

Signals of muscle relaxant drug interactions associated with unintentional traumatic injury: A population-based screening study

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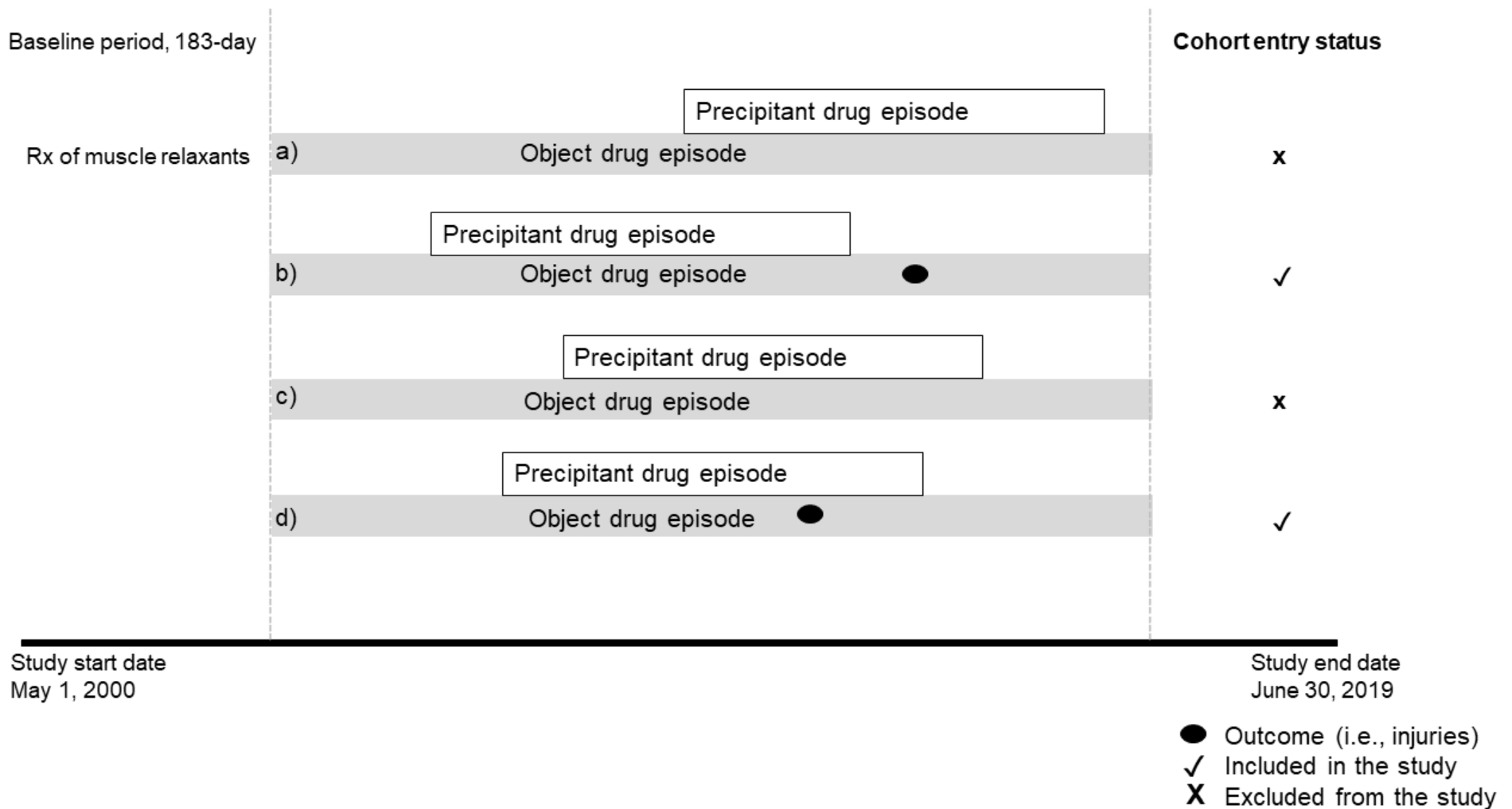
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Supplemental Figure S1. Examples of eligibility and non-eligibility in the self-controlled case series studies



