



Figure S1. Identification of study individuals and application of inclusion and exclusion criteria

GIB: gastrointestinal bleeding. ICH: non-traumatic intracranial hemorrhage.

Table S1. ICD-9-CM diagnosis codes used to identify acute infections

ICD-9-CM code	Description
001.*	Cholera
002.*	Typhoid and paratyphoid fevers
003.*	Other salmonella infections
004.*	Shigellosis
005.*	Other food poisoning (bacterial)
006.*, except 006.1	Amebiasis
007.*	Other protozoal intestinal diseases
008.*	Intestinal infections due to other organisms
009.*	Ill-defined intestinal infections
018.0*	Miliary tuberculosis
020.*	Plague
021.*	Tularemia
022.*	Anthrax
023.*	Brucellosis
024	Glanders
025	Melioidosis
026.*	Rat-bite fever
027.*	Other zoonotic bacterial diseases
030.*	Leprosy
031.*	Diseases due to other mycobacteria
032.*	Diphtheria
033.*	Whooping cough
034.*	Streptococcal sore throat and scarlet fever
035	Erysipelas
036.*	Meningococcal infection
037	Tetanus
038.*	Septicemia
039.*, except 039.4	Actinomycotic infections
040.*, except 040.1	Other bacterial diseases
041.*, except 041.81	Bacterial infection in conditions classified elsewhere and of unspecified site
045.*	Acute poliomyelitis
047.*	Meningitis due to enterovirus
048	Other enterovirus diseases of central nervous system
049.*	Other non-arthropod-borne viral diseases of central nervous system
050.*	Smallpox
051.*	Cowpox and paravaccinia
052.*	Chickenpox
053.*, except 053.12, 053.13	Herpes zoster
054.*	Herpes simplex
055.*	Measles
056.*	Rubella
057.*	Other viral exanthemata
058.*	Other human herpesvirus
059.*	Other poxvirus infections
060.*	Yellow fever
061	Dengue
062.*	Mosquito-borne viral encephalitis
063.*	Tick-borne viral encephalitis
064	Viral encephalitis transmitted by other and unspecified arthropods

ICD-9-CM code	Description
065.*	Arthropod-borne hemorrhagic fever
066.*	Other arthropod-borne viral diseases
070.*, except 070.22, 070.23, 070.32, 070.33, 070.44, 070.54	Viral hepatitis
071	Rabies
072.*	Mumps
073.*	Ornithosis
074.*	Specific diseases due to coxsackie virus
075	Infectious mononucleosis
076.*	Trachoma
077.*	Other diseases of conjunctiva due to viruses and chlamydiae
078.*	Other diseases due to viruses and chlamydiae
079.*, except 079.51, 079.52, 079.53	Viral and chlamydial infection in conditions classified elsewhere and of unspecified site
080	Louse-borne (epidemic) typhus
081.*	Other typhus
082.*	Tick-borne rickettsioses
083.*	Other rickettsioses
084.*	Malaria
085.*	Leishmaniasis
086.*	Trypanosomiasis
087.*	Relapsing fever
088.*	Other arthropod-borne diseases
090.*	Congenital syphilis
091.*	Early syphilis symptomatic
092.*	Early syphilis latent
093.*	Cardiovascular syphilis
094.*	Neurosyphilis
095.*	Other forms of late syphilis with symptoms
096	Late syphilis, latent
097.*	Other and unspecified syphilis
098.*, except 098.2, 098.3*	Gonococcal infections
099.*	Other venereal diseases
100.*	Leptospirosis
101	Vincent's angina
103.*	Pinta
104.*	Other spirochetal infection
110.*	Dermatophytosis
111.*	Dermatomycosis other and unspecified
112.*	Candidiasis
114.*, except 114.4	Coccidioidomycosis
115.*	Histoplasmosis
116.*, except 116.2	Blastomycotic infection
118	Opportunistic mycoses
121.*	Other trematode infections
122.*	Echinococcosis
123.*	Other cestode infection
124	Trichinosis
125.*	Filarial infection and dracontiasis

