Appendix Note 1: Calculation of Absolute Event Rates

We used the method of predictive margins.[1] Specifically, for each person-quarter in the sample, we predicted the probability of the event, both with concurrent warfarin use and without concurrent use. All other variables were held fixed at their actual values in this prediction exercise. The difference in the two probabilities thus represented the predicted effect of concurrent warfarin use, and was averaged across the sample. To limit computational burden, individual-level random effects were evaluated at zero. Adverse event rates per thousand person-years were estimated by multiplying the effect of warfarin use on the event rate per person per quarter by 4 quarters, and then by 1,000 persons.

Reference

1.   Graubard BI, Korn EL. Predictive margins with survey data. Biometrics 1999;55:652-9.

Appendix Table 1:

ICD-9 Codes Related to Identification of Fall-Related Fracture

Description	ICD-9 Code
Fall-related fracture site	
Fracture of vertebral column without mention of spinal cord injury	805xx
Fracture of vertebral column with spinal cord injury	806xx
Fracture of pelvis	808xx
Fracture of humerus	812xx
Fracture of radius and ulna	813xx
Fracture of carpal bone(s)	814xx
Fracture of metacarpal bone(s)	815xx
Fracture of one or more phalanges of hand	816xx
Multiple fractures of hand bones	817xx
Ill-defined fractures of upper limb	818xx
Fracture of neck of femur	820xx
Fracture of other and unspecified parts of femur	821xx
Fracture of patella	822xx
Fracture of tibia and fibula	823xx
Fracture of ankle	824xx
Other multiple and ill-defined fractures of lower limb	827xx
Fall cause of injury	
Accidental fall on or from stairs or steps	E880xx
Accidental fall on or from ladders or scaffolding	E881xx
Other accidental falls from one level to another	E884xx
Accidental fall on same level from slipping tripping or stumbling	E885xx
Other and unspecified fall	E888xx

Notes: Based on Johnston et al. (2012). Fall-related fractures in Figure 5 were defined by a diagnosis of one of these fracture codes, without having an external cause of injury code other than the fall causes listed.

Appendix Table 2: Odds ratios for hypoglycemia hospitalization or ED visit,

complete results

Covariate	Odds ratio (95% CI)
Constant	6.81E-6 (3.61E-6 - 1.29E-5)
Warfarin use	1.22 (1.04 - 1.42)
Age	1.01 (1.01 - 1.02)
Female	1.34 (1.21 - 1.49)
Non-white race / ethnicity	1.69 (1.53 - 1.87)
Acute myocardial infarction or ischemic heart disease	1.20 (1.06 - 1.35)
Alzheimer's disease or dementia	1.82 (1.63 - 2.03)
Asthma	0.85 (0.74 - 0.97)
Atrial fibrillation	0.96 (0.84 - 1.10)
Cancer (breast, colorectal, endometrial, lung or prostate)	0.92 (0.80 - 1.05)
Chronic kidney disease	1.91 (1.73 - 2.10)
Chronic obstructive pulmonary disease	1.33 (1.20 - 1.48)
Congestive heart failure	1.45 (1.30 - 1.62)
Depression	1.15 (1.04 - 1.27)
Dyslipidemia	0.91 (0.79 - 1.04)
Hypertension	1.39 (1.05 - 1.84)
Osteoporosis	1.05 (0.93 - 1.18)
Rheumatoid / Osteoarthritis	1.14 (1.03 - 1.26)
Stroke / TIA	1.29 (1.16 - 1.44)
σ	1.93 (1.80 - 2.06)
$\sigma^2/(\sigma^2+\theta^2)$	0.53 (0.50 - 0.56)
Other Statistics	
Person-quarters, n	4,355,418
Persons, n	465,918
Log likelihood value	-18039.44

Notes: Age and comorbidities are measured as of beginning of each calendar-quarter analyzed. σ is the standard deviation of beneficiary-level random effects; θ is the standard deviation of the idiosyncratic disturbance. Results correspond to *ED visit or admission, adjusted* in Figure 1.

Appendix Table 3:

Utilization of other diabetes medications

Other medication \ Person-quarters, n (%)	Full sample (n=4355418)	Person-quarters with warfarin use (n=416479)	Person-quarters without warfarin use (n=3938939)	p value
Metformin	1827689 (41.964%)	137884 (33.107%)	1689805 (42.900%)	< 0.001
Thiazolidinedione	770041 (17.680%)	51595 (12.388%)	718446 (18.240%)	< 0.001
Meglitinide	46773 (1.074%)	5026 (1.207%)	41747 (1.060%)	0.001
Glyburide	55805 (1.281%)	4909 (1.179%)	50896 (1.292%)	< 0.001
Insulin	708374 (16.264%)	82536 (19.818%)	625838 (15.888%)	< 0.001