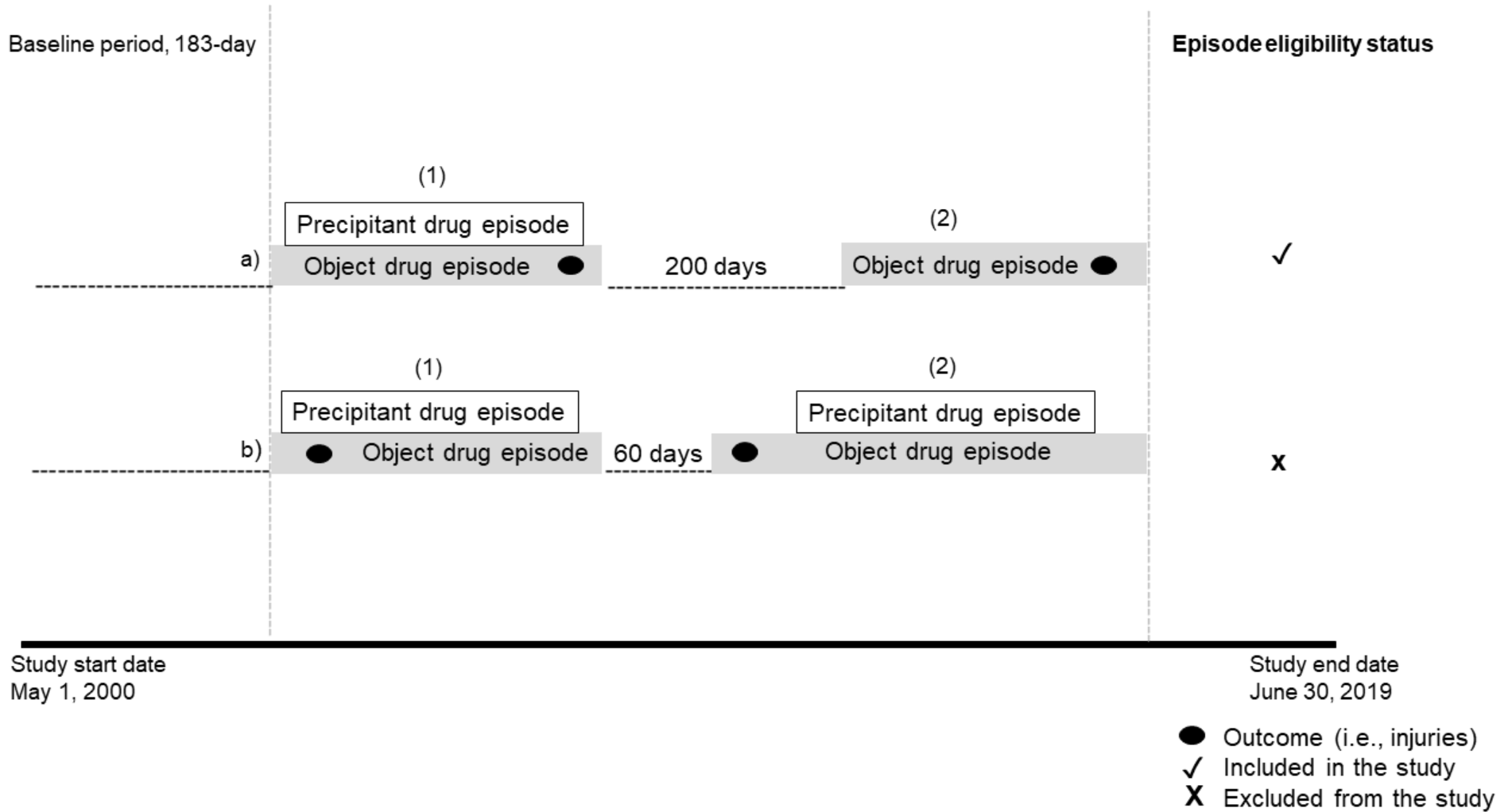
The figure illustrates scenarios of cohort entry

Patient a was excluded because of muscle relaxant use during the baseline period.

Patients b and d were included given the absence of baseline muscle relaxant use and presence of an injury during the observation period.

Patient c was excluded given the absence of an injury during the observation period.

Supplemental Figure S2. Scenarios of subsequent episode eligibility



The figure illustrates subsequent episodes eligibility status.

For patient a, the subsequent episode is included since the washout period between episodes 1 and 2 is ≥ 183 days.

For patient b, the subsequent episode is excluded since the washout period between episodes 1 and 2 is < 183 days.

