

Supplementary Appendix

Adjusted hazard ratios with 95% CI for the association between pioglitazone use and all-cause mortality. Full model results.

Variables	HR	95% CI of HR	p-value
Pioglitazone exposure: never	Reference		
Pioglitazone exposure: ever	0.67	(0.64, 0.70)	<0.001
FIN	Reference		
NL HOSP	0.75	(0.69, 0.82)	<0.001
SWE	0.74	(0.65, 0.84)	<0.001
UK GP	0.78	(0.72, 0.84)	<0.001
UK GP-HOSP	0.66	(0.61, 0.71)	<0.001
NL GP	0.46	(0.41, 0.52)	<0.001
AD prior to CED: no treatment	Reference		
AD prior to CED: metformin only	0.80	(0.74, 0.87)	<0.001
AD prior to CED: SU only	0.94	(0.86, 1.02)	0.145
AD prior to CED: metformin and SU	0.58	(0.53, 0.63)	<0.001
AD prior to CED: insulin (only or comb.)	0.69	(0.62, 0.77)	<0.001
AD prior to CED: other	0.63	(0.56, 0.70)	<0.001
history of other TZD: never	Reference		
history of other TZD: ever	0.86	(0.79, 0.93)	<0.001
Add-on	Reference		
Switch	1.09	(1.04, 1.14)	<0.001
PS quintile group: 1	Reference		
PS quintile group: 2	1.06	(0.99, 1.12)	0.074
PS quintile group: 3	1.11	(1.03, 1.19)	0.006
PS quintile group: 4	1.16	(1.07, 1.26)	<0.001
PS quintile group: 5	1.14	(1.04, 1.25)	0.004
duration of treated diabetes: <1 year	Reference		
duration of treated diabetes: 1-<2 years	0.85	(0.77, 0.92)	<0.001
duration of treated diabetes: 2-<4 years	0.78	(0.72, 0.85)	<0.001
duration of treated diabetes: 4-<6 years	0.79	(0.73, 0.86)	<0.001
duration of treated diabetes: >=6 years	0.86	(0.79, 0.94)	0.001
diabetic coma: never	Reference		
diabetic coma: ever	1.37	(1.27, 1.49)	<0.001
diabetic lower limb severity: never	Reference		
diabetic lower limb severity: ever	1.88	(1.76, 2.02)	<0.001
diabetic renal complication: never	Reference		
diabetic renal complication: ever	1.47	(1.39, 1.55)	<0.001
diabetic retinopathy or maculopathy: never	Reference		
diabetic retinopathy or maculopathy: ever	0.98	(0.93, 1.04)	0.486
diabetic ketoacidosis: never	Reference		
diabetic ketoacidosis: ever	1.75	(1.40, 2.20)	<0.001
MI or stroke: never	Reference		
MI or stroke: ever	1.84	(1.76, 1.92)	<0.001
CHF: never	Reference		
CHF: ever	2.92	(2.79, 3.07)	<0.001
Cohort entry year: 2000-2003	Reference		
Cohort entry year: 2004-2007	0.88	(0.83, 0.93)	<0.001
Cohort entry year: 2007-2011	0.72	(0.66, 0.77)	<0.001
Duration of membership: 1-2 years	Reference		
Duration of membership: 3-4 years	1.03	(0.95, 1.12)	0.426
Duration of membership: 5-6 years	0.99	(0.91, 1.07)	0.767

Duration of membership: >=7 years	0.86	(0.80, 0.93)	<0.001
Number of AD drugs prior to CED: 0	Reference		
Number of AD drugs prior to CED: 1	1.32	(1.15, 1.51)	<0.001
Number of AD drugs prior to CED: 2	1.47	(1.27, 1.71)	<0.001
Number of AD drugs prior to CED: 3	1.32	(1.11, 1.55)	0.001
Number of AD drugs prior to CED: >3	1.26	(1.03, 1.53)	0.026
age at CED: 40-49 years	Reference		
age at CED: 50-59 years	1.70	(1.48, 1.96)	<0.001
age at CED: 60-69 years	2.88	(2.52, 3.29)	<0.001
age at CED: >=70 years	6.66	(5.84, 7.60)	<0.001
sex: male	Reference		
sex: female	0.88	(0.85, 0.91)	<0.001
history of metformin: never	Reference		
history of metformin: ever	0.82	(0.75, 0.89)	<0.001
history of SU: never	Reference		
history of SU: ever	1.34	(1.25, 1.44)	<0.001
history of insulin: never	Reference		
history of insulin: ever	1.38	(1.31, 1.45)	<0.001
history of other AD: never	Reference		
history of other AD: ever	0.93	(0.87, 0.99)	0.027