## Sodium Glucose Co-transporter 2 (SGLT2) inhibitors in Heart Failure with Preserved Ejection Fraction: A systematic review and meta-analysis

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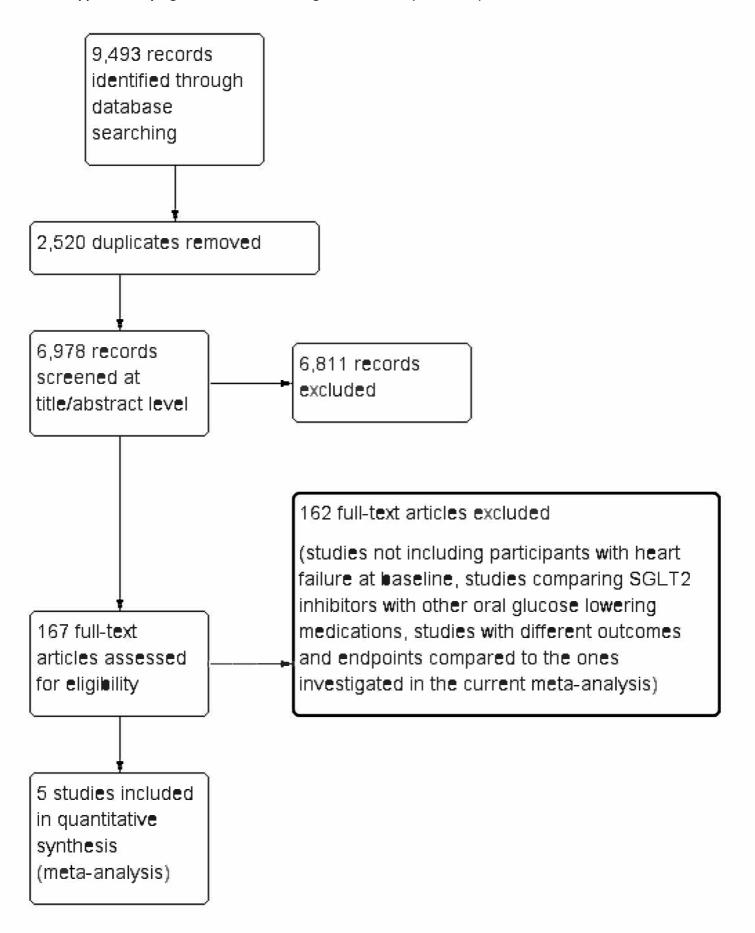
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## **Supplementary Figure 1.** Inclusion criteria during the study screening process

- (1) Randomised controlled trials comparing SGLT2 inhibitors with placebo
- (2) Studies that included adults (>18 years old) with heart failure and ejection fraction > 40% at baseline
- (3) Studies that assessed mortality and / or clinical events (hospitalisation for heart failure)
- (4) Studies with follow-up period greater than 6 months



**Supplementary Figure 3.** Effect of SGLT2 inhibitors vs placebo on the hospitalisation for heart failure for the total population

				SGLT2 Placebo			Hazard Ratio		Hazard Ratio			
	Study or Subg roup	log[Hazard Ratio]	SE	Total	Total	Weig ht	IV, Random, 95% CI		IV, Rando	m, 95% CI		
-	DECLARE TIMI 58	-0.3011	0.2209	399	409	13.1%	0.74 [0.48, 1.14]		-	ē)		
	EMPEROR-Preserved	-0.3425	0.0859	2997	2991	86.9%	0.71 [0.60, 0.84]		_			
	Total (95% CI)			3396	3400	100.0%	0.71 [0.61, 0.84]		<b>♦</b>			
Heterogeneity: $Tau^2 = 0.00$ ; $Chi^2 = 0.03$ , $df = 1$ (P = 0.86); $I^2 = 0\%$ Test for overall effect: Z = 4.21 (P < 0.0001)								0.01	0.1 1 Favours SGLT2	10 Favours placebo	100	