Supplemental Table S1. Outcome definitions

Outcome	Discharge diagnosis position and claim type	ICD-9-CM discharge diagnosis code(s)	Performance characteristics and/or other supporting information	Adaptation to ICD-10-CM era
<p>Unintentional traumatic injury <i>(primary outcome)</i></p>	<p>Any-position discharge diagnosis on an ED claim</p> <p>or</p> <p>Principal inpatient discharge diagnosis on an inpatient hospitalization claim</p>	<p>fracture (800–829) dislocation (830–839) sprain/strain (840–848) intracranial injury (850–854) internal injury of thorax, abdomen, or pelvis (860–869) open wound (870–897) injury to blood vessels (900–904) crushing injury (925–929) injury to nerves or spinal cord (950–957) certain traumatic complications and unspecified injuries (958–959)</p>	<p>Adapted from the injury definition used by the American College of Surgeons' NTDB Data Standard (version 03.2015).</p> <p>NTDB's injury definition explicitly excludes the following: late effects of injuries, poisonings, toxic effects, and other external causes; superficial injury; contusion with intact skin surface; and effects of a foreign body entering through orifice.</p> <p>Our adapted definition further excluded burns (as these are unlikely due to a drug interaction), consistent with work by Sears et al. <i>J Occup Rehabil</i> 2015;25(4).</p>	<p>Adapted from the injury definition used by the American College of Surgeons' NTDB Data Standard (updated October 2019)</p> <p>The definition included: injuries to specific body parts (S00–S99 with a 7th character modifier of A, B, or C only; excluding superficial injuries indicated by S00, S10, S20, S30, S40, S50, S60, S70, S80, or S90), unspecified multiple injuries (T07 with a 7th character modifier of A only), injury of unspecified body region (T14 with a 7th character modifier of A only), and traumatic compartment syndrome (T79.A1–T79.A9 with 7th character modifier of A only).</p> <p>This definition excludes: late effects of injury (identified by other 7th character modifiers); poisonings, toxic effects, and other external causes; superficial injury; effects of a foreign body entering through orifice; and burns.</p>
<p>Typical hip fracture <i>(secondary outcome)</i></p>	<p>Principal inpatient discharge diagnosis on an inpatient hospitalization claim</p>	<p>closed transcervical fracture (820.00–820.09) open transcervical fracture (820.10–820.19) closed fracture of unspecified trochanteric section of femur (820.20) closed fracture of intertrochanteric section of femur (820.21) open fracture of unspecified trochanteric section of femur (820.30) open fracture of intertrochanteric section of femur (820.31) closed fracture of unspecified part of neck of femur (820.8) open fracture of unspecified part of neck of femur (820.9)</p>	<p>The inclusion of codes for typical closed hip fractures is supported by FDA Sentinel and findings by Narogroeknawin et al. <i>Journal of Clinical Densitometry</i> 2012;15(1) using 2004–2008 health system data from the University of Alabama at Birmingham. The PPV for typical closed hip fracture ICD-9 discharge diagnosis codes in a principal position was 94%.</p> <p>The rationale for including typical open hip fractures codes was that such fractures can be caused by an injury.</p> <p>A hip fracture algorithm including typical open and closed hip fracture codes in 1996–1997 Norwegian data had a PPV and sensitivity of 84% and 90%, respectively (Lofthus et al. J Clin Epidemiol 2005;58). Typical open and closed hip fracture codes are a component of AHRQ's hip fracture mortality rate quality indicator.</p> <p>The rationale for excluding pathologic fracture codes (e.g., ICD-9 733.14) was that such fractures are due to a localized process such as malignancy or infection (Curtis et al. <i>Osteoporos Int</i> 2009;20); their exclusion should have had minimal impact on precision, as ~3% of closed hip fractures are coded as pathologic.</p> <p>The rationale for excluding atypical (i.e., subtrochanteric and diaphyseal) hip fracture codes (e.g., ICD-9 820.22) was that such fractures are associated with no or minimal trauma and commonly attributed to the use of bisphosphonates and/or glucocorticoids (Shane et al. <i>JBMR</i> 2014;29).</p>	<p>An ICD-10-CM algorithm was mapped from ICD-9-CM codes for transcervical, trochanteric, pertrochanteric, and femoral neck fractures.</p> <p>We used a principal inpatient discharge diagnosis of fracture of head and neck of femur (ICD-10-CM S72.0* with a 7th character modifier of A, B, or C only) or pertrochanteric fracture (ICD-10-CM S72.1* with a 7th character modifier of A, B, or C only).</p> <p>This definition is partially supported by a validation of Finnish registry data by Sund et al (Methods Inf Med 2007;46:558-566) that reported specificities and sensitivities of 99% (95–100%) and 69% (53–84%) for trochanteric fractures and 81% (68–92%) and 97% (92–100%) for femoral neck fractures; these findings were highlighted in a systemic review by Hudson et al (J Clin Epi 2013;66:278-285). While Canadian-based ICD-10 validation work by Park-Wyllie et al (JAMA 2011;305:783-789) initially seemed relevant, the authors validated atypical fracture codes (ICD-10 S72.2, S72.3) that we exclude for reasons based above.</p>
<p>Unintentional motor vehicle crash while subject was driving <i>(secondary outcome)</i></p>	<p>Unintentional traumatic injury (see primary above)</p> <p>and</p> <p>Any-position discharge diagnosis, arising from the same hospital presentation as the injury, on an ED or inpatient</p>	<p>MVTA, injuring the driver, in collision with train (E810.0) MVTA, injuring the driver, in re-entrant collision with another motor vehicle (E811.0) MVTA, injuring the driver, other, in collision with motor vehicle (E812.0) MVTA, injuring the driver, in collision with other vehicle (E813.0) MVTA, injuring the driver, in collision with pedestrian (E814.0) MVTA, injuring the driver, other, in collision on highway (E815.0) MVTA, injuring the driver, loss of control, without collision on highway (E816.0)</p>	<p>The PPV and sensitivity for the motor vehicle crash component of the outcome definition are 88–89% and 97%, respectively (LeMier et al. Inj Prev 2001;7 and Bowman et al. Perspect Health Inf Manag 2011;8).</p> <p>The inclusion of motor vehicle accident codes of an unintentional manner and exclusion of self-inflicted, assault, and undetermined manner motor vehicle accident codes is supported by the CDC Injury Center's E-Code Grouping Matrix.</p>	<p>In the transition from ICD-9-CM to ICD-10-CM, ECOI E-codes were supplanted by codes beginning with V, W, X and Y (ICD-10-CM Chapter 20: External Causes of Morbidity). ICD-10-CM codes beginning with the letter V are used for transportation related injuries.</p> <p>A code's second character indicates the victim's mode of transport (e.g., car occupant, pedestrian). We required that outcome-defining events had a second character indicating a motor vehicle. The third character indicates the accident's circumstance (e.g., collision with car, non-collision transport accident). The fourth character generally indicates the victim's activity (e.g., driver vs. passenger) and whether the incident occurred in a traffic or non-traffic situation. We required that outcome-defining events had a fourth character indicating the driver. The fifth and sixth characters are generally X-filled</p>

