Supplemental Table 3. Study and population characteristics

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Surgical populations | | | | | | | | | | | | | | |
| First Author | Year | Country | Study design | Surgical population | Medico-administrative database | Sample size | Age | Females (N (%)) | Pre-surgical opioid prescription status | Additional inclusion/exclusion criteriaπ | Acute post-operative opioid prescription status | Follow-up (months)† | Outcome | |
| Prolonged opioid prescription | Long-term opioid prescription |
| Anthony24 | 2017 | USA | R-MA | Ortho | Humana | 4946 | n/a | n/a | n, m | none | Continuous prescriptions since event | 12 | **√** | **√** |
| Bedard25 | 2018 | USA | R-MA | Arthro | Humana | 4205 | AE | 2283 (54.3) | n, m | none | Continuous prescriptions since event | 12 | **√** | **√** |
| Bedard26 | 2017 | USA | R-MA | Arthro | Humana | 37 393 | AE | 15 349 (41.0) | n, m | none | Continuous prescriptions since event | 12 | **√** | **√** |
| Bedard27 | 2017 | USA | R-MA | Arthro | Humana | 73 959 | AE | 47 180 (63.8) | n, m | none | Continuous prescriptions since event | 12 | **√** | **√** |
| Brummett28 | 2017 | USA | R-MA | Mixed | Clinformatics Data Mart | 36 177 | A | 23 913 (66.1) | n | none | Peri-operative prescription as inclusion criteria | 3-6 | **√** | - |
| Clarke29 \*\* | 2014 | CA | R-MA | Mixed | CIHI / OHIP /Registered Persons Database /Ontario Drug Benefit Database | 39 140 | E | 18 753 (47.9) | n | ≠ palliative care | Acute postoperative opioid prescription required in criteria for prolonged opioid therapy | 6 | **√** | - |
| Soneji47 \*\*,¥ | 2016 | 12 | **√** | **√** |
| Connolly30 | 2017 | USA | R-MA | Ortho | Clinformatics Data Mart | 8377 | A | 4702 (56.1) | n,p,m | ≠ cancer, fracture, infection, spine inflammation, hx trauma; ≠ pregnancy; insurance | Unknown | 24 | - | **√** |
| First Author | Year | Country | Study design | Surgical population | Medico-administrative database | Sample size | Age | Females (N (%)) | Pre-surgical opioid status | Additional inclusion/exclusion criteriaπ | Acute post-operative opioid status | Follow-up (months)† | Outcome | |
| Prolonged opioid prescription | Long-term opioid prescription |
| Deyo18 ¥ | 2018 | USA | R-MA | Ortho | Oregon’s prescription drug monitoring program | 2491 | AE | 1486 (59.7) | n,p,m | ≠ fracture or inflammatory spondylopathy, ≠ cancer or spinal infection | Unknown | 7 | - | **√** |
| Hadland-smyth32¥ | 2018 | USA | R-MA | Arthro | Veterans’ Affairs datasets through VA Informatics and Computing Infrastructure | 6195 | AE | -- | n,p,m | none | Continuous prescriptions since event | 12 | - | **√** |
| Hansen33 | 2017 | AU | R-MA | Arthro | Australian Government Department of Veterans’ Affairs’ administrative database | 13,584 (15,020 cx) | AE | 7442 (49.5) | n,p,m | ≠ cancer | Continuous prescriptions since event | > 6 | - | **√** |
| Inacio35 | 2016 | AU | R-MA | Arthro | Australian Government Department of Veterans’ Affairs’ administrative database | 8925 (9525 cx) | E | 4891 (51.3) | n,p,m | ≠ cancer | Continuous prescriptions since event | 3-6 | **√** | - |
| Johnson36 | 2016 | USA | R-MA | Plastic | MarketScan (Truven Health Analytics) | 77 573 | AE | 46 893 (60.5) | n | ≠ dx opioid dependence or abuse; isolated injuries | Peri-operative prescription as inclusion criteria | 6 | **√** | - |
| Kim38 | 2017 | USA | R-MA | Arthro | Clinformatics Data Mart | 57 545 | AE | 32 801 (57.0) | n,p,m | ≠ cancer; no sx for fracture; no arthroplasty past 12m | Peri-operative prescription as inclusion criteria | 12 | - | **√** |
| Kim37 | 2018 | USA | R | Arthro | n/a | 54 | AE | 31 (57.4) | p | none | Unknown | 6 | **√** | - |
| First Author | Year | Country | Study design | Surgical population | Medico-administrative database | Sample size | Age | Females (N (%)) | Pre-surgical opioid status | Additional inclusion/exclusion criteriaπ | Acute post-operative opioid status | Follow-up (months)† | Outcome | |
| Prolonged opioid prescription | Long-term opioid prescription |
| Lawrence39 | 2008 | USA | P | Ortho | n/a | 91 | AE | -- | p, m | No neck pain greater than radicular pain | Continuous prescriptions since event | 3-24 | - | **√** |
| Mohanty40 | 2017 | USA | TC | Bariatric | Michigan Bariatric Surgery Collaborative | 14 063 | -- | -- | n, m | none | Unknown | 12 | - | **√** |
| Mosher41 | 2018 | USA | R-MA | Mixed | Austin Information Technology Center | 26 476 | AE | 1807 (6.8) | n | ≠ metastatic cancer, palliative care or opioid-dependence tx | Peri-operative prescription as inclusion criteria | > 3 | **√** | - |
| Moyer42 | 2011 | USA | P | Plastic | n/a | 6 | A | 3 (50.0) | p | Hyperalgesic/painful burn scars | Acute postoperative opioid prescription required in criteria for long-term opioid prescription | 13.0±4.3 | - | **√** |
| Mueller43 | 2017 | USA | R-MA | Arthro | MarketScan (Truven Health Analytics) | 6695 | A | 2856 (42.7) | n, p, m | ≠ cancer | Acute postoperative opioid prescription required in criteria for long-term opioid prescription | 12 |  | **√** |
| Politzer44 | 2017 | USA | R-MA | Arthro | Humana | 66 950 | AE | 42 458 (63.4) | n, m | none | Continuous prescriptions since event | > 6 | - | **√** |
| Qureshi45 | 2018 | USA | R-MA | Neuro-surgical | PearlDiver Database | 1321 | A | 625 (47.3) | P | ≠ concomitant spine fusion, spinal infections, cancer, trauma | Continuous prescriptions since event | > 3 | **√** | - |
