor agonist, the reduction in MACE outcome was higher in women than men (RR=0.86 vs. 0.89, respectively). We found no statistically significant difference in the MACE risk between males and females treated with SGLT-2 inhibitors and GLP-1 receptor agonists.

Our results are also consistent with Singh and his colleagues, who found that compared to placebo, reduction in MACE outcome was similar in both men and women treated with GLP-1 receptor agonists. However, there was a significant difference in men treated with SGLT-2 inhibitors [25].

Many potential explanations can be attributed to these differences in results between genders.

For example, body fats are usually higher in women than men. Also, blood flood flow to the organs and plasma volume is low. This affects the pharmacokinetics and pharmacodynamics of SGLT-2 inhibitors and GLP-1 receptor agonists in many ways and may play a crucial role in this variation [26].

Also, the extent to which patients comply with therapy suggestions, drugs, and protocols may affect this variation. This is because the side effect of cardiovascular drugs is relatively higher in women than men. The intake of diabetic medications may be relatively low, which can explain the variation in response to the diabetic drugs between genders [27].

Strength points and limitations

There were many strong points. All studies included in our meta-analysis were randomized controlled trials with high quality and low risk of bias. The included studies included a large sample size to better understand and evaluate the evidence. Moreover, we strictly adhered to the PRISMA checklist and carefully performed a precise search in the electronic database. In addition, no publication bias was detected. The limitation points in our study included a lack of gender-wise specification in the included studies, a low sample size of Black population compared to the other races, high heterogeneity in some subgroups.

5. Conclusion

This meta-analysis showed that SGLT-2 inhibitors and GLP-1 receptor agonists significantly reduced the risk of MACE outcome among White and Asian populations, and both males and females; however, both treatments failed to reduce the MACE outcomes in Black patients with T2DM and high-risk CVD. Subgroup analysis showed no significant differences between SGLT2 inhibitors and GLP-1 receptor agonists on the MACE outcomes stratified by race (White, Black, Asian, or others), ethnicity (Hispanic or non-Hispanic), or gender (male or female). In patients with HFrEF, the meta-analysis showed that SGLT2 inhibitors reduced the MACE risk in all subgroups, including the Black population. Further multicenter RCTs with a larger sample size are recommended to evaluate the effect of these drugs to better understand the ethnic difference in CV outcomes.

Compliance with ethical standards

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Disclosure of conflict of interest

There is no conflict of interest of the authors.

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