	hospitalization claim	<p>MVTA, injuring the driver, noncollision, while boarding or alighting (E817.0)</p> <p>MVTA, injuring the driver, other noncollision (E818.0)</p> <p>MVTA, injuring the driver, unspecified nature (E819.0)</p> <p>MVNTA, injuring the driver, motor-driven snow vehicle (E820.0)</p> <p>MVNTA, injuring the driver, off-road motor vehicle (E821.0)</p> <p>MVNTA, injuring the driver, other, in collision with moving object (E822.0)</p> <p>MVNTA, injuring the driver, other, in collision with stationary object (E823.0)</p> <p>MVNTA, injuring the driver, other, while boarding or alighting (E824.0)</p> <p>MVNTA, injuring the driver, unspecified nature (E825.0)</p>		<p>placeholders intended for future expansion. The seventh character indicates an initial encounter vs. subsequent encounter vs. sequela. We required that outcome-defining events had a seventh character indicating an initial encounter.</p> <p>We excluded MVC events with one of the following any-position emergency department or any-position inpatient discharge diagnoses co-occurring with an ECOI of interest: intentional self-harm by crashing of motor vehicle (X82*); assault by crashing of motor vehicle (Y03*); or crashing of motor vehicle, undetermined intent (Y32*).</p>
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AHRQ = Agency for Healthcare Research and Quality; CDC = Centers for Disease Control and Prevention; ED = emergency department; FDA = Food and Drug Administration; ICD-9-CM = international classification of diseases 9th revision clinical modification; MVC= motor vehicle crash; MVTA = motor vehicle traffic accident; MVNTA = motor vehicle nontraffic accident; NTDB = National Trauma Data Bank; PPV = positive predictive value

