Supplementary Table S1: ICD-9 and E codes used to identify participants with a fall-related injury

ICD-9 or E Code	Definition
Fracture	
800	Fracture of vault of skull
801	Fracture of base of skull
802	Fracture of face bones
803	Other and unqualified skull fractures
804	Multiple fractures involving skull or face with other bones
805	Fracture of vertebral column without mention of spinal cord injury
806	Fracture of vertebral column with spinal cord injury
807.0-807.2	Fracture of rib(s), sternum, larynx, and trachea
808.0-808.9	Fracture of pelvis
810	Fracture of clavicle
811	Fracture of scapula
812	Fracture of humerus
813	Fracture of radius and ulna
814	Fracture of carpal bone(s)
815	Fracture of metacarpal bone(s)
816	Fracture of one or more phalanges of hand
817	Multiple fractures of hand bones
818.0-818.1	Ill-defined fractures of upper limb
819.0-819.1	Multiple fractures involving both upper limbs and upper limb with rib(s) and sternum
820	Fracture of neck of femur
821	Fracture of other and unspecified parts of femur
822	Fracture of patella
823	Fracture of tibia and fibula
824	Fracture of ankle
825	Fracture of one or more tarsal and metatarsal bones
826	Fracture of one or more phalanges of foot
827	Other multiple and ill-defined fractures of lower limb
828	Multiple fractures involving both lower limbs lower with upper limb and lower limb(s) with rib(s) and sternum
829	Fracture of unspecified bones
Intracranial Injury	
850	Concussion
851	Cerebral laceration and contusion
852	Subarachnoid subdural and extradural hemorrhage following injury
853	Other and unspecified intracranial hemorrhage following injury
854	Intracranial injury of other and unspecified nature
Dislocation	
830	Dislocation of jaw
831	Dislocation of shoulder
832	Dislocation of elbow
833	Dislocation of wrist
834	Dislocation of finger
835	Dislocation of hip
836	Dislocation of knee
837	Dislocation of ankle

838	Dislocation of foot
839	Other multiple and ill-defined dislocations
Contusion	
920	Contusion of face, scalp, and neck except eye(s)
921	Contusion of eye and adnexa
922	Contusion of trunk
923	Contusion of upper limb
924	Contusion of lower limb and of other and unspecified sites
Accidental Fall	
E880	Accidental fall on or from stairs or steps
E881	Accidental fall on or from ladders or scaffolding
E882	Accidental fall from or out of building or other structure
E883	Accidental fall into hole or other opening in surface
E884	Other accidental falls from one level to another
E885	Accidental fall on same level from slipping tripping or stumbling
E886	Fall on same level from collision, pushing, or shoving, by or with other person
E887	Fracture, cause unspecified
E888	Other and unspecified fall
V15.88	History of falls

Abbreviations: ICD-9 = International Classification of Diseases, Ninth Revision

Supplementary Table S2: Classification of medications and minimum effective dose

Drug Class	Individual Medications	Minimum Effective Geriatric Daily Dose
Benzodiazepines/Sedative Hypnotics		
	Alprazolam	0.25 mg
	Chlordiazepoxide	10 mg
	Clonazepam	0.5 mg
	Clorazepate	7.5 mg
	Diazepam	1 mg
	Eszopiclone	1 mg
	Flurazepam	15 mg
	Lorazepam	0.5 mg
	Oxazepam	20 mg
	Temazepam	7.5 mg
	Triazolam	0.0625 mg
	Zaleplon	5 mg
	Zolpidem	5 mg
	Buspirone	15 mg
	Chloral hydrate	250 mg
Opioids [a]		
	Codeine	200 mg (0.15)
	Fentanyl transdermal	12.5 mg (2.4)
	Hydrocodone	30 mg (1.00)
	Hydromorphone	7.5 mg (4.00)
	Levorphanol	2.7 mg (11.00)
	Meperidine	300 mg (0.10)
	Methadone	10 mg (3.00)
	Morphine	30 mg
	Opium tinctures/suppositories	300 mg (0.10)
	Oxycodone	20 mg (1.5)
	Propoxyphene	130.4 mg (0.23)
	Tramadol	300 mg (0.10)
Antipsychotics		
	Aripiprazole	10 mg
	Chlorpromazine[b]	10 mg
	Clozapine[b]	12.5 mg
	Haloperidol	0.5 mg
	Lurasidone	40 mg
	Olanzapine[b]	5 mg
	Perphenazine	12 mg
	Quetiapine	50 mg
	Risperidone	1 mg
	Thioridazine[b]	10 mg
	Thiothixene	6 mg
	Trifluoperazine[b]	0.5 mg
Antidepressants		
Tricyclic antidepressants	Nortriptyline[b]	30 mg
	Desipramine[b]	25 mg
	Clomipramine[b]	25 mg
	Amitriptyline[b]	10 mg