| Rios46 | 1998 | USA | R | Digest. | Medical University of South Carolina | 17 | A | 11 (64.7) | P | Chronic pancreatitis; duct ≤ 7mm diameter; ≠ prior ductal or resectional surgery | Acute postoperative opioid prescription required in criteria for prolonged opioid therapy | 10.3 (3-16) | - | **√** |
| First Author | Year | Country | Study design | Surgical population | Medico-administrative database | Sample size | Age | Females (N (%)) | Pre-surgical opioid status | Additional inclusion/exclusion criteriaπ | Acute post-operative opioid prescription status | Follow-up (months)† | Outcome | |
| Prolonged opioid prescription | Long-term opioid prescription |
| Rozet10 | 2014 | USA | R | Arthro | Veteran’s Administration Puget Sound Health Care System | 145 | A | 18 (12.4) | n, m | ≠ arthro on contralateral leg or anterior/posterior cruciate ligament repair; ≠ procedure < 6m before indexed sx | Acute postoperative opioid prescription required in criteria for prolonged opioid therapy | 3.5 | **√** | - |
| Schoenfeld11 | 2017 | USA | R-MA | Ortho | TRICARE insurance claims from the Military Health System Data Repository | 9991 | A | 3694 (37.0) | n | ≠ cancer or trauma; ≠ eligible for Medicare or Medicaid | Continuous prescriptions since event | 12 | **√** | **√** |
| Sun48 ¥ | 2016 | USA | R-MA | Mixed | MarketScan (Truven Health Analytics) | 641 941 | A | 472 276 (73.6) | n | 3yr enrollment insurance plan | Unknown | 12 | - | **√** |
| Westermann50 | 2017 | USA | R-MA | Ortho | Humana | 35 155 | AE | 16 523 (47.0) | n,p | none | Unknown | 12 | **√** | **√** |
| Yang51 | 2015 | USA | R | Digest. | Beth Israel Deaconess Medical Center | 66 | AE | 34 (51.5) | n,p | Diagnosis of recurrent acute or chronic pancreatitis | Unknown | 36 | - | **√** |
| Zarling52 | 2016 | USA | R | Arthro | Michigan Automated Prescription System database | 315 | AE | 208 (66.0) | p, m | none | Opioid prescription examined by periods of 6 weeks postoperatively | 12 | - | **√** |
| Trauma populations | | | | | | | | | | | | | | |
| First Author | Year | Country | Study design | Trauma type | Medico-administrative database | Sample size | Age | Females (N(%)) | Pre-trauma opioid prescription status | Inclusion criteriaπ | Acute post-operative opioid prescription status | Follow-up (months)¥ | Outcome | |
| Prolonged opioid prescription | Long-term opioid prescription |
| Al Dabbagh23 | 2014 | SWE | R-MA | Mixed | Swedish National Hospital Discharge Register/National Pharmacy Register/Total Population Register | 639 | AE | 250 (39.1) | n | No associated fracture | Peri-operative prescription as inclusion criteria | 17 (7-27) | **√** | **√** |
| Al Dabbagh3¥ | 2016 | SWE | R-MA | Mixed | Swedish National Hospital Discharge Register/Swedish Prescribed Drug Register | 891 | AE | 501 (56.2) | n | No associated skeletal injuries | Peri-operative prescription as inclusion criteria | 20 (11-32) | **√** | **√** |
| Daoust31 | 2017 | CA | R-MA | Mixed | Quebec Trauma Registry/Medical Consultations and Medications Database | 39 833 | E | 27 564 (69.2) | n,p,m | none | Long-term opioid prescription associated with initial injury | 12 | - | **√** |
| Holman34 | 2013 | USA | R-MA | Ortho | Utah Controlled Substance Database | 613 | AE | -- | n,p,m | ≠ multisystem or multiple-limb trauma | Continuous prescriptions since event | > 3 | **√** | - |
| Weiss49 | 2012 | SWE | R-MA | Fracture | Swedish National Hospital Discharge Registry/National Pharmacy Register | 1017 | AE | -- | n | ≠ fracture | Peri-operative prescription as inclusion criteria | 14 (5-24) | **√** | **√** |
| Zwisler53 | 2015 | DEN | R | Mixed | Odense University Hospital trauma database | 938 | AE | 284 (30.3) | n, m | none | Unknown | > 6 | - | **√** |

\*\* Same patient cohort; † Follow-up time recorded in this table refers to the last time points at which data was collected. **Median** (range) is used for studies with varying time points across patients. **¥**Based on correspondence with the author. **R**: longitudinal retrospective study design. **P**: longitudinal prospective study design. **R-MA**= longitudinal retrospective study design using medico-administrative databases only. **TC**: transversal/cross-sectional study. **Arthro**: Arthroplasty (knee, hip or shoulder). **SWE**: Sweden, **DEN**: Denmark, **CA**: Canada. **A**: Adults (18-65 years old). **AE**: Adults and elderly (> 18 years old). **p** = patients with pre-event prolonged opioid prescription; **n** = patients with no/short-term opioid prescription pre-event; **m** = pre-event mixed patient group (unable to determine opioid status); **hx**: history; **dx**: diagnosis; **sx**: symptoms; **tx**: treatments. **CIHI**: Canadian Institute for Health Information. **OHIP**: Ontario Health Insurance Plan.

*Note:* Several studies extracted data from the same databases (see Table 1 for details). In the vast majority of studies, there is no overlap in the examined populations. One exception was the cohorts in Bedard31 and Politzer48 that significantly overlapped in the composition of their samples. The two studies however, used different definitions of prolonged opioid prescription, and therefore we report them in this review (see Supplementary Table 4, http://links.lww.com/SLA/B673). These articles were not part of the meta-analyses. Other two studies using the same cohort are from Clarke33 and Soneji;51 the former is reporting on the 6-month outcomes, while the latter is reporting on > 6-month outcomes, and therefore both were eligible for inclusion. The Clarke and Soneji studies also had 26% of their patients who underwent cancer-related surgeries. However, the authors directly stated that they selected their surgical procedures as to minimize the presence of preoperative chronic pain problems (which would then reduce the risk factor of cancer-related chronic analgesia that motivated the use of this exclusion criteria to start with). As such these article were retained.