Supplemental Table S2. Characteristics of cohorts of new users of muscle relaxants experiencing a typical hip fracture or motor vehicle crash (secondary outcomes) in which the subject was driving, by object drug of interest

	Baclofen	Carisoprodol	Chlorzoxazone	Cyclobenzaprine	Dantrolene	Metaxalone	Methocarbamol	Orphenadrine	Tizanidine	
Typical hip fracture	N	239	90	14	542	2	49	84	18	270
	Demographics									
	Age in years, median (Q1-Q3)	72.5 (63.6-79.9)	72.7 (60.5-78.4)	68.0 (59.0-78.0)	74.5 (64.6-80.6)	52.8 (42.0-63.6)	71.6 (58.9-78.6)	73.0 (60.8-78.9)	78.6 (70.2-81.5)	73.2 (65.9-79.7)
	Female, %	66.5	74.4	85.7	74.7	0.0	71.4	71.4	61.1	73.0
	Race, %									
	Caucasian	73.6	70.0	71.4	75.1	50.0	79.6	76.2	55.6	70.0
	African American	9.2	11.1	21.4	7.4	0.0	8.2	9.5	5.6	11.5
	Hispanic	6.3	5.6	7.1	6.6	0.0	2.0	4.8	5.6	5.2
	Asian	1.3	1.1	0.0	1.1	0.0	0.0	3.6	0.0	1.1
	Unknown	9.6	12.2	0.0	9.8	50.0	10.2	6.0	33.3	12.2
	Geographic division, %									
	New England	3.3	0.0	0.0	3.5	0.0	2.0	1.2	0.0	1.1
	Middle Atlantic	5.9	3.3	14.3	5.7	0.0	8.2	1.2	5.6	3.7
	East North Central	10.0	2.2	7.1	14.0	50.0	18.4	11.9	11.1	14.8
	West North Central	7.9	5.6	7.1	8.9	50.0	12.2	14.3	16.7	7.8
	South Atlantic	34.7	35.6	35.7	28.6	0.0	32.7	20.2	33.3	33.3
	East South Central	3.8	4.4	0.0	4.6	0.0	0.0	8.3	11.1	6.7
	West South Central	11.3	15.6	14.3	14.4	0.0	14.3	14.3	5.6	20.4
	Mountain	8.4	13.3	14.3	10.3	0.0	12.2	9.5	11.1	7.0
	Pacific	14.2	18.9	7.1	10.0	0.0	0.0	19.0	5.6	4.8
Unknown	0.4	1.1	0.0	0.0	0.0	0.0	0.0	0.0	0.4	
Typical hip fracture, sum	239	90	14	542	2	49	84	18	272	
Motor vehicle crash	N	92	100	7	336	1	53	66	17	172
	Demographics									
	Age in years, median (Q1-Q3)	59.7 (47.1-68.6)	47.7 (37.4-57.0)	31.3 (25.5-46.3)	52.3 (39.1-63.7)	75.9 (75.9-75.9)	39.6 (27.8-50.0)	47.8 (32.5-59.3)	36.4 (29.7-54.3)	58.0 (48.9-68.0)
	Female, %	69.6	55.0	28.6	65.5	100.0	52.8	57.6	64.7	58.7
	Race, %									
	Caucasian	51.1	63.0	57.1	57.1	0.0	64.2	56.1	64.7	57.0
	African American	21.7	11.0	14.3	23.2	100.0	15.1	13.6	17.6	22.7
	Hispanic	8.7	12.0	0.0	7.4	0.0	3.8	10.6	5.9	9.9
	Asian	1.1	2.0	14.3	1.5	0.0	1.9	1.5	0.0	0.0
	Unknown	17.4	12.0	14.3	10.7	0.0	15.1	18.2	11.8	10.5
	Geographic division, %									
	New England	2.2	2.0	0.0	2.1	0.0	1.9	4.5	5.9	1.7
	Middle Atlantic	2.2	0.0	0.0	1.2	0.0	1.9	4.5	0.0	1.2
	East North Central	9.8	8.0	0.0	12.8	0.0	17.0	18.2	35.3	14.0
	West North Central	7.6	7.0	28.6	9.8	0.0	9.4	3.0	5.9	5.2
	South Atlantic	37.0	33.0	0.0	38.7	100.0	43.4	22.7	29.4	41.9
	East South Central	8.7	6.0	28.6	6.5	0.0	5.7	3.0	5.9	12.8
	West South Central	13.0	18.0	0.0	12.8	0.0	11.3	16.7	0.0	9.3
	Mountain	10.9	10.0	28.6	9.5	0.0	7.5	22.7	11.8	9.3
	Pacific	8.7	16.0	14.3	6.3	0.0	1.9	4.5	5.9	4.1
Unknown	0.0	0.0	0.0	0.3	0.0	0.0	0.0	0.0	0.6	
MVC in which the subject was driving, sum	94	101	10	345	1	53	67	17	177	