**Supplementary Figure 4.** Effect of SGLT2 inhibitors vs placebo on cardiovascular death for the total population

			SGLT2 Placebo Hazard Ratio					Hazard Ratio		
Study or Subgroup	log[Hazard Ratio]	SE	Total	Total	Weight	IV, Random, 95% C		IV, Random, 95% C		
DECLARE TIMI 58	0.3646	0.2811	399	409	15.8%	1.44 [0.83, 2.50]				
VERTIS CV	0.077	0.267	680	327	17.2%	1.08 [0.64, 1.82]		<del></del>		
EMPEROR-Preserved	-0.0943	0.0919	2997	2991	67.0%	0.91 [0.76, 1.09]		•		
Total (95% CI)			4076	3727	100.0%	1.01 [0.80, 1.28]		•		
Heterogeneity: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 2.61, df = 2 (P = 0.27); l <sup>2</sup> = 23%								0.1 1	10	100
Test for overall effect: Z =	0.01	Favours SGLT2 Favours		100						

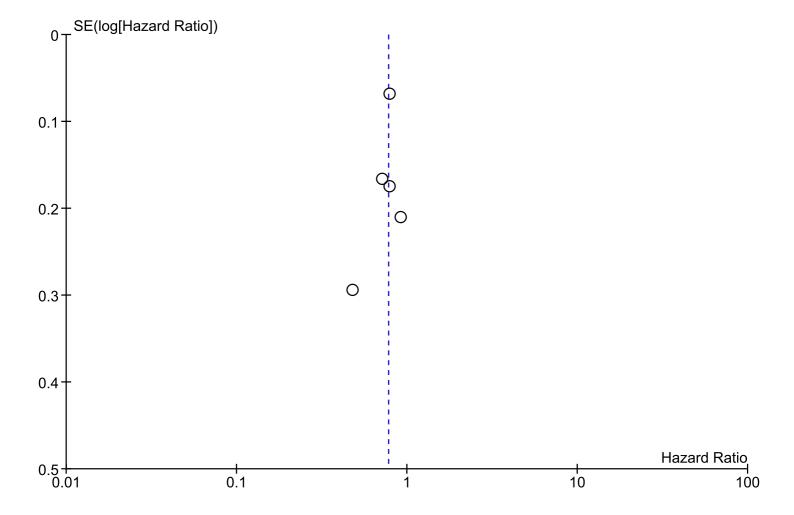
**Supplementary Figure 5.** Effect of SGLT2 inhibitors vs placebo on all-cause mortality for the total population

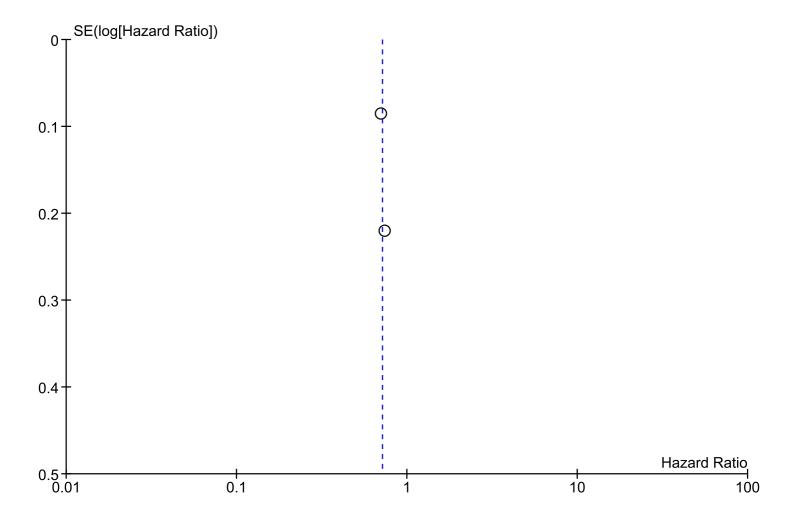
			SGLT2 P	Placebo		Hazard Ratio		Hazard Ratio	
_Study or Subgroup	log[Hazard Ratio]	SE	Total	Total	Weight	IV, Random, 95% C		IV, Random, 95% CI	
VERTIS CV	0.01	0.2171	680	327	8.7%	1.01 [0.66, 1.55]		S	
DECLARE TIMI 58	0.0583	0.2045	399	409	9.8%	1.06 [0.71, 1.58]			
EMPEROR-Preserved	0	0.0711	2997	2991	81.4%	1.00 [0.87, 1.15]			
Total (95% CI)			4076	3727	100.0%	1.01 [0.89, 1.14]			
Heterogeneity: Tau <sup>2</sup> = 0.0 Test for overall effect: Z =		2 (P = 0.	96); I² = 0%	6			0.01	0.1 1 10  Favours SGLT2 Favours placebo	100