Supplemental Table 6. Results of individual risk factors for opioid prescription 3-6 months and >6 months post-surgery or trauma among individuals with no/short-term opioid prescription pre-event

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Risk factor category** | | **Risk factor** | **Studies** | **Data source for risk factor** | **Period considered preop/ pretrauma** | **N** | **Out-come** | **Type of effect size** | **Effect size (95% CI)** |
| Socio  demographic | Female sex (ref: male sex) | | Brummett (2017) | -- | -- | 36,177 | Rx\_3-6 | OR | 0.99 (0.90, 1.10) |
| Female sex (ref: male sex) | | Clarke (2014) | -- | -- | 39,140 | Rx\_3-6 | OR | 1.10 (0.96, 1.27) |
| Female sex (ref: male sex) | | Johnson (2016) | -- | -- | 59,725 | Rx\_3-6 | OR | 1.1 (1.0, 1.2) |
| **Female sex (ref: male sex)** | | **Mosher (2018)** | **--** | **--** | **26,476** | **Rx\_3-6** | **OR** | **0.73 (0.63, 0.86)** |
| Female sex (ref: male sex) | | Holman (2013) | -- | -- | 613 | Rx\_3-6 | RR | 1.06 (0.79, 1.43) |
| Female sex (ref: male sex) | | Al Dabbagh (2014) | -- | -- | **639** | Rx\_>6 | HR | 1.1 (0.9, 1.4) |
| Female sex (ref: male sex) | | Al Dabbagh (2016) | -- | -- | 891 | Rx\_>6 | HR | 1.2 (1.0, 1.4) |
| Female sex (ref: male sex) | | Schoenfeld (2017) | -- | -- | 9991 | Rx\_>6 | HR | 0.99 (0.93, 1.07) |
| **Female sex (ref: male sex)** | | **Daoust (2017)** | **--** | **--** | **39,833** | **Rx\_>6** | **OR** | **1.27 (1.16, 1.38)** |
| Female sex (ref: male sex) | | Sun (2016) | -- | -- | 641,941 | Rx\_>6 | OR | 1.34 (-, -) |
| **Age (5yr increment)** | | **Holman (2013)** | **--** | **--** | **613** | **Rx\_3-6** | **RR** | **1.06 (1.02, 1.11)** |
| **Age: 66-75 (ref: age 86+)** | | **Clarke (2014)** | **--** | **--** | **39,140** | **Rx\_3-6** | **OR** | **1.63 (1.08, 2.46)** |
| Age: 76-85 (ref: age 86+) | | Clarke (2014) | -- | -- | 39,140 | Rx\_3-6 | OR | 1.47 (0.97, 2.22) |
| **Age: 18-34 (ref: 50-64)** | | **Mosher (2018)** | **--** | **--** | **26,476** | **Rx\_3-6** | **OR** | **0.72 (0.61, 0.86)** |
| Age: 35-49 (ref: 50-64) | | Mosher (2018) | -- | -- | 26,476 | Rx\_3-6 | OR | 0.91 (0.81, 1.02) |
| **Age: 65-79 (ref: 50-64)** | | **Mosher (2018)** | **--** | **--** | **26,476** | **Rx\_3-6** | **OR** | **0.59 (0.54, 0.65)** |
| **Age: 80+ (ref: 50-64)** | | **Mosher (2018)** | **--** | **--** | **26,476** | **Rx\_3-6** | **OR** | **0.41 (0.35, 0.49)** |
| **Age: missing (ref: 50-64)** | | **Mosher (2018)** | **--** | **--** | **26,476** | **Rx\_3-6** | **OR** | **0.49 (0.31, 0.79)** |
| Age: 35-44 (ref: age 18-34) | | Johnson (2016) | -- | -- | 59,725 | Rx\_3-6 | OR | 1 (0.9, 1.2) |
| Age: 45-54 (ref: age 18-34) | | Johnson (2016) | -- | -- | 59,725 | Rx\_3-6 | OR | 1 (0.9, 1.1) |
| Age: 55-64 (ref: age 18-34) | | Johnson (2016) | -- | -- | 59,725 | Rx\_3-6 | OR | 0.9 (0.8, 1) |
| **Age: 65+ (ref: age 18-34)** | | **Johnson (2016)** | **--** | **--** | **59,725** | **Rx\_3-6** | **OR** | **0.8 (0.7, 0.9)** |
| **Age: 30-39 (ref: age 18-29)** | | **Brummett (2017)** | **--** | **--** | **36,177** | **Rx\_3-6** | **OR** | **0.76 (0.64, 0.9)** |
| **Age: 40-49 (ref: age 18-29)** | | **Brummett (2017)** | **--** | **--** | **36,177** | **Rx\_3-6** | **OR** | **0.72 (0.61, 0.84)** |
| Age: 50-59 (ref: age 18-29) | | Brummett (2017) | -- | -- | 36,177 | Rx\_3-6 | OR | 0.88 (0.75, 1.04) |
| Age: 60-64 (ref: age 18-29) | | Brummett (2017) | -- | -- | 36,177 | Rx\_3-6 | OR | 0.9 (0.74, 1.1) |
| **Age: 50+ (ref: age <50)** | | **Sun (2016)** | **--** | **--** | **641,941** | **Rx\_>6** | **OR** | **1.74 (1.45, 2.09)** |
| **Age: older age (ref: younger age)** | | **Al Dabbagh (2014)** | **--** | **--** | **639** | **Rx\_>6** | **HR** | **1.5 (1.3, 1.9)** |
| **Age: older age (ref: younger age)** | | **Al Dabbagh (2016)** | **--** | **--** | **891** | **Rx\_>6** | **HR** | **1.9 (1.5, 2.3)** |
| **Age: older age (ref: younger age)** | | **Weiss (2012)** | **--** | **--** | **396** | **Rx\_>6** | **HR** | **2.0 (1.5, 2.7)** |
| Race - Black (ref: White) | | Mosher (2018) | -- | -- | 26,476 | Rx\_3-6 | OR | 0.96 (0.83, 1.13) |
| **Race – Other/unknown (ref: White)** | | **Mosher (2018)** | **--** | **--** | **26,476** | **Rx\_3-6** | **OR** | **0.78 (0.66, 0.92)** |
| Race - African American (ref: White) | | Brummett (2017) | -- | -- | 36,177 | Rx\_3-6 | OR | 1.13 (0.97, 1.3) |
| Race - Asian (ref: White) | | Brummett (2017) | -- | -- | 36,177 | Rx\_3-6 | OR | 0.73 (0.51, 1.04) |
| Race - Hispanic (ref: White) | | Brummett (2017) | -- | -- | 36,177 | Rx\_3-6 | OR | 0.98 (0.84, 1.15) |
| Rural region (ref: urban) | | Clarke (2014) | -- | -- | 39,140 | Rx\_3-6 | OR | 0.98 (0.83, 1.15) |
| Isolated region (ref: urban) | | Mosher (2018) | -- | -- | 26,476 | Rx\_3-6 | OR | 1.02 (0.92, 1.14) |
| **Small rural region (ref: urban)** | | **Mosher (2018)** | **--** | **--** | **26,476** | **Rx\_3-6** | **OR** | **1.29 (1.14, 1.47)** |
| Large rural region (ref: urban) | | Mosher (2018) | -- | -- | 26,476 | Rx\_3-6 | OR | 1.02 (0.9, 1.17) |
| Married (ref: other civil status) | | Schoenfeld (2017) | -- | -- | 9,991 | Rx\_>6 | HR | 0.96 (0.91, 1.03) |