ICD-9-CM code	Description
126.*	Ancylostomiasis and necatoriasis
127.*	Other intestinal helminthiases
128.*	Other and unspecified helminthiases
129	Intestinal parasitism, unspecified
130.*	Toxoplasmosis
131.*	Trichomoniasis
132.*	Pediculosis and phthirus infestation
133.*	Acariasis
134.*	Other infestation
135	Sarcoidosis
136.*	Other and unspecified infectious and parasitic diseases
320.*	Bacterial meningitis
321.*	Meningitis due to other organisms
322.*	Meningitis of unspecified cause
323.*	Encephalitis myelitis and encephalomyelitis
460	Acute nasopharyngitis [common cold]
461.*	Acute sinusitis
462	Acute pharyngitis
463	Acute tonsillitis
464.*	Acute laryngitis and tracheitis
465.*	Acute upper respiratory infections of multiple or unspecified sites
466.*	Acute bronchitis and bronchiolitis
480.*	Viral pneumonia
481	Pneumococcal pneumonia [Streptococcus pneumoniae pneumonia]
482.*	Other bacterial pneumonia
483.*, except 483.0	Pneumonia due to other specified organism
484.*	Pneumonia in infectious diseases classified elsewhere
485	Bronchopneumonia, organism unspecified
486	Pneumonia, organism unspecified
487.*	Influenza
488.*	Influenza due to certain identified influenza viruses
590.1*	Acute pyelonephritis
595.0	Acute cystitis
598.0*	Urethral stricture due to infection
599.0	Urinary tract infection, site not specified

Table S2. Sensitivity analysis: Confounder-adjusted outcome occurrence rate ratios for the association between serious bleeding and warfarin when used concomitantly with a sulfonylurea or metformin, controlling for warfarin average daily dose

Outcome	Person-days during observation time	Number of outcomes during observation time	Precipitant drug	Person-days during precipitant-exposed time ^a	Number of outcomes during precipitant-exposed time	Rate ratio ^b	95% CI
Serious bleeding ^c	1,145,524	6,141	glimepiride	79,273	404	1.01	0.80, 1.29
			glipizide	211,829	1,079	1.00	0.85, 1.18
			glyburide	148,852	732	0.82	0.68, 0.99
			metformin	305,793	1,469	0.84	0.73, 0.96
Gastrointestinal bleeding	1,036,482	5,318	glimepiride	72,370	358	1.13	0.87, 1.46
			glipizide	192,598	919	0.96	0.81, 1.15
			glyburide	131,004	616	0.87	0.71, 1.07
			metformin	271,692	1,236	0.90	0.78, 1.04
Non-traumatic intracranial hemorrhage	118,037	845	glimepiride	7,243	49	0.55	0.28, 1.06
			glipizide	21,872	164	1.30	0.81, 2.09
			glyburide	19,944	120	0.56	0.34, 0.92
			metformin	35,475	239	0.51	0.35, 0.74

CI: confidence interval (based on a two-tailed test). ^aPrecipitant-exposed time: days of warfarin-precipitant drug concomitant use during observation time since the initiation of the concomitant use. ^bRate ratio: [(outcome occurrence rate during precipitant-exposed time) / (outcome occurrence rate during precipitant-unexposed time)], for each warfarin-precipitant drug pair. ^cSerious bleeding as a composite outcome; occurrence of gastrointestinal bleeding or non-traumatic intracranial hemorrhage or both.

Table S3. Sensitivity analysis: Confounder-adjusted outcome occurrence rate ratios for the association between serious bleeding and warfarin when used concomitantly with a sulfonylurea or metformin, controlling for warfarin monitoring

Outcome	Person-days during observation time	Number of outcomes during observation time	Precipitant drug	Person-days during precipitant-exposed time ^a	Number of outcomes during precipitant-exposed time	Rate ratio ^b	95% CI
Serious bleeding ^c	1,433,447	7,388	glimepiride	101,700	496	0.93	0.75, 1.15
			glipizide	259,066	1,276	0.97	0.83, 1.12
			glyburide	183,101	913	0.89	0.75, 1.05
			metformin	385,586	1,757	0.85	0.75, 0.96
Gastrointestinal bleeding	1,303,047	6,419	glimepiride	92,882	441	0.98	0.78, 1.24
			glipizide	236,553	1,090	0.96	0.82, 1.12
			glyburide	162,723	756	0.88	0.74, 1.06
			metformin	343,808	1,487	0.91	0.80, 1.04
Non-traumatic intracranial hemorrhage	141,179	996	glimepiride	9,457	58	0.67	0.36, 1.26
			glipizide	25,667	191	1.01	0.68, 1.51
			glyburide	22,488	161	0.81	0.52, 1.26
			metformin	43,526	276	0.50	0.36, 0.70

CI: confidence interval (based on a two-tailed test). ^aPrecipitant-exposed time: days of warfarin-precipitant drug concomitant use during observation time since the initiation of the concomitant use. ^bRate ratio: [(outcome occurrence rate during precipitant-exposed time) / (outcome occurrence rate during precipitant-unexposed time)], for each warfarin-precipitant drug pair. ^cSerious bleeding as a composite outcome; occurrence of gastrointestinal bleeding or non-traumatic intracranial hemorrhage or both.

