

Table S1. Observational studies that compared cardiovascular effects of SGLT2is in different age subgroups

Reference s	Countr y	SGLT2i (n)	Comparator (n)	Age categor y	MACE	All -cause mortality + hHF	All-cause mortality	CV mortality	MACE + hHF	hHF
Birkeland et al. 2017 [58]	Nordic	All	Glucose-lowering agents	< 65 years	1.01 (0.85;1.20)	NA	NA	1.10 (0.65;1.84)	NA	NA
				≥ 65 years	0.66 (0.56;0.78)	NA	NA	0.45 (0.32;0.65)	NA	NA
Gautam et al. 2017 [60]	USA	All	DPP4-is	< 65 years	NA	NA	NA	NA	NA	0.77 (0.57;1.05) <i>P</i> < 0.09
				≥ 65 years	NA	NA	NA	NA	NA	0.60 (0.41;0.87) <i>P</i> = 0.008
Dawwas et al. 2019 [61]	USA	All	Sulphonylureas	≤ 65 years	0.59 (0.52;0.66)	NA	NA	NA	NA	NA
				> 65 years	0.89 (0.65;1.00)	NA	NA	NA	NA	NA
Pasternak et al. 2019 [59]	Nordic	All	DPP-4is	< 65 years	NA	NA	NA	NA	1.13 (0.94;1.35)	NA
				≥ 65 years	NA	NA	NA	NA	0.81	NA

				years					(0.69;0.96) ) <i>P</i> interaction 0.01	
Han et al. 2020 [45]	South Korea	All	DPP-4is	< 75 years	NA	0.77 (0.67;0.88 ) <i>P</i> = 0.001	0.72 (0.58;0.89 ) <i>P</i> = 0.002	NA	NA	0.79 (0.66;0.93 ) <i>P</i> = 0.006
				≥ 75 years	NA	0.93 (0.81;1.06 ) <i>P</i> = 0.283 <i>P</i> interaction < 0.001	0.93 (0.77;1.11 ) <i>P</i> = 0.422 <i>P</i> interaction < 0.001	NA	NA	0.95 (0.79;1.14 ) <i>P</i> = 0.582 <i>P</i> interaction < 0.001
Htoo et al. 2022 [48]	US	Empagliflozi n	Sitagliptin	< 75 years	0.72 (0.61;0.85 )	NA	NA	NA	NA	0.40 (0.30;0.54 )
				≥ 75 years	0.63 (0.52;0.77 ) <i>P</i> interaction 0.34	NA	NA	NA	NA	0.46 (0.33;0.64 ) <i>P</i> interaction 0.50
Htoo et al. 2022 [48]	US	Empagliflozi n	Liraglutide	< 75 years	0.91 (0.77;1.07 )	NA	NA	NA	NA	0.67 (0.50;0.91 )
				≥ 75 years	0.96 (0.77;1.20 ) <i>P</i>	NA	NA	NA	NA	0.70 (0.50;0.97 ) <i>P</i>

					interaction 0.62					interaction 0.90
Nakai et al. 2022 [47]	Japan	All	DPP-4is	< 65 years	NA	NA	0.51 (0.25;0.84)	NA	NA	0.38 (0.27;0.54)
				65;74 years	NA	NA	0.79 (0.49;1.27)	NA	NA	0.48 (0.36;0.85)
				≥ 75 years	NA	NA	0.58 (0.61;0.90)	NA	NA	0.52 (0.45;0.61)
							<i>P</i> interaction 0.81			<i>P</i> interaction 0.16

DPP-4is: dipeptidyl peptidase-4 inhibitors. hHF: hospitalization for heart failure. MACE: major cardiovascular adverse event. NA: not available. SGLT2i : sodium-glucose cotransporter type 2 inhibitor.