| **Military rank - Junior enlisted (ref: Rank – officer)** | | **Schoenfeld (2017)** | **--** | **--** | **9,991** | **Rx\_>6** | **HR** | **0.8 (0.72, 0.9)** |
| Military rank - other (ref: Rank – officer) | | Schoenfeld (2017) | -- | -- | 9,991 | Rx\_>6 | HR | 1.07 (0.95, 1.19) |
| **Military rank - Senior enlisted (ref: Rank – officer)** | | **Schoenfeld (2017)** | **--** | **--** | **9,991** | **Rx\_>6** | **HR** | **0.94 (0.89, 0.99)** |
| **Education – High school (ref: college or more)** | | **Brummett (2017)** | **--** | **--** | **36,177** | **Rx\_3-6** | **OR** | **1.22 (1.04, 1.43)** |
| Education – < High school (ref: college or more) | | Brummett (2017) | -- | -- | 36,177 | Rx\_3-6 | OR | 1.08 (0.53, 2.18) |
| **Education – Some college (ref: college or more)** | | **Brummett (2017)** | **--** | **--** | **36,177** | **Rx\_3-6** | **OR** | **1.19 (1.03, 1.38)** |
| Neighborhood income (fifth) – 2nd lowest (ref: lowest) | | Clarke (2014) | -- | -- | 39,140 | Rx\_3-6 | OR | 0.98 (0.82, 1.16) |
| Neighborhood income (fifth) – 3rd lowest (ref: lowest) | | Clarke (2014) | -- | -- | 39,140 | Rx\_3-6 | OR | 0.9 (0.75, 1.07) |
| **Neighborhood income (fifth) – 2nd highest (ref: lowest)** | | **Clarke (2014)** | **--** | **--** | **39,140** | **Rx\_3-6** | **OR** | **0.76 (0.63, 0.92)** |
| **Neighborhood income (fifth) – highest (ref: lowest)** | | **Clarke (2014)** | **--** | **--** | **39,140** | **Rx\_3-6** | **OR** | **0.77 (0.64, 0.93)** |
| Median household income $40,000-$49,000 (ref: < $40,000) | | Johnson (2016) | -- | -- | 59,725 | Rx\_3-6 | OR | 1 (0.9, 1.2) |
| Median household income $50,000-$59,000 (ref: < $40,000) | | Johnson (2016) | -- | -- | 59,725 | Rx\_3-6 | OR | 1 (0.8, 1.2) |
| **Median household income $60,000-$69,000 (ref: < $40,000)** | | **Johnson (2016)** | **--** | **--** | **59,725** | **Rx\_3-6** | **OR** | **0.8 (0.7, 0.9)** |
| **Median household income $70,000+ (ref: < $40,000)** | | **Johnson (2016)** | **--** | **--** | **59,725** | **Rx\_3-6** | **OR** | **0.7 (0.6, 0.9)** |
| Insurance plan –comprehensive (ref: preferred provider organization) | | Johnson (2016) | -- | -- | 59,725 | Rx\_3-6 | OR | 1.1 (1, 1.3) |
| Insurance plan –health maintenance organization (ref: preferred provider organization) | | Johnson (2016) | -- | -- | 59,725 | Rx\_3-6 | OR | 1 (0.9, 1.1) |
| Insurance plan –other (ref: preferred provider organization) | | Johnson (2016) | -- | -- | 59,725 | Rx\_3-6 | OR | 1 (0.9, 1.1) |
| Insurance plan –point of service (ref: preferred provider organization) | | Johnson (2016) | -- | -- | 59,725 | Rx\_3-6 | OR | 1.1 (1, 1.2) |
| Health behaviors | **Tobacco dependence** | | **Brummett (2017)** | **ICD9** | **1 year** | **36,177** | **Rx\_3-6** | **OR** | **1.35 (1.21, 1.49)** |
| **Tobacco dependence** | | **Johnson (2016)** | **ICD9** | **1 year** | **59,725** | **Rx\_3-6** | **OR** | **1.6 (1.0, 2.6)** |
| Alcohol dependence | | Johnson (2016) | ICD9 | **1 year** | 59,725 | Rx\_3-6 | OR | 1.3 (0.9, 2) |
| **Alcohol or drug dependence** | | **Daoust (2017)** | **ICD9** | **1 year** | **39,833** | **Rx\_>6** | **OR** | **1.28 (0.94, 1.74)** |
| **Alcohol dependence** | | **Sun (2016)** | **ICD9** | **1 year** | **641,941** | **Rx\_>6** | **OR** | **1.83 (-, -)** |
| **Alcohol or drug dependence** | | **Brummett (2017)** | **CCS-AHRQ** | **1 year** | **36,177** | **Rx\_3-6** | **OR** | **1.34 (1.05, 1.72)** |
| Drug dependence | | Johnson (2016) | ICD9 | 1 year | 59,725 | Rx\_3-6 | OR | 0.9 (0.6, 1.5) |
| **Drug dependence** | | **Sun (2016)** | **ICD9** | **1 year** | **641,941** | **Rx\_>6** | **OR** | **3.15 (1.1, 9.05)** |
| Pre-event medication use | **ACE inhibitors** | | **Clarke (2014)** | **ODBD** | **3 months** | **39,140** | **Rx\_3-6** | **OR** | **1.26 (1.09, 1.44)** |
| Angiotensin receptor blockers | | Clarke (2014) | ODBD | 3 months | 39,140 | Rx\_3-6 | OR | 1.08 (0.9, 1.28) |
| **Antidepressants** | | **Mosher (2014)** | **VHA** | **1 year** | **26,476** | **Rx\_3-6** | **OR** | **1.26 (1.16, 1.37)** |
| **Antidepressants (SSRIs)** | | **Clarke (2018)** | **ODBD** | **3 months** | **39,140** | **Rx\_3-6** | **OR** | **1.41 (1.10, 1.80)** |
| **Antidepressants** | | **Sun (2016)** | **TMSD** | **1 year** | **641,941** | **Rx\_>6** | **OR** | **1.65 (1.38, 1.98)** |
| Antipsychotics | | Sun (2016) | TMSD | 1 year | 641,941 | Rx\_>6 | OR | 1.14 (0.88, 1.48) |
| Beta blockers | | Clarke (2014) | ODBD | 3 months | 39,140 | Rx\_3-6 | OR | 1.05 (0.92, 1.21) |
| **Benzodiazepine** | | **Clarke (2014)** | **ODBD** | **3 months** | **39,140** | **Rx\_3-6** | **OR** | **1.26 (1.07, 1.48)** |
| **Benzodiazepine** | | **Sun (2016)** | **TMSD** | **1 year** | **641,941** | **Rx\_>6** | **OR** | **1.82 (1.48, 2.24)** |
| **Benzodiazepine in past year (ref: none in past year)** | | **Mosher (2018)** | **VHA** | **1 year** | **26,476** | **Rx\_3-6** | **OR** | **0.84 (0.72, 0.98)** |
| **Benzodiazepine current use (ref: none in past year)** | | **Mosher (2018)** | **VHA** | **1 year** | **26,476** | **Rx\_3-6** | **OR** | **1.56 (1.41, 1.73)** |
| **Muscle relaxant in past year (ref: none in the past year)** | | **Mosher (2018)** | **VHA** | **1 year** | **26,476** | **Rx\_3-6** | **OR** | **1.17 (1.01, 1.35)** |
| **Muscle relaxant current use (ref: none in past year)** | | **Mosher (2018)** | **VHA** | **1 year** | **26,476** | **Rx\_3-6** | **OR** | **1.69 (1.52, 1.89)** |
| **Pre-event long-term opioid use (ref: pre-event opioid naïve)** | | **Holman (2013)** | **UCSB** | **3 months** | **613** | **Rx\_3-6** | **RR** | **5.14 (3.84, 6.87)** |