Note: *Adjusting for use of other diabetes meds* sensitivity analysis in Figure 3 adjusts for these medications.
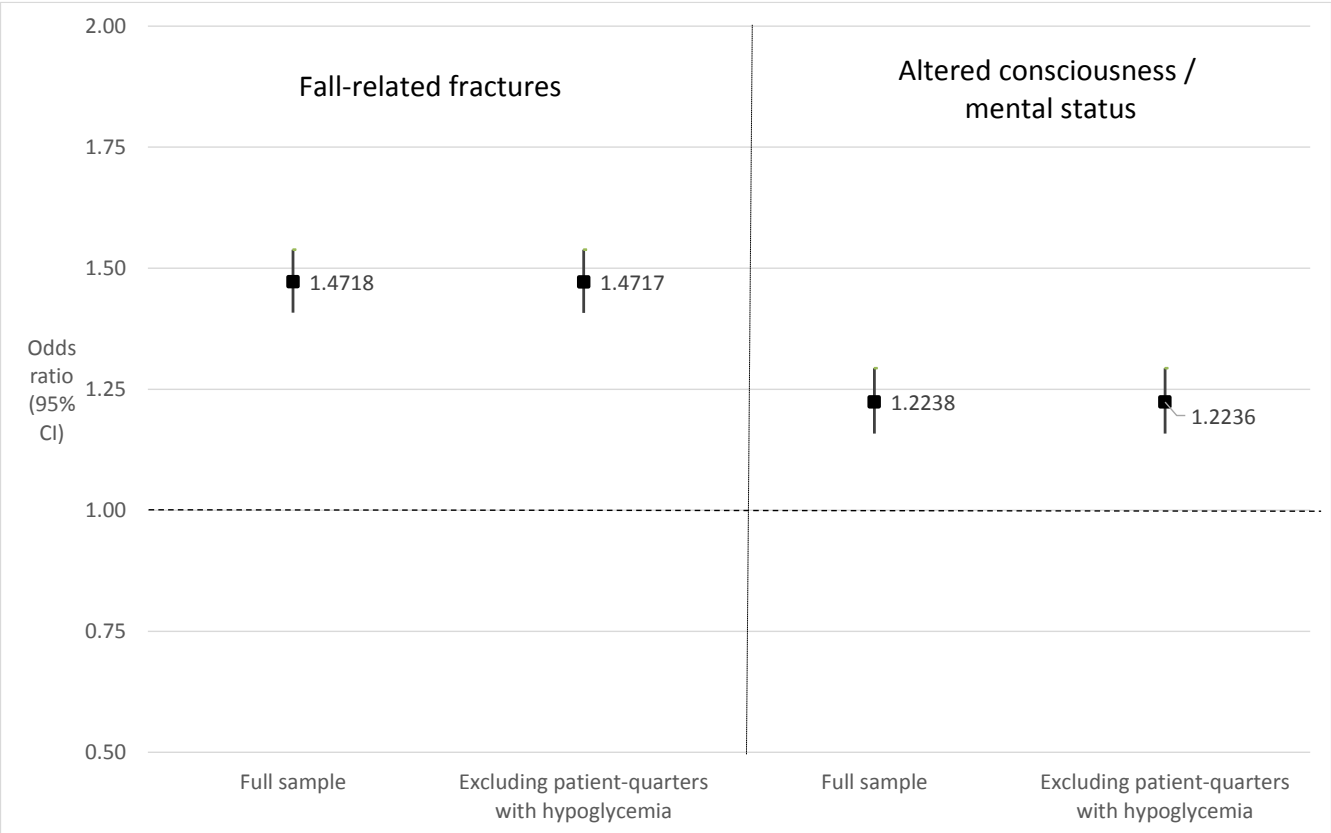
Appendix Table 4:

Warfarin use concurrent with various diabetes medications

Diabetes medication \ Person-quarters, n (%)	Full sample	Person-quarters with warfarin use	Person-quarters without warfarin use
Glipizide / glimepiride	4355418	416479 (9.6%)	3938939 (90.4%)
Metformin	2582813	167608 (6.5%)	2415205 (93.5%)
Thiazolidinediones	7144591	522901 (7.3%)	6621690 (92.7%)
Meglitinides	4426422	479423 (10.8%)	3946999 (89.2%)
Glyburide	2215598	184317 (8.3%)	2031281 (91.7%)
Insulin	330665	35759 (10.8%)	294906 (89.2%)

Notes: Adjusted analyses of warfarin use together with metformin, thiazolidinediones, meglitinides, glyburide and insulin are reported in Figure 4. All other tables and figures correspond to primary analysis of glipizide / glimepiride.

Appendix Figure 1: Odds ratios for hospitalization or ED visit for fall-related fracture and altered consciousness / mental status in person-quarters with concurrent use of warfarin and glipizide / glimepiride, full sample versus person-quarters without hypoglycemia

Note: *Full sample* corresponds to Figure 5 and Appendix Table 4.