MVC = motor vehicle crash in which the subject was driving; Q = quartile

Supplemental Table S3. Summary of time-varying confounder prevalence during observation periods, by object drugs of interest

Outcome	Time-varying covariates	Object drug cohort								
		Baclofen	Carisoprodol	Chlorzoxazone	Cyclobenzaprine	Dantrolene	Metaxalone	Methocarbamol	Orphenadrine	Tizanidine
% unless otherwise noted										
Unintentional traumatic injury (primary)	Object drug average daily dose (mg), median (Q1-Q3)	30 (20.0-30.0)	1050 (700-1167)	1500 (1125-2000)	15 (10.0-30.0)	100 (50.0-100)	2400 (1600-2400)	1500 (1000-2250)	200 (200-200)	8 (4.0-12.0)
	Unintentional traumatic injury, ever prior to the day of observation*, person-days	845,733	509,403	24,917	1,317,657	7,195	111,379	231,729	44,360	1,190,419
	Unintentional traumatic injury, ever prior to the first day of observation*, % episodes	72.9	66.9	71.4	71.2	59.5	69.3	74.9	71.9	72.9
	Fracture	42.7	27.5	24.2	27.1	36.0	22.6	31.3	23.6	38.7
	Dislocation/sprain/strain	66.7	81.2	78.7	80.1	64.0	84.1	80.4	80.8	71.7
	Intracranial injury	9.9	5.7	4.4	5.7	20.0	4.9	6.6	4.9	8.1
	Internal injury of thorax, abdomen, or pelvis	4.9	2.6	2.0	2.3	8.0	1.9	3.0	2.0	3.5
	Open wound	34.4	23.5	23.1	21.7	32.0	17.7	24.2	20.6	31.0
	Injury to blood vessels	1.0	0.7	1.1	0.5	8.0	0.3	0.7	0.2	0.8
	Crushing injury	1.2	0.9	0.9	0.8	0.0	0.4	0.8	0.6	1.2
	Injury to nerves or spinal cord	4.5	2.5	2.6	2.2	16.0	1.8	2.4	1.5	3.7
	Certain traumatic complications, unspecified injuries, and other specified injuries	57.8	38.9	41.5	40.1	68.0	29.4	44.1	36.5	55.1
Typical hip fracture (secondary)	Object drug average daily dose (mg), median (Q1-Q3)	20 (15.0-40.0)	1050 (700-1400)	1500 (1500-2000)	10 (10.0-20.0)	150 (50.0-400)	1200 (800-2400)	2250 (1125-3000)	194 (100-200)	6.0 (4.0-8.0)
	Hip Fracture, typical, ever prior to the day of observation*, person-days	15,881	6,151	425	17,936	70	911	1,902	438	12,492
	Hip Fracture, typical, ever prior to the first day of observation*, % episodes	9.2	7.8	7.1	9.8	0.0	18.4	9.5	5.6	6.7
Motor vehicle crash (secondary)	Object drug average daily dose (mg), median (Q1-Q3)	30 (30.0-60.0)	1050 (700-1050)	1500 (1000-1500)	20.0 (10.0-30.0)	100 (100-100)	2400 (2400-2400)	1500 (750-2250)	200 (200-300)	8.0 (4.0-12.0)
	MVC in which the subject was driving, ever prior to the day of observation*, person-days	5,501	4,889	119	10,796	33	744	1,242	330	12,183
	MVC in which the subject was driving, ever prior to the first day of observation*, % episodes	12.0	9.0	42.9	13.7	0.0	9.4	15.2	5.9	9.9

MVC = motor vehicle crash in which the subject was driving; Q = quartile

* diagnosis (any position, any claim type) ever prior to the day of observation

Supplemental Table S4. Confounder adjusted rate ratios after semi-Bayes shrinkage for muscle relaxant drug interaction with opioids and risk of unintentional traumatic injury

