

**Supplementary Table 3.** Fully adjusted HRs of selected study endpoints for different SGLT2i treatment strategies stratified by the time of SGLT2i initiation, before and after the EMPAREG study.

		Exposure	All individuals			Before EMPAREG			After EMPAREG		
			HR*	95% CI	p value	HR*	95% CI	p value	HR*	95% CI	p value
Mortality	ITT	Non-initiator	1.0			1.0			1.0		
		SGLT2i initiator	0.56	0.49–0.63	<0.01	0.54	0.46–0.65	<0.01	0.56	0.46–0.68	<0.01
	OT	Non-initiator	1.0			1.0			1.0		
		SGLT2i initiator	0.34	0.27–0.42	<0.01	0.36	0.27–0.48	<0.01	0.32	0.23–0.43	<0.01
	AT	Non-use	1.0			1.0			1.0		
		Current use of SGLT2i	0.35	0.30–0.41	<0.01	0.36	0.29–0.45	<0.01	0.34	0.26–0.43	<0.01
		Recent use of SGLT2i	1.08	0.75–1.55	0.69	1.09	0.66–1.80	0.73	1.05	0.62–1.79	0.86
		Past use of SGLT2i	1.21	0.97–1.51	0.09	1.09	0.79–1.49	0.60	1.37	1.00–1.88	0.05
	Severe renal disease	ITT	Non-initiator	1.0			1.0			1.0	
SGLT2i initiator			0.55	0.46–0.67	<0.01	0.47	0.36–0.61	<0.01	0.65	0.49–0.86	<0.01
OT		Non-initiator	1.0			1.0			1		
		SGLT2i initiator	0.34	0.25–0.47	<0.01	0.24	0.14–0.39	<0.01	0.48	0.32–0.73	<0.01
AT		Non-use	1.0			1.0			1.0		
		Current use of SGLT2i	0.31	0.24–0.40	<0.01	0.22	0.15–0.32	<0.01	0.47	0.33–0.66	<0.01
		Recent use of SGLT2i	0.70	0.38–1.32	0.27	0.47	0.17–1.26	0.13	1.03	0.46–2.32	0.95
		Past SGLT2i	0.82	0.58–1.17	0.28	0.63	0.38–1.04	0.07	1.09	0.66–1.79	0.73
CV		ITT	Non-initiator	1.0			1.0			1.0	
	SGLT2i initiator		0.75	0.61–0.93	0.01	0.72	0.54–0.98	0.04	0.82	0.60–1.11	0.2
	OT	Non-initiator	1.0			1.0			1.0		
		SGLT2i initiator	0.54	0.40–0.74	<0.01	0.44	0.27–0.73	<0.01	0.67	0.44–1.01	0.06
	AT	Non-use	1.0			1.0			1.0		
		Current use of SGLT2i	0.76	0.61–0.95	0.02	0.66	0.48–0.90	0.01	0.9	0.66–1.24	0.53
		Recent use of SGLT2i	1.62	0.95–2.78	0.08	1.68	0.82–3.44	0.15	1.49	0.65–3.41	0.34
		Past use of SGLT2i	1.19	0.78–1.81	0.41	0.97	0.52–1.79	0.92	1.54	0.86–2.74	0.14
	MI	ITT	Non-initiator	1.0			1.0			1.0	
SGLT2i initiator			0.98	0.74–1.28	0.86	0.97	0.66–1.45	0.90	1.0	0.68–1.47	1.0
OT		Non-initiator	1.0			1.0					

		Exposure	All individuals			Before EMPAREG			After EMPARG		
			HR*	95% CI	p value	HR*	95% CI	p value	HR*	95% CI	p value
	AT	SGLT2i initiator	0.67	0.45–0.99	0.05	0.6	0.31–1.16	0.13	0.76	0.45–1.27	0.29
		Non-use	1.0			1.0			1.0		
		Current use of SGLT2i	0.94	0.71–1.25	0.67	0.89	0.59–1.34	0.57	1.01	0.68–1.50	0.96
		Recent use of SGLT2i	1.92	0.97–3.77	0.06	2.01	0.81–5.02	0.13	1.77	0.64–4.90	0.27
		Past use of SGLT2i	1.05	0.57–1.94	0.88	0.94	0.38–2.35	0.90	1.21	0.52–2.82	0.65
IS	ITT	Non-initiator	1.0			1.0			1.0		
		SGLT2i initiator	0.51	0.36–0.74	<0.01	0.52	0.31–0.86	0.01	0.53	0.31–0.92	0.02
	OT	Non-initiator	1.0			1.0			1.0		
		SGLT2i initiator	0.37	0.21–0.65	<0.01	0.35	0.16–0.78	0.01	0.41	0.18–0.93	0.03
	AT	Non-use	1.0			1.0			1.0		
		Current use of SGLT2i	0.57	0.39–0.83	<0.01	0.49	0.29–0.83	0.01	0.67	0.38–1.15	0.14
		Recent use of SGLT2i	1.11	0.41–3.01	0.84	0.99	0.24–4.05	0.99	1.21	0.29–5.02	0.79
		Past use of SGLT2i	1.24	0.66–2.31	0.50	0.77	0.28–2.14	0.62	1.99	0.89–4.45	0.09

Reference group=non-initiator/non-use.

\*Adjusted estimates obtained using a Cox proportional hazard regression model including all variables in **Supplementary table 1**.