	Amitriptyline/Perphenazine[b]	10 mg
	Doxepin[b]	10 mg
	Imipramine[b]	25 mg
SSRIs	Paroxetine[b]	10 mg
	Citalopram	20 mg
	Escitalopram	10 mg
	Fluoxetine	20 mg
	Fluvoxamine	50 mg
SNRIs	Sertraline	25 mg
	Duloxetine	20 mg
Other	Venlafaxine	50 mg
	Bupropion	150 mg
	Maprotiline	25 mg
	Mirtazapine	15 mg
	Trazodone	25 mg
	Nefazodone	100 mg
	Phenelzine	7.5 mg
	Tranylcypromine	30 mg
Skeletal muscle relaxants		
	Baclofen	10 mg
	Carisoprodol	750 mg
	Cyclobenzaprine[b]	5 mg
	Dantrolene	25 mg
	Methocarbamol	600 mg
	Tizanidine hydrochloride	12 mg
Anticholinergics		
	Hydroxyzine	75 mg
	Cyproheptadine	4 mg
	Procyclidine	2.5 mg
	Glycopyrrolate	0.6 mg
	Solifenacin	5 mg
	Prochlorperazine	15 mg
	Promethazine	50 mg
	Scopolamine oral	0.0195 mg
	Scopolamine patch	0.33 mg
	Benztropine	0.5 mg
	Trihexyphenidyl	6 mg
	Darifenacin	7.5 mg
	Oxybutynin oral	5 mg
	Tolterodine	2 mg
	Trospium	20 mg
	Atropine	0.0582 mg
	Belladonna suppository[b]	1 suppository = 1 SSD
	Levorotatory alkaloids of belladonna[b]	1 tablet = 1 SSD
	Dicyclomine	40 mg
	Homatropine	6 mg
	Hyoscyamine	0.75 mg
	Propantheline bromide	22.5 mg

Abbreviations: TCA = tricyclic antidepressants, SSRI = selective serotonin reuptake inhibitor, SNRI = serotonin norepinephrine reuptake inhibitor, MAOI = monamine oxidase inhibitor
[a]For opioids, number in parentheses after dose refers to morphine equivalents
[b]These medications have anticholinergic activity and were included in creating the anticholinergic exposure variable.

Supplementary Table S3: ICD-9 codes used for covariates

ICD-9 Code	Definition
Depression	
296.2	Major depressive disorder, single episode
296.3	Major depressive disorder, recurrent episode
298.0	Depressive type psychosis
300.4	Dysthymic disorder
301.12	Chronic depressive personality disorder
309.1	Prolonged depressive reaction
311	Depressive disorder, not elsewhere classified
Anxiety	
300.0	Anxiety states
300.2	Phobic disorders
309.2	Adjustment disorder
Parkinson's Disease	
332.0	Primary Parkinsonism
Insomnia	
780.5	Sleep disturbances
327.0	Organic sleep disorders of initiating and maintaining sleep
Urinary Incontinence	
788.3	Urinary incontinence, unspecified

Abbreviations: ICD-9 = International Classification of Diseases, Ninth Revision

Supplementary Table S4. Average change in SDD from index of CNS-active medications according to use at index (restricted to index during 1994-2003)