Object drug	Precipitant drug	Adjusted RR	95% CI	
Baclofen	Codeine	0.93	0.73	1.20
Carisoprodol	Codeine	0.71	0.53	0.95
Chlorzoxazone	Codeine	0.87	0.43	1.77
Cyclobenzaprine	Codeine	1.01	0.90	1.14
Metaxalone	Codeine	1.08	0.74	1.56
Methocarbamol	Codeine	0.89	0.67	1.20
Orphenadrine	Codeine	1.37	0.82	2.28
Tizanidine	Codeine	1.00	0.82	1.23
Baclofen	Hydrocodone	0.97	0.88	1.08
Carisoprodol	Hydrocodone	0.92	0.84	1.02
Chlorzoxazone	Hydrocodone	1.01	0.73	1.41
Cyclobenzaprine	Hydrocodone	1.02	0.98	1.07
Dantrolene	Hydrocodone	1.00	0.44	2.26
Metaxalone	Hydrocodone	0.98	0.86	1.11
Methocarbamol	Hydrocodone	0.95	0.85	1.06
Orphenadrine	Hydrocodone	0.86	0.71	1.05
Tizanidine	Hydrocodone	0.88	0.81	0.95
Baclofen	Hydromorphone	0.75	0.53	1.05
Carisoprodol	Hydromorphone	1.11	0.74	1.66
Chlorzoxazone	Hydromorphone	1.36	0.61	2.99
Cyclobenzaprine	Hydromorphone	0.69	0.54	0.90
Metaxalone	Hydromorphone	1.36	0.74	2.50
Methocarbamol	Hydromorphone	0.69	0.44	1.07
Orphenadrine	Hydromorphone	0.93	0.39	2.25
Tizanidine	Hydromorphone	0.73	0.54	0.99
Tizanidine	Levorphanol	1.08	0.43	2.69
Baclofen	Meperidine	1.31	0.60	2.88
Carisoprodol	Meperidine	0.99	0.55	1.79
Cyclobenzaprine	Meperidine	1.09	0.65	1.84
Metaxalone	Meperidine	1.15	0.50	2.64
Methocarbamol	Meperidine	0.97	0.43	2.16
Tizanidine	Meperidine	0.73	0.34	1.55
Baclofen	Methadone	0.69	0.42	1.14
Carisoprodol	Methadone	0.96	0.55	1.65
Cyclobenzaprine	Methadone	0.83	0.54	1.27
Metaxalone	Methadone	0.70	0.31	1.58
Methocarbamol	Methadone	0.86	0.46	1.61
Tizanidine	Methadone	0.84	0.53	1.33
Baclofen	Morphine	1.46	1.13	1.87
Carisoprodol	Morphine	0.80	0.55	1.15
Chlorzoxazone	Morphine	0.66	0.28	1.55
Cyclobenzaprine	Morphine	0.89	0.71	1.13
Metaxalone	Morphine	0.88	0.49	1.58
Methocarbamol	Morphine	0.74	0.50	1.11
Orphenadrine	Morphine	0.71	0.27	1.84
Tizanidine	Morphine	0.94	0.75	1.19
Baclofen	Oxycodone	0.80	0.70	0.90
Carisoprodol	Oxycodone	0.90	0.78	1.04

Chlorzoxazone	Oxycodone	1.00	0.62	1.62
Cyclobenzaprine	Oxycodone	0.77	0.72	0.82
Dantrolene	Oxycodone	1.16	0.45	3.02
Metaxalone	Oxycodone	0.69	0.56	0.85
Methocarbamol	Oxycodone	0.75	0.65	0.86
Orphenadrine	Oxycodone	0.63	0.46	0.87
Tizanidine	Oxycodone	0.90	0.81	0.99
Baclofen	Oxymorphone	1.76	0.98	3.18
Carisoprodol	Oxymorphone	0.89	0.47	1.69
Cyclobenzaprine	Oxymorphone	0.88	0.47	1.65
Metaxalone	Oxymorphone	1.46	0.57	3.72
Methocarbamol	Oxymorphone	1.23	0.68	2.22
Tizanidine	Oxymorphone	0.69	0.46	1.05
Baclofen	Tapentadol	0.62	0.34	1.14
Carisoprodol	Tapentadol	1.09	0.48	2.49
Cyclobenzaprine	Tapentadol	0.75	0.40	1.40
Metaxalone	Tapentadol	0.75	0.29	1.92
Methocarbamol	Tapentadol	1.00	0.45	2.22
Tizanidine	Tapentadol	0.95	0.58	1.54
Baclofen	Tramadol	1.07	0.94	1.21
Carisoprodol	Tramadol	0.84	0.69	1.03
Chlorzoxazone	Tramadol	1.06	0.64	1.76
Cyclobenzaprine	Tramadol	0.99	0.92	1.07
Dantrolene	Tramadol	1.00	0.40	2.46
Metaxalone	Tramadol	1.14	0.92	1.42
Methocarbamol	Tramadol	1.15	0.97	1.36
Orphenadrine	Tramadol	0.73	0.52	1.03
Tizanidine	Tramadol	0.97	0.88	1.08