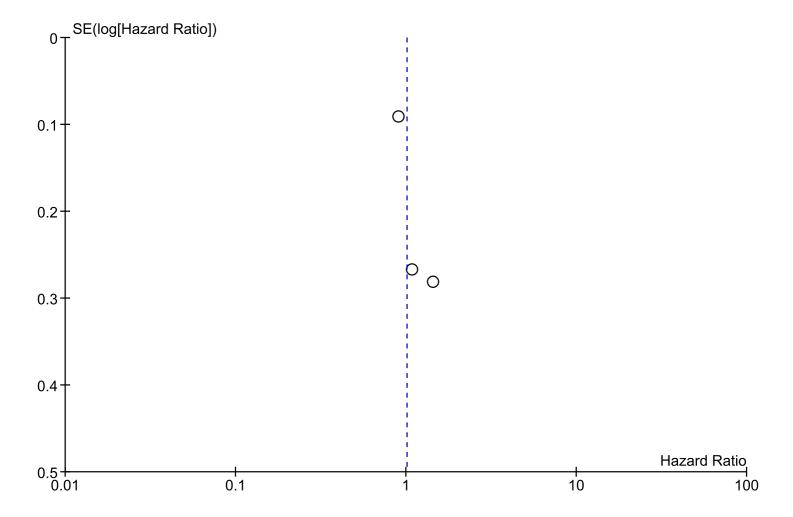
**Supplementary Figure 6.** Effect of SGLT2 inhibitors vs placebo on the risk of cardiovascular death or hospitalisation for heart failure for the patients with  $EF \ge 50\%$ 

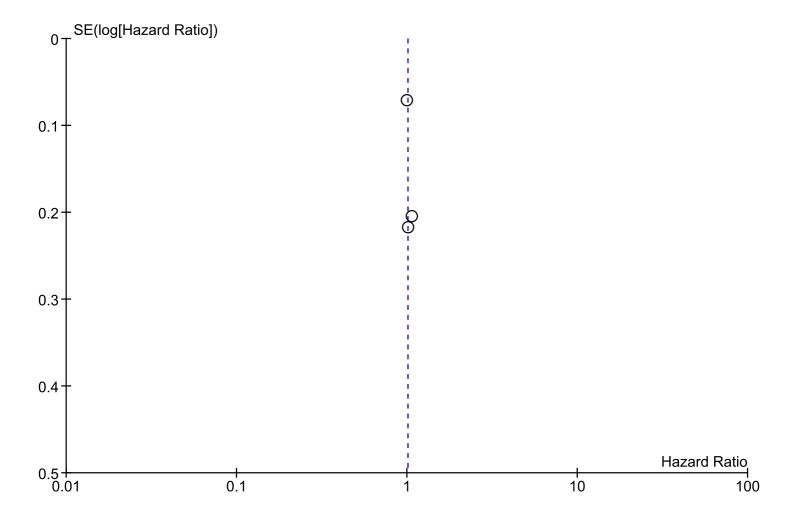
			SGLT2	Placebo		Hazard Ratio	Hazard Ratio			
Study or Subgroup	log[Hazard Ratio]	SE	Total	Total	Weight	IV, Random, 95% C	i <u>IV, I</u>	Random, 95%	CI	
EMPEROR-Preserved Subgroup EF ≥50% to < 60%	-0.2231	0.1139	1028	1030	36.6%	0.80 [0.64, 1.00]		-		
EMPEROR-Preserved Subgroup EF ≥ 60%	-0.1393	0.1183	974	973	34.8%	0.87 [0.69, 1.10]		-		
SCORED	-0.3285	0.166	843	824	20.9%	0.72 [0.52, 1.00]		-		
SOLOIST WHF	-0.734	0.2936	127	129	7.7%	0.48 [0.27, 0.85]	Ş.	- <del>1</del> :		
Total (95% CI)			2972	2956	100.0%	0.77 [0.66, 0.91]		•		
Heterogeneity: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 3.86, df = 3 (P = 0.	28); I <sup>2</sup> = 22%						0.01 0.1		10	100
Test for overall effect: Z = 3.02 (P = 0.002)								GLT2 Favours		100

**Supplementary Figure 7.** Funnel plot for the risk of cardiovascular death or hospitalisation for heart failure for the total population









**Supplementary Figure 11.** Funnel plot for the cardiovascular death or hospitalisation for heart failure for the patients with  $EF \ge 50\%$ 

