

Table S1 Sensitivity analysis: confounder-adjusted outcome occurrence rate ratios for the association between warfarin and serious hypoglycemia when used concomitantly with a sulfonylurea or metformin with additional adjustment for the average daily dose of object drug

Object drug (N=number of outcomes ^a)	Risk Window (days) ^b	Rate ratio ^c (95% CI)
Glimepiride (N=573)	Overall	1.48 (1.05–2.07)
	0–30	1.65 (1.15–2.37)
	31–60	1.23 (0.78–1.93)
	61–120	1.16 (0.70–1.92)
	>120	1.59 (0.97–2.62)
Glipizide (N=1,391)	Overall	1.24 (1.00–1.53)
	0–30	1.25 (0.99–1.60)
	31–60	0.93 (0.69–1.28)
	61–120	1.06 (0.77–1.48)
	>120	1.72 (1.27–2.34)
Glyburide (N=1,243)	Overall	1.16 (0.92–1.47)
	0–30	1.20 (0.93–1.55)
	31–60	0.93 (0.67–1.29)
	61–120	1.09 (0.77–1.55)
	>120	1.58 (1.12–2.23)
Metformin (N=1,098)	Overall	1.61 (1.27–2.05)
	0–30	1.50 (1.13–1.98)
	31–60	1.26 (0.90–1.78)
	61–120	2.01 (1.47–2.74)
	>120	1.87 (1.35–2.60)

CI, confidence interval.

^aNumber of outcomes: number of serious hypoglycemia occurrences during the observation time for each object-precipitant drug pair. ^bRisk window (days): days within the exposed time (i.e., concomitant-use period) in the observation time since the initiation of the concomitant-use time. ^cRate ratio: ((outcome occurrence rate of exposed time) / (outcome occurrence rate of unexposed time)), for each object-precipitant drug pair.

Table S2 Sensitivity analysis: outcome occurrence rate ratios for the association between warfarin and serious hypoglycemia when used concomitantly with a sulfonylurea or metformin , by concomitancy-triggering drug

Object drug (N=number of outcomes ^a)	Concomitancy- triggering drug	Risk Window (days) ^b	Rate ratio ^c (95% CI)	
Glimepiride (N=654)	Warfarin-triggered ^d	Overall	2.03 (1.39–2.97)	
		0–30	1.97 (1.28–3.03)	
		31–60	1.85 (1.08–3.16)	
		61–120	2.03 (1.13–3.63)	
		>120	2.78 (1.52–5.09)	
		Overall	0.89 (0.55–1.43)	
	Antidiabetes-triggered ^e	0–30	1.04 (0.63–1.72)	
		31–60	0.76 (0.40–1.44)	
		61–120	0.38 (0.15–0.97)	
		>120	0.98 (0.45–2.14)	
		Overall	0.42 (0.16–1.15)	
		0–30	0.51 (0.17–1.51)	
	Combination-triggered ^f	31–60	0.38 (0.11–1.28)	
		61–120	0.49 (0.13–1.81)	
		>120	0.25 (0.05–1.21)	
		Overall	1.51 (1.18–1.93)	
		0–30	1.55 (1.17–2.07)	
		31–60	1.21 (0.82–1.80)	
Glipizide (N=1,554)	Warfarin-triggered	61–120	1.11 (0.71–1.74)	
		>120	2.19 (1.48–3.24)	
		Overall	0.90 (0.66–1.24)	
		0–30	0.94 (0.65–1.34)	
		31–60	0.62 (0.39–0.99)	
		61–120	0.87 (0.54–1.42)	
	Antidiabetes-triggered	>120	1.37 (0.82–2.30)	
		Overall	1.09 (0.72–1.67)	
		0–30	0.95 (0.54–1.66)	
		31–60	0.72 (0.36–1.43)	
		61–120	1.00 (0.47–2.13)	
		>120	1.53 (0.86–2.71)	
	Glyburide (N=1,405)	Warfarin-triggered	Overall	1.13 (0.87–1.48)
			0–30	1.22 (0.90–1.67)
			31–60	0.66 (0.40–1.06)
			61–120	1.17 (0.75–1.82)
			>120	1.66 (1.06–2.60)
			Overall	1.05 (0.75–1.45)
Antidiabetes-triggered		0–30	0.96 (0.66–1.39)	
		31–60	0.86 (0.54–1.36)	
		61–120	0.91 (0.55–1.53)	
		>120	2.05 (1.26–3.32)	
		Overall	1.27 (0.79–2.05)	
		0–30	1.45 (0.88–2.40)	
Combination-triggered		31–60	1.00 (0.53–1.87)	
		61–120	1.05 (0.49–2.28)	
		>120	1.13 (0.46–2.77)	

Object drug (N=number of outcomes ^a)	Concomitancy- triggering drug	Risk Window (days) ^b	Rate ratio ^c (95% CI)
Metformin (N=1,197)	Warfarin-triggered	Overall	1.55 (1.19–2.02)
		0–30	1.11 (0.77–1.61)
		31–60	1.14 (0.73–1.78)
		61–120	2.01 (1.36–2.95)
		>120	2.48 (1.72–3.58)
	Antidiabetes-triggered	Overall	1.51 (1.08–2.12)
		0–30	1.73 (1.19–2.53)
		31–60	1.21 (0.74–1.98)
		61–120	1.24 (0.74–2.06)
		>120	1.63 (0.98–2.69)
	Combination-triggered	Overall	1.66 (0.98–2.79)
		0–30	1.37 (0.70–2.65)
		31–60	1.21 (0.56–2.61)
		61–120	3.13 (1.55–6.31)
		>120	1.66 (0.64–4.28)

CI, confidence interval.