| Pre-event short-term opioid use (ref: pre-event opioid naïve) | | Holman (2013) | UCSB | 3 months | 613 | Rx\_3-6 | RR | 1.66 (0.7, 3.94) |
| **Pre-event short-term opioid use (30 days) (ref: pre-event opioid naïve)** | | **Brummett (2017)** | **MA** | **1 year** | **36,177** | **Rx\_3-6** | **OR** | **1.93 (1.71, 2.19)** |
| **Number pre-event opioid prescription > 1 (ref: 0)** | | **Daoust (2017)** | **RAMQ** | **1 year** | **39,833** | **Rx\_>6** | **OR** | **11.4 (10.5, 12.5)** |
| **Number pre-event opioid prescription = 1 (ref: 0)** | | **Daoust (2017)** | **RAMQ** | **1 year** | **39,833** | **Rx\_>6** | **OR** | **2.26 (2, 2.56)** |
| Statins | | Clarke (2014) | ODBD | 3 months | 39,140 | Rx\_3-6 | OR | 1 (0.88, 1.14) |
| MSK conditions | **Arthritis** | | **Brummett (2017)** | **ICD9** | **1 year** | **36,177** | **Rx\_3-6** | **OR** | **1.56 (1.4, 1.73)** |
| **Back pain** | | **Brummett (2017)** | **ICD9** | **1 year** | **36,177** | **Rx\_3-6** | **OR** | **1.57 (1.42, 1.75)** |
| **Back diagnosis: deformity (ref: disc degeneration)** | | **Schoenfeld (2017)** | **MDR** | **--** | **9,991** | **Rx\_>6** | **HR** | **0.73 (0.59, 0.91)** |
| **Back diagnosis: fracture (ref: disc degeneration)** | | **Schoenfeld (2017)** | **MDR** | **--** | **9,991** | **Rx\_>6** | **HR** | **0.81 (0.69, 0.95)** |
| **Back diagnosis: other (ref: disc degeneration)** | | **Schoenfeld (2017)** | **MDR** | **--** | **9,991** | **Rx\_>6** | **HR** | **1.29 (1.14, 1.45)** |
| Back diagnosis: revision (ref: disc degeneration) | | Schoenfeld (2017) | MDR | -- | 9,991 | Rx\_>6 | HR | 1.09 (0.9, 1.33) |
| Back diagnosis: spondylolisthesis (ref: disc degeneration) | | Schoenfeld (2017) | MDR | -- | 9,991 | Rx\_>6 | HR | 1.05 (0.92, 1.19) |
| Back diagnosis: stenosis (ref: disc degeneration) | | Schoenfeld (2017) | MDR | -- | 9,991 | Rx\_>6 | HR | 1.04 (0.98, 1.1) |
| **Chronic pain** | | **Mosher (2018)** | **ICD9** | **1 year** | **26,476** | **Rx\_3-6** | **OR** | **1.18 (1.04, 1.21)** |
| Chronic pain history | | Johnson (2016) | ICD9 | 1 year | 59,725 | Rx\_3-6 | OR | 1 (0.9, 1.2) |
| **Chronic pain other than reason for surgery** | | **Brummett (2017)** | **ICD9** | **1 year** | **36,177** | **Rx\_3-6** | **OR** | **1.39 (1.26, 1.54)** |
| Psychiatric diagnoses | Adjustment disorder | | Brummett (2017) | CCS-AHRQ | 1 year | 36,177 | Rx\_3-6 | OR | 0.86 (0.68, 1.07) |
| **Anxiety disorder** | | **Brummett (2017)** | **CCS-AHRQ** | **1 year** | **36,177** | **Rx\_3-6** | **OR** | **1.25 (1.10, 1.42)** |
| Anxiety disorder | | Mosher (2018) | ICD9 | 1 year | 26,476 | Rx\_3-6 | OR | 1.07 (0.95, 1.21) |
| Anxiety disorder | | Schoenfeld (2017) | ICD9 | 1 year | 9,991 | Rx\_>6 | HR | 0.85 (0.67, 1.06) |
| Anxiety disorder | | Daoust (2017) | ICD9 | 1 year | 39,833 | Rx\_>6 | OR | 1.12 (0.99, 1.27) |
| **Depressive disorder** | | **Brummett (2017)** | **CCS-AHRQ** | **1 year** | **36,177** | **Rx\_3-6** | **OR** | **1.15 (1.01, 1.30)** |
| Depressive disorder | | Mosher (2018) | ICD9 | 1 year | 26,476 | Rx\_3-6 | OR | 0.92 (0.82, 1.03) |
| **Depressive disorder** | | **Daoust (2017)** | **ICD9** | **1 year** | **39,833** | **Rx\_>6** | **OR** | **1.32 (1.13, 1.53)** |
| **Depressive disorder** | | **Sun (2016)** | **ICD9** | **1 year** | **641,941** | **Rx\_>6** | **OR** | **1.15 (-, -)** |
| **Depressive disorder** | | **Schoenfeld (2017)** | **ICD9** | **1 year** | **9,991** | **Rx\_>6** | **HR** | **0.84 (0.77, 0.9)** |
| Disruptive disorders | | Brummett (2017) | CCS-AHRQ | 1 year | 36,177 | Rx\_3-6 | OR | 1.03 (0.78, 1.34) |
| Mental health care visit | | Mosher (2018) | VHA | 1 year | 26,476 | Rx\_3-6 | OR | 0.98 (0.89, 1.07) |
| Other psychiatric disorder | | Brummett (2017) | CCS-AHRQ | 1 year | 36,177 | Rx\_3-6 | OR | 0.85 (0.67, 1.08) |
| Psychiatric disorder | | Johnson (2016) | ICD9 | 1 year | 59,725 | Rx\_3-6 | OR | 1.1 (1, 1.2) |
| Psychosis | | Sun (2016) | ICD9 | 1 year | 641,941 | Rx\_>6 | OR | 1.03 (0.68, 1.55) |
| Peri-event factors  (type of surgery or trauma) | **Elective surgery (ref: trauma surgery)** | | **Johnson (2016)** | **TMSD** | **--** | **59,725** | **Rx\_3-6** | **OR** | **1.2 (1.1, 1.3)** |
| Major surgery (ref: minor surgery) | | Brummett (2017) | MA | -- | 36,177 | Rx\_3-6 | OR | 1.09 (0.96, 1.23) |
| **Back surgical procedure: decompression (ref: lumbar interbody arthrodesis)** | | **Schoenfeld (2017)** | **MDR** | **--** | **9,991** | **Rx\_>6** | **HR** | **1.34 (1.25, 1.43)** |
| **Back surgical procedure: discectomy (ref: lumbar interbody arthrodesis)** | | **Schoenfeld (2017)** | **MDR** | **--** | **9,991** | **Rx\_>6** | **HR** | **1.43 (1.36, 1.5)** |
| Back surgical procedure: lumbar posterolateral arthrodesis (ref: lumbar interbody arthrodesis) | | Schoenfeld (2017) | MDR | -- | 9,991 | Rx\_>6 | HR | 1.03 (0.95, 1.12) |
| Surgery type: pelvis or acetabulum (ref: lower extremity) | | Holman (2013) | MA | -- | 613 | Rx\_3-6 | RR | 1.33 (0.91, 1.94) |
| Surgery type: upper extremity (ref: lower extremity) | | Holman (2013) | MA | -- | 613 | Rx\_3-6 | RR | 0.68 (0.36, 1.27) |
| Surgery type: CABG via sternotomy (ref: open prostatectomy) | | Clarke (2014) | OHIP | -- | 39,140 | Rx\_3-6 | OR | 0.95 (0.71, 1.29) |
| **Surgery type: minimally invasive lung resection (ref: open prostatectomy)** | | **Clarke (2014)** | **OHIP** | **--** | **39,140** | **Rx\_3-6** | **OR** | **1.95 (1.36, 2.78)** |