CI= confidence interval; RR= rate ratio

Supplemental Table S5. Summary of unadjusted and adjusted signals, with and without semi-Bayes shrinkage, for muscle relaxants plus candidate interacting precipitant and unintentional traumatic injury, typical hip fracture, and motor vehicle crash in which the subject was driving

Outcomes of interest	Object drug cohort	Unadjusted analyses			Adjusted analyses		
		Candidate interacting precipitants examined, sum	Before semi-Bayes shrinkage, DDI signals, sum (%)*	After semi-Bayes shrinkage, DDI signals, sum (%)*	Candidate interacting precipitants examined, sum	Before semi-Bayes shrinkage, DDI signals, sum (%)*	After semi-Bayes shrinkage, DDI signals, sum (%)*
Unintentional traumatic injury (primary)	Baclofen	396	10 (2.5)	4 (1.0)	396	15 (3.8)	5 (1.3)
	Carisoprodol	357	4 (1.1)	1 (0.3)	357	5 (1.4)	2 (0.6)
	Chlorzoxazone	128	2 (1.6)	0 (0.0)	128	3 (2.3)	2 (1.6)
	Cyclobenzaprine	465	7 (1.5)	3 (0.6)	465	4 (0.9)	0 (0.0)
	Dantrolene	13	1 (7.7)	0 (0.0)	13	1 (7.7)	0 (0.0)
	Metaxalone	268	5 (1.9)	1 (0.4)	268	3 (1.1)	0 (0.0)
	Methocarbamol	322	12 (3.7)	4 (1.2)	323	11 (3.4)	4 (1.2)
	Orphenadrine	165	4 (2.4)	1 (0.6)	165	3 (1.8)	0 (0.0)
	Tizanidine	428	5 (1.2)	3 (0.7)	428	5 (1.2)	3 (0.7)
Typical hip fracture (secondary)	Baclofen	137	1 (0.7)	0 (0.0)	129	3 (2.3)	0 (0.0)
	Carisoprodol	96	1 (1.0)	0 (0.0)	91	4 (4.4)	0 (0.0)
	Chlorzoxazone	6	0 (0.0)	0 (0.0)	6	1 (16.7)	0 (0.0)
	Cyclobenzaprine	189	0 (0.0)	0 (0.0)	179	9 (5.0)	0 (0.0)
	Dantrolene	-	-	-	-	-	-
	Metaxalone	35	0 (0.0)	0 (0.0)	32	0 (0.0)	0 (0.0)
	Methocarbamol	57	1 (1.8)	0 (0.0)	53	2 (3.8)	0 (0.0)
	Orphenadrine	12	0 (0.0)	0 (0.0)	9	1 (11.1)	0 (0.0)
	Tizanidine	142	3 (2.1)	0 (0.0)	140	3 (2.1)	0 (0.0)
Motor vehicle crash (secondary)	Baclofen	75	0 (0.0)	0 (0.0)	63	0 (0.0)	0 (0.0)
	Carisoprodol	54	0 (0.0)	0 (0.0)	47	3 (6.4)	0 (0.0)
	Chlorzoxazone	1	0 (0.0)	0 (0.0)	-	-	-
	Cyclobenzaprine	112	0 (0.0)	0 (0.0)	96	1 (1.0)	0 (0.0)
	Dantrolene	-	-	-	-	-	-
	Metaxalone	10	0 (0.0)	0 (0.0)	8	0 (0.0)	0 (0.0)
	Methocarbamol	26	0 (0.0)	0 (0.0)	19	1 (5.3)	0 (0.0)
	Orphenadrine	2	0 (0.0)	0 (0.0)	-	-	-
	Tizanidine	105	1 (1.0)	0 (0.0)	93	5 (5.4)	0 (0.0)

DDI = drug-drug interaction

* lower bound of the 95% confidence interval for the RR of interest excluded the null value