CNS use at index	Fall-related injury at index	SDD at index	Average change in SDD from index		
			3 months	6 months	12 months
Primary Analysis					
Users at index	Yes	2.8 (3.9)	-0.22 (-0.47, 0.03)	-0.34 (-0.64, -0.04)	-0.45 (-0.79, -0.11)
	No	2.3 (2.7)	-0.70 (-0.81, -0.59)	-0.71 (-0.83, -0.58)	-0.67 (-0.83, -0.52)
	p-value[1]		<0.001	0.021	0.255
Non-users at index	Yes		0.24 (0.13, 0.35)	0.20 (0.14, 0.26)	0.19 (0.13, 0.25)
	No		0.20 (0.17, 0.24)	0.21 (0.17, 0.25)	0.26 (0.21, 0.30)
	p-value[1]		0.516	0.819	0.050
Sensitivity Analysis (without opioids)					
Users at index	Yes		0.00 (-0.26, 0.28)	-0.22 (-0.54, 0.12)	-0.34 (-0.71, 0.03)
	No		-0.54 (-0.67, -0.40)	-0.53 (-0.68, -0.39)	-0.53 (-0.71, -0.34)
	p-value[1]		<0.001	0.065	0.396
Non-users at index	Yes		0.16 (0.10, 0.21)	0.17 (0.12, 0.22)	0.15 (0.10, 0.21)
	No		0.18 (0.15, 0.22)	0.19 (0.15, 0.23)	0.24 (0.19, 0.28)
	p-value[1]		0.469	0.473	0.014

Abbreviations: CNS = central nervous system; SDD = standardized daily dose
[1]p-value corresponding to test of whether average change in SDD from index differs between those with fall-related injury and those without
*Estimates for average change in SDD at each time point (relative to index) are based on adjusted regression models and standardized to a common distribution of covariates. Regression models were adjusted for the following covariates (as of index): age (spline 2df), calendar time (spline 2df), class(es) of CNS medications used, clinical encounter type at index, ACT cohort, gender, race/ethnicity, education, self-rated health, frail (per gait speed), cognition, treatment for hypertension, treatment for diabetes, osteoarthritis, coronary artery disease, stroke, anxiety, depression, urinary incontinence, Parkinson's disease, insomnia, and prior falls.

Supplementary Table S5. Average change in SDD from index of CNS-active medications according to use at index (restricted to index during 2004-2014)

CNS use at index	Fall-related injury at index	SDD at index	Average change in SDD from index		
			3 months	6 months	12 months
Primary Analysis					
Users at index	Yes	2.1 (1.7)	-0.53 (-0.69, -0.37)	-0.44 (-0.61, -0.27)	-0.39 (-0.57, -0.21)
	No	2.1 (2.0)	-0.62 (-0.75, -0.50)	-0.57 (-0.68, -0.46)	-0.63 (-0.77, -0.49)
	p-value[1]		0.344	0.210	0.033
Non-users at index	Yes		0.11 (0.07, 0.16)	0.16 (0.10, 0.21)	0.15 (0.09, 0.20)
	No		0.21 (0.17, 0.26)	0.23 (0.18, 0.27)	0.22 (0.17, 0.27)
	p-value[1]		0.001	0.033	0.021
Sensitivity Analysis (without opioids)					
Users at index	Yes		-0.41 (-0.59, -0.23)	-0.35 (-0.56, -0.15)	-0.26 (-0.49, -0.03)
	No		-0.50 (-0.66, -0.34)	-0.46 (-0.60, -0.31)	-0.56 (-0.73, -0.39)
	p-value[1]		0.373	0.302	0.015
Non-users at index	Yes		0.10 (0.06, 0.14)	0.13 (0.07, 0.18)	0.13 (0.08, 0.19)
	No		0.19 (0.15, 0.23)	0.20 (0.15, 0.24)	0.20 (0.15, 0.24)
	p-value[1]		0.002	0.021	0.049

Abbreviations: CNS = central nervous system; SDD = standardized daily dose
[1]p-value corresponding to test of whether average change in SDD from index differs between those with fall-related injury and those without
*Estimates for average change in SDD at each time point (relative to index) are based on adjusted regression models and standardized to a common distribution of covariates. Regression models were adjusted for the following covariates (as of index): age (spline 2df), calendar time (spline 2df), class(es) of CNS medications used, clinical encounter type at index, ACT cohort, gender, race/ethnicity, education, self-rated health, frail (per gait speed), cognition, treatment for hypertension, treatment for diabetes, osteoarthritis, coronary artery disease, stroke, anxiety, depression, urinary incontinence, Parkinson's disease, insomnia, and prior falls.