| Surgery type: minimally invasive colorectal surgery (ref: open prostatectomy) | | Clarke (2014) | OHIP | -- | 39,140 | Rx\_3-6 | OR | 1 (0.76, 1.32) |
| **Surgery type: minimally invasive hysterectomy (ref: open prostatectomy)** | | **Clarke (2014)** | **OHIP** | **--** | **39,140** | **Rx\_3-6** | **OR** | **0.45 (0.33, 0.62)** |
| Surgery type: minimally invasive prostatectomy (ref: open prostatectomy) | | Clarke (2014) | OHIP | -- | 39,140 | Rx\_3-6 | OR | 0.37 (0.14, 1.01) |
| Surgery type: open colorectal surgery (ref: open prostatectomy) | | Clarke (2014) | OHIP | -- | 39,140 | Rx\_3-6 | OR | 0.84 (0.67, 1.07) |
| **Surgery type: open hysterectomy (ref: open prostatectomy)** | | **Clarke (2014)** | **OHIP** | **--** | **39,140** | **Rx\_3-6** | **OR** | **0.73 (0.55, 0.98)** |
| **Surgery type: open lung resection (ref: open prostatectomy)** | | **Clarke (2014)** | **OHIP** | **--** | **39,140** | **Rx\_3-6** | **OR** | **2.58 (2.03, 3.28)** |
| **ISS score ≥ 15** | | **Daoust (2017)** | **QTR** | **--** | **39,833** | **Rx\_>6** | **OR** | **0.81 (0.69, 0.95)** |
| Number of injuries = 2 (ref: 1) | | Daoust (2017) | QTR | -- | 39,833 | Rx\_>6 | OR | 1.01 (0.92, 1.1) |
| Number of injuries ≥ 3 (ref: 1) | | Daoust (2017) | QTR | -- | 39,833 | Rx\_>6 | OR | 0.95 (0.85, 1.07) |
| Face injury | | Daoust (2017) | QTR | -- | 39,833 | Rx\_>6 | OR | 1.08 (0.95, 1.24) |
| Head injury | | Daoust (2017) | QTR | -- | 39,833 | Rx\_>6 | OR | 0.97 (0.84, 1.11) |
| **Lower extremity injury** | | **Daoust (2017)** | **QTR** | **--** | **39,833** | **Rx\_>6** | **OR** | **1.25 (1.15, 1.36)** |
| **Spine injury** | | **Daoust (2017)** | **QTR** | **--** | **39,833** | **Rx\_>6** | **OR** | **1.62 (1.46, 1.8)** |
| **Thorax injury** | | **Daoust (2017)** | **QTR** | **--** | **39,833** | **Rx\_>6** | **OR** | **1.15 (1.03, 1.28)** |
| **Neck pain** | | **Brummett (2017)** | **QTR** | **--** | **36,177** | **Rx\_3-6** | **OR** | **1.22 (1.07, 1.39)** |
| Trauma with surgery (ref: trauma without surgery) | | Daoust (2017) | QTR | -- | 39,833 | Rx\_>6 | OR | 0.99 (0.91, 1.07) |
| Trauma with surgery (ref: trauma without surgery) | | Al Dabbagh (2014) | ICD9 | -- | 639 | Rx\_>6 | HR | 1.1 (0.9, 1.4) |
| Trauma with surgery (ref: trauma without surgery) | | Weiss (2012) | MA | -- | 396 | Rx\_>6 | HR | 0.9 (0.7, 1.3) |
| Fall mechanism unspecified (ref: same level fall) | | Al Dabbagh (2014) | ICD9 | -- | 639 | Rx\_>6 | HR | 1.0 (0.5, 1.8) |
| Fall mechanism unspecified (ref: same level fall) | | Al Dabbagh (2016) | ICD10 | -- | 891 | Rx\_>6 | HR | 0.8 (0.6, 1.0) |
| Fall mechanism other (ref: same level fall) | | Al Dabbagh (2014) | ICD9 | -- | 639 | Rx\_>6 | HR | 1.1 (0.8, 1.4) |
| Fall mechanism other (ref: same level fall) | | Al Dabbagh (2016) | ICD10 | -- | 891 | Rx\_>6 | HR | 1.1 (0.7, 1.5) |
| Fall mechanism unknown (ref: same level fall) | | Al Dabbagh (2014) | ICD9 | -- | 639 | Rx\_>6 | HR | 0.9 (0.6, 1.2) |
| Fall mechanism unknown (ref: same level fall) | | Al Dabbagh (2016) | ICD10 | -- | 891 | Rx\_>6 | HR | 1.0 (0.7, 1.3) |
| Fall mechanism transport accident (ref: same level fall) | | Al Dabbagh (2014) | ICD9 | -- | 639 | Rx\_>6 | HR | 0.9 (0.7, 1.2) |
| Fall mechanism transport accident (ref: same level fall) | | Al Dabbagh (2016) | ICD10 | -- | 891 | Rx\_>6 | HR | 1.1 (0.9, 1.4) |
| Fall mechanism transport accident (ref: same level fall) | | Weiss (2012) | MA | -- | 396 | Rx\_>6 | HR | 1.2 (0.8, 1.9) |
| Fall mechanism – from height (ref: same level fall) | | Al Dabbagh (2014) | ICD9 | -- | 639 | Rx\_>6 | HR | 0.8 (0.6, 1.1) |
| Fall mechanism – from height (ref: same level fall) | | Al Dabbagh (2016) | ICD10 | -- | 891 | Rx\_>6 | HR | 1.2 (0.8, 1.8) |
| Fall mechanism – from height (ref: same level fall) | | Weiss (2012) | MA | -- | 396 | Rx\_>6 | HR | 1.1 (0.7, 1.8) |
| Fracture type – open (ref: closed) | | Al Dabbagh (2014) | ICD9 | -- | 639 | Rx\_>6 | HR | 0.9 (0.7, 1.1) |
| Fracture type – open (ref: closed) | | Al Dabbagh (2016) | ICD10 | -- | 891 | Rx\_>6 | HR | 0.6 (0.4, 1.0) |
| **Fracture type – unspecified (ref: closed)** | | **Al Dabbagh (2014)** | **ICD9** | **--** | **639** | **Rx\_>6** | **HR** | **0.6 (0.4, 0.9)** |
| Fracture type – unspecified (ref: closed) | | Al Dabbagh (2016) | ICD10 | -- | 891 | Rx\_>6 | HR | 0.9 (0.7, 1.2) |
| Injury: mva (ref: falls) | | Daoust (2017) | QTR | -- | 39,833 | Rx\_>6 | OR | 0.87 (0.75, 1) |
| Injury: other (ref: falls) | | Daoust (2017) | QTR | -- | 39,833 | Rx\_>6 | OR | 1.15 (0.97, 1.37) |
| Injury: weapon or blunt object (ref: falls) | | Daoust (2017) | QTR | -- | 39,833 | Rx\_>6 | OR | 0.98 (0.73, 1.31) |
| Peri- event factors (medication) | **OME total dose during surgical window ≥ 300mg (ref: < 300mg)** | | **Brummett (2017)** | **MA** | **--** | **36,177** | **Rx\_3-6** | **OR** | **1.12 (1.03, 1.27)** |
| **Number of days’ supply of first prescription: 8-14 days (ref: ≤7days)** | | **Mosher (2018)** | **VHA** | **--** | **26,476** | **Rx\_3-6** | **OR** | **1.24 (1.12, 1.37)** |
| **Number of days’ supply of first prescription: 15-29 days (ref: ≤7days)** | | **Mosher (2018)** | **VHA** | **--** | **26,476** | **Rx\_3-6** | **OR** | **1.56 (1.39, 1.76)** |
| **Number of days’ supply of first prescription ≥ 30 days (ref: ≤7days)** | | **Mosher (2018)** | **VHA** | **--** | **26,476** | **Rx\_3-6** | **OR** | **2.59 (2.35, 2.86)** |
| **Daily morphine equivalent (mg): 15.01 to ≤30 (ref: ≤15)** | | **Mosher (2018)** | **VHA** | **--** | **26,476** | **Rx\_3-6** | **OR** | **1.11 (1.02, 1.21)** |