^aNumber of outcomes: number of serious hypoglycemia occurrence during the observation time for each object-precipitant drug pair. ^bRisk window (days): days within the exposed time (i.e., concomitant-use period) in the observation time since the initiation of the concomitant-use time. ^cRate ratio: ((outcome occurrence rate of exposed time) / (outcome occurrence rate of unexposed time)), for each object-precipitant drug pair. ^dWarfarin-triggered: observation time (person-days) in which the concomitant use of object and precipitant drugs was initiated by warfarin during the ongoing anti diabetic treatment. ^eAnti diabetes-triggered: observation time (person-days) in which the concomitant use of object and precipitant drugs was initiated by an antidiabetic drug during the ongoing warfarin treatment. ^fCombination-triggered: observation time (person-days) in which the concomitant use of object and precipitant drugs was initiated by warfarin and an antidiabetic drug on the same day (i.e., prescriptions of warfarin and an antidiabetic drug were dispensed on the same day).

Table S3 Sensitivity analysis: confounder-adjusted outcome occurrence rate ratios for the association between warfarin and serious hypoglycemia when used concomitantly with a sulfonylurea or metformin, excluding individuals who had death outcome during the observation time

Object drug (N=number of outcomes ^a)	Risk Window (days) ^b	Rate ratio ^c (95% CI)
Glimepiride (N=621)	Overall	1.67 (1.19–2.33)
	0–30	1.77 (1.24–2.53)
	31–60	1.46 (0.95–2.24)
	61–120	1.43 (0.87–2.35)
	>120	1.83 (1.12–2.99)
Glipizide (N=1,454)	Overall	1.16 (0.95–1.43)
	0–30	1.18 (0.94–1.49)
	31–60	0.83 (0.61–1.13)
	61–120	1.02 (0.74–1.40)
	>120	1.65 (1.23–2.22)
Glyburide (N=1,340)	Overall	1.13 (0.90–1.41)
	0–30	1.14 (0.89–1.45)
	31–60	0.90 (0.66–1.23)
	61–120	1.06 (0.76–1.48)
	>120	1.63 (1.18–2.26)
Metformin (N=1,174)	Overall	1.69 (1.35–2.12)
	0–30	1.51 (1.15–1.99)
	31–60	1.39 (1.00–1.92)
	61–120	1.98 (1.46–2.69)
	>120	2.15 (1.58–2.92)

CI, confidence interval.

^aNumber of outcomes: number of severe hypoglycemia occurrence during the observation time for each object-precipitant drug pair. ^bRisk window (days): days within the exposed time (i.e., concomitant-use period) in the observation time since the initiation of the concomitant-use time. ^cRate ratio: ((outcome occurrence rate of exposed time) / (outcome occurrence rate of unexposed time)), for each object-precipitant drug pair.

Number (%) of person-days excluded: glimepiride, N=10,156 (3.9%); glipizide, N=21,074 (3.4%); glyburide, N=19,128 (3.2%); metformin, N=9,456 (1.7%).

Table S4 Sensitivity analysis: confounder-adjusted outcome occurrence rate ratios for the association between warfarin and serious hypoglycemia when used concomitantly with a sulfonylurea or metformin, excluding individuals with potentially incomplete data

Object drug (N=number of outcomes ^a)	Risk Window (days) ^b	Rate ratio ^c (95% CI)
Glimepiride (N=382)	Overall	2.18 (1.41–3.36)
	0–30	2.43 (1.54–3.85)
	31–60	1.43 (0.79–2.58)
	61–120	1.75 (0.91–3.37)
	>120	3.54 (1.83–6.82)
Glipizide (N=845)	Overall	1.03 (0.77–1.36)
	0–30	0.87 (0.62–1.22)
	31–60	1.04 (0.70–1.55)
	61–120	0.96 (0.61–1.49)
	>120	1.54 (1.02–2.32)
Glyburide (N=833)	Overall	1.21 (0.90–1.63)
	0–30	1.26 (0.91–1.73)
	31–60	0.98 (0.65–1.48)
	61–120	1.01 (0.63–1.63)
	>120	1.83 (1.15–2.89)
Metformin (N=677)	Overall	1.65 (1.18–2.29)
	0–30	1.29 (0.87–1.92)
	31–60	1.12 (0.69–1.80)
	61–120	2.02 (1.30–3.13)
	>120	2.70 (1.79–4.09)

CI, confidence interval.

^aNumber of outcomes: number of serious hypoglycemia occurrence during the observation time for each object-precipitant drug pair. ^bRisk window (days): days within the exposed time (i.e., concomitant-use period) in the observation time since the initiation of the concomitant-use time. ^cRate ratio: ((outcome occurrence rate of exposed time) / (outcome occurrence rate of unexposed time)), for each object-precipitant drug pair.

Number (%) of person-days excluded: glimepiride, N=111,584 (42.4%); glipizide, N=322,493 (51.5%); glyburide, N=274,695 (45.3%); metformin, N=245,490 (44.3%).