Table S4. Sensitivity analysis: Confounder-adjusted outcome occurrence rate ratios for the association between serious bleeding and warfarin when used concomitantly with a sulfonyleurea or metformin, with observation time only from individuals who were alive during that observation time

Outcome	Person-days during observation time	Number of outcomes during observation time	Precipitant drug	Person-days during precipitant-exposed time ^a	Number of outcomes during precipitant-exposed time	Rate ratio ^b	95% CI
Serious bleeding ^c	1,312,744	6,420	glimepiride	90,841	428	1.02	0.80, 1.29
			glipizide	235,160	1,052	0.94	0.80, 1.10
			glyburide	167,117	799	0.93	0.77, 1.11
			metformin	353,794	1,535	0.87	0.76, 0.99
Gastrointestinal bleeding	1,205,234	5,784	glimepiride	84,518	397	0.95	0.75, 1.22
			glipizide	215,850	955	0.97	0.82, 1.15
			glyburide	150,026	683	0.91	0.75, 1.10
			metformin	319,827	1,357	0.92	0.80, 1.05
Non-traumatic intracranial hemorrhage	99,936	652	glimepiride	5,472	32	2.42	0.99, 5.91
			glipizide	18,459	100	0.74	0.47, 1.16
			glyburide	16,193	118	1.02	0.61, 1.69
			metformin	30,462	181	0.49	0.33, 0.73

CI: confidence interval (based on a two-tailed test). ^aPrecipitant-exposed time: days of warfarin-precipitant drug concomitant use during observation time since the initiation of the concomitant use. ^bRate ratio: [(outcome occurrence rate during precipitant-exposed time) / (outcome occurrence rate during precipitant-unexposed time)], for each warfarin-precipitant drug pair. ^cSerious bleeding as a composite outcome; occurrence of gastrointestinal bleeding or non-traumatic intracranial hemorrhage or both.

Number of person-days excluded: Serious bleeding, 120,703 person-days; Gastrointestinal bleeding, 97,813 person-days; Non-traumatic intracranial hemorrhage, 41,243 person-days.

Table S5. Sensitivity analysis: Confounder-adjusted outcome occurrence rate ratios for the association between serious bleeding and warfarin when used concomitantly with a sulfonylurea or metformin, excluding individuals with potentially incomplete data

Outcome	Person-days during observation time	Number of outcomes during observation time	Precipitant drug	Person-days during precipitant-exposed time ^a	Number of outcomes during precipitant-exposed time	Rate ratio ^b	95% CI
Serious bleeding ^c	790,061	4,399	glimepiride	56,059	295	1.02	0.77, 1.36
			glipizide	136,046	741	0.91	0.75, 1.11
			glyburide	96,773	562	0.88	0.70, 1.09
			metformin	199,242	996	0.90	0.76, 1.05
Gastrointestinal bleeding	719,129	3,797	glimepiride	52,950	263	1.02	0.76, 1.37
			glipizide	124,653	635	0.91	0.74, 1.12
			glyburide	84,337	461	0.92	0.73, 1.16
			metformin	177,671	825	0.96	0.81, 1.14
Non-traumatic intracranial hemorrhage	78,706	618	glimepiride	3,748	35	0.93	0.34, 2.57
			glipizide	13,252	108	0.80	0.46, 1.40
			glyburide	14,136	103	0.61	0.34, 1.10
			metformin	22,289	174	0.52	0.33, 0.83

CI: confidence interval (based on a two-tailed test). ^aPrecipitant-exposed time: days of warfarin-precipitant drug concomitant use during observation time since the initiation of the concomitant use. ^bRate ratio: [(outcome occurrence rate during precipitant-exposed time) / (outcome occurrence rate during precipitant-unexposed time)], for each warfarin-precipitant drug pair. ^cSerious bleeding as a composite outcome; occurrence of gastrointestinal bleeding or non-traumatic intracranial hemorrhage or both.

Number of person-days excluded: Serious bleeding, 643,386 person-days; Gastrointestinal bleeding, 583,918 person-days; Non-traumatic intracranial hemorrhage, 62,473 person-days.