| **Daily morphine equivalent (mg): 30.01 to ≤45 (ref: ≤15)** | | **Mosher (2018)** | **VHA** | **--** | **26,476** | **Rx\_3-6** | **OR** | **1.18 (1.05, 1.33)** |
| **Daily morphine equivalent (mg): > 45 (ref: ≤15)** | | **Mosher (2018)** | **VHA** | **--** | **26,476** | **Rx\_3-6** | **OR** | **1.7 (1.49, 1.94)** |
| Type of opioid prescribed: Oxycodone (ref: Hydrocodone) | | Mosher (2018) | VHA | -- | 26,476 | Rx\_3-6 | OR | 0.96 (0.88, 1.05) |
| **Type of opioid prescribed: Tramadol (ref: Hydrocodone)** | | **Mosher (2018)** | **VHA** | **--** | **26,476** | **Rx\_3-6** | **OR** | **1.55 (1.39, 1.72)** |
| **Type of opioid prescribed: other (ref: Hydrocodone)** | | **Mosher (2018)** | **VHA** | **--** | **26,476** | **Rx\_3-6** | **OR** | **1.23 (1.05, 1.45)** |
| **Opioid prescription filled within 3month of trauma (ref: no opioid prescription filled)** | | **Daoust (2017)** | **RAMQ** | **--** | **39,833** | **Rx\_>6** | **OR** | **3.05 (2.83, 3.29)** |
| Peri-event factors -acute postope-ratively | Perioperative complications (ref: no complications) | | Schoenfeld (2017) | MDR | -- | 9,991 | Rx\_>6 | HR | 1.05 (0.94, 1.17) |
| Length of hospitalization (days) | | Schoenfeld (2017) | MDR | -- | 9,991 | Rx\_>6 | HR | 1 (0.99, 1) |
| **Discharged to rehab (ref: discharged home)** | | **Kim (2017)** | **OCDMD** | **--** | **7,425** | **Rx\_>6** | **OR** | **2.24 (1.21, 4.13)** |
| Comorbidities | **Charlson comorbidity score** | | **Brummett (2017)** | **ICD9** | **1 year** | **36,177** | **Rx\_3-6** | **OR** | **1.1 (1.08, 1.13)** |
| **Comorbidity score (20 diseases examined)** | | **Kim (2017)** | **OCDMD** | **1 year** | **7,425** | **Rx\_>6** | **OR** | **1.25 (1.08, 1.44)** |
| Charlson comorbidity score = 1 (ref: 0) | | Schoenfeld (2017) | ICD9 | 1 year | 9,991 | Rx\_>6 | HR | 0.94 (0.89, 1) |
| Charlson comorbidity score = 2+ (ref: 0) | | Schoenfeld (2017) | ICD9 | 1 year | 9,991 | Rx\_>6 | HR | 1.06 (0.94, 1.2) |
| **Elixhauser score = 2 (ref: ≤1)** | | **Johnson (2016)** | **ICD9** | **1 year** | **59,725** | **Rx\_3-6** | **OR** | **1.4 (1.3, 1.5)** |
| **Elixhauser score = 3 (ref: ≤1)** | | **Johnson (2016)** | **ICD9** | **1 year** | **59,725** | **Rx\_3-6** | **OR** | **1.6 (1.4, 1.7)** |
| **Elixhauser score = >3 (ref: ≤1)** | | **Johnson (2016)** | **ICD9** | **1 year** | **59,725** | **Rx\_3-6** | **OR** | **2.2 (2, 2.3)** |
| Endo/ Metab | Diabetes | | Clarke (2014) | ICD10 | 3 years | 39,140 | Rx\_3-6 | OR | 1.15 (1, 1.31) |
| Onco-logy | Malignancy: metastatic (ref: no malignancy) | | Clarke (2014) | ICD10 | 3 years | 39,140 | Rx\_3-6 | OR | 1.41 (0.88, 2.25) |
| Malignancy: primary (ref: no malignancy) | | Clarke (2014) | ICD10 | 3 years | 39,140 | Rx\_3-6 | OR | 1.05 (0.91, 1.21) |
| Respi-ratory | **Pulmonary disease** | | **Clarke (2014)** | **ICD10** | **3 years** | **39,140** | **Rx\_3-6** | **OR** | **1.53 (1.7, 1.99)** |
| Vascular | Coronary artery disease | | Clarke (2014) | ICD10 | 3 years | 39,140 | Rx\_3-6 | OR | 0.95 (0.75, 1.21) |
| Cerebrovascular disorder | | Clarke (2014) | ICD10 | 3 years | 39,140 | Rx\_3-6 | OR | 1.06 (0.71, 1.58) |
| **Heart failure** | | **Clarke (2014)** | **ICD10** | **3 years** | **39,140** | **Rx\_3-6** | **OR** | **1.32 (1.02, 1.74)** |
| Hypertension | | Clarke (2014) | ICD10 | 3 years | 39,140 | Rx\_3-6 | OR | 1.06 (0.92, 1.23) |
| Peripheral vascular disease | | Clarke (2014) | ICD10 | 3 years | 39,140 | Rx\_3-6 | OR | 0.85 (0.57, 1.2) |
| Renal disease | | Clarke (2014) | ICD10 | 3 years | 39,140 | Rx\_3-6 | OR | 1.01 (0.74, 1.39) |

*Note:* **Rx\_3-6** = opioid prescription 3-6 months post-event; **Rx\_>6** = opioid prescription > 6 months post-event; **OR** = Odds ratio; **HR** = Hazard ratio, **SSRI**: selective serotonin reuptake inhibitor; **MA**: medico-administrative database/medical records; **ICD**: International Classification of Diseases (when available, the version number is written next to the ICD acronym); **CCS-AHRQ**: Clinical Classification System from the Agency of Healthcare Research and Quality; **OHIP**: Ontario Health Insurance Plan; **ODBD**: Ontario Drug Benefit Database; **QTR**: Quebec Trauma Registry; **RAMQ**: Régie de l’assurance maladie du Québec; **UCSB**: Utah Controlled Substance Database; **TMSD**: Truven MarketScan Database; **MDR**: Military Health System Data Repository; **OCDMD**: Optum Clinformatics Data Mart Database; **VHA**: Veterans Health Affairs

Supplemental Table 7. Results of individual risk factors for opioid prescription 3-6 months and >6 months post-surgery or trauma among individuals with prolonged opioid prescription pre-event

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Risk factor category** | | **Risk factor** | **Studies** | **Data source for risk factor** | **Period considered preop/ pretrauma** | **N** | **Out-come** | **Type of effect size** | **Effect size (95% CI)** |
| Socio  demographic | Female sex (ref: male sex) | | Qureshi (2018) | -- | -- | 1,321 | Rx\_3-6 | OR | 0.88 (0.71, 1.10) |
| Female sex (ref: male sex) | | Kim (2018) | -- | -- | 54 | Rx\_3-6 | OR | 0.38 (0.08, 1.84) |
| Female sex (ref: male sex) | | Hadlandsmyth (2018) | -- | -- | 1,229 | Rx\_>6 | RR | 0.91 (0.74, 1.11) |
| Female sex (ref: male sex) | | Hansen (2017) | -- | -- | 720 | Rx\_>6 | OR | 0.81 (0.57, 1.15) |
| **Age (10yrs increment)** | | **Inacio (2016)** | **--** | **--** | **593** | **Rx\_3-6** | **OR** | **0.96 (0.93, 0.99)** |
| Age: 70-80 (ref: < 70) | | Kim (2018) | -- | -- | 54 | Rx\_3-6 | OR | 0.22 (0.02, 2.12) |
| **Age: 38-60 (ref: 80+)** | | **Hansen (2017)** | **--** | **--** | **720** | **Rx\_>6** | **OR** | **0.32 (0.18, 0.58)** |
| **Age: 61-80 (ref: 80+)** | | **Hansen (2017)** | **--** | **--** | **720** | **Rx\_>6** | **OR** | **0.67 (0.48, 0.95)** |
| Age: 60-70 (ref: <60) | | Hadlandsmyth (2018) | -- | -- | 1,229 | Rx\_>6 | RR | 0.99 (0.89, 1.1) |
| Age: 70+ (ref: <60) | | Hadlandsmyth (2018) | -- | -- | 1,229 | Rx\_>6 | RR | 0.92 (0.79, 1.09) |
| Race: African American (ref: White) | | Hadlandsmyth (2018) | -- | -- | 1,229 | Rx\_>6 | RR | 1.01 (0.88, 1.15) |
| Race: other (ref: White) | | Hadlandsmyth (2018) | -- | -- | 1,229 | Rx\_>6 | RR | 1.19 (0.9, 1.58) |
| Race: unknown (ref: White) | | Hadlandsmyth (2018) | -- | -- | 1,229 | Rx\_>6 | RR | 1.16 (0.96, 1.39) |
| Health behaviors | **Tobacco dependence** | | **Qureshi (2018)** | ICD9 | 4 months | 1,321 | **Rx\_3-6** | **OR** | **1.96 (1.56, 2.46)** |
| Tobacco dependence | | Kim (2018) | MA | 3 months | 54 | Rx\_3-6 | OR | 6.94 (0.49, 97.52) |
| Drug dependence | | Hadlandsmyth (2018) | ICD9 | 1 year | 1,229 | Rx\_>6 | RR | 0.95 (0.83, 1.08) |
| Alcohol dependence | | Qureshi (2018) | ICD9 | 4 months | 1,321 | Rx\_3-6 | OR | 0.9 (0.56, 1.44) |
| Pre-event medication use | **Antidepressant current use (ref: none in the past year)** | | **Hadlandsmyth (2018)** | **VHA** | **1 year** | **1,229** | **Rx\_>6** | **RR** | **1.27 (1.02, 1.59)** |
| Antidepressant in the past year (ref: none in the past year) | | Hadlandsmyth (2018) | VHA | 1 year | 1,229 | Rx\_>6 | RR | 1.1 (0.97, 1.24) |
| Antiepileptic current use (ref: none in the past year) | | Hadlandsmyth (2018) | VHA | 1 year | 1,229 | Rx\_>6 | RR | 0.89 (0.59, 1.34) |
| **Antiepileptic in the past year (ref: none in the past year)** | | **Hadlandsmyth (2018)** | **VHA** | **1 year** | **1,229** | **Rx\_>6** | **RR** | **1.13 (1.02, 1.26)** |
| Benzodiazepine current use (ref: none in the past year) | | Hadlandsmyth (2018) | VHA | 1 year | 1,229 | Rx\_>6 | RR | 1.06 (0.79, 1.44) |
| Benzodiazepine in the past year (ref: none in the past year) | | Hadlandsmyth (2018) | VHA | 1 year | 1,229 | Rx\_>6 | RR | 1.09 (0.98, 1.21) |
| Hypnotic current use (ref: none in the past year) | | Hadlandsmyth (2018) | VHA | 1 year | 1,229 | Rx\_>6 | RR | 0.8 (0.55, 1.17) |
| Hypnotic in the past year (ref: none in the past year) | | Hadlandsmyth (2018) | VHA | 1 year | 1,229 | Rx\_>6 | RR | 1.03 (0.91, 1.17) |
| **Preoperative hypnotic use** | | **Inacio (2016)** | **DVA** | **1 year** | **593** | **Rx\_3-6** | **OR** | **2.52 (1.48, 4.3)** |
| Muscle relaxant current use (ref: none in the past year) | | Hadlandsmyth (2018) | VHA | 1 year | 1,229 | Rx\_>6 | RR | 0.9 (0.67, 1.19) |
| Muscle relaxant in the past year (ref: none in the past year) | | Hadlandsmyth (2018) | VHA | 1 year | 1,229 | Rx\_>6 | RR | 1.1 (0.99, 1.22) |
| Average OME (10mg increment) | | Inacio (2016) | DVA | 1 year | 593 | Rx\_3-6 | OR | 1.06 (1, 1.11) |
| Pre-event OME >12mg daily | | Kim (2018) | MA | 3 months | 54 | Rx\_3-6 | OR | 5.97 (0.49, 72.23) |
| **Pre-event opioid use (ref: no opioid use pre-event)** | | **Qureshi (2018)** | **PDD** | **4 months** | **1,321** | **Rx\_3-6** | **OR** | **3.4 (NA, NA)** |
| **Number of day using opioids pre-event = 157-224 (ref: 94-156)** | | **Inacio (2016)** | **DVA** | **1 year** | **593** | **Rx\_3-6** | **OR** | **3.63 (2.08, 6.34)** |
| **Number of days using opioids pre-event ≥ 225 (ref: 94-156)** | | **Inacio (2016)** | **DVA** | **1 year** | **593** | **Rx\_3-6** | **OR** | **5.18 (2.92, 9.19)** |
| NSAID | | Hansen (2017) | DVA | 1 year | 720 | Rx\_>6 | OR | 1 (0.7, 1.43) |
| MSK condition | **Back pain** | | **Inacio (2016)** | **ICD10** | **1 year** | **593** | **Rx\_3-6** | **OR** | **1.99 (1.2, 3.23)** |
| Back pain | | Hansen (2017) | ICD10 | 1 year | 720 | Rx\_>6 | OR | 0.57 (0.3, 1.08) |
| Chronic pain | | Hadlandsmyth (2018) | ICD9 | 1 year | 1,229 | Rx\_>6 | RR | 1.07 (0.96, 1.2) |
| **Fibromyalgia** | | **Qureshi (2018)** | **ICD9** | **4 months** | **1,321** | **Rx\_3-6** | **OR** | **2.12 (1.56, 2.89)** |
| Primary gonarthrosis | | Hansen (2017) | ICD10 | 1 year | 720 | Rx\_>6 | OR | 1.12 (0.87, 1.45) |
| Neuro | **Migraine** | | **Qureshi (2018)** | **ICD9** | **4 months** | **1,321** | **Rx\_3-6** | **OR** | **1.42 (1.02, 1.97)** |
| Migraine | | Inacio (2016) | ICD10 | 1 year | 593 | Rx\_3-6 | OR | 1.76 (0.18, 17.25) |
| Psychiatric diagnoses | **Depressive disorder** | | **Qureshi (2018)** | **ICD9** | **4 months** | **1,321** | **Rx\_3-6** | **OR** | **1.63 (1.29, 2.05)** |
| Depressive disorder | | Inacio (2016) | ICD10 | 1 year | 593 | Rx\_3-6 | OR | 1.14 (0.67, 1.95) |
| Psychiatric disorder | | Kim (2018) | MA | 3 months | 54 | Rx\_3-6 | OR | 1.53 (0.21, 5.29) |
| Psychiatric disorder | | Hadlandsmyth (2018) | ICD9 | 1 year | 1,229 | Rx\_>6 | RR | 0.97 (0.87, 1.09) |
| Psychosis | | Inacio (2016) | ICD10 | 1 year | 593 | Rx\_3-6 | OR | 1.47 (0.39, 5.42) |
| Peri-operative factors | Bilateral surgery (ref: unilateral surgery) | | Hansen (2017) | DVA | -- | 720 | Rx\_>6 | OR | 1.08 (0.72, 1.59) |
| Length hospitalization (days) | | Hadlandsmyth (2018) | VHA | -- | 1,229 | Rx\_>6 | RR | 1 (1, 1) |
| Length hospitalization: 11-20 days (ref: <11) | | Hansen (2017) | DVA | -- | 720 | Rx\_>6 | OR | 0.97 (0.63, 1.49) |
| Length hospitalization ≥ 21 days (ref: <11) | | Hansen (2017) | DVA | -- | 720 | Rx\_>6 | OR | 1.47 (0.73, 2.94) |
| Posttraumatic osteoarthritis | | Kim (2018) | MA | -- | 54 | Rx\_3-6 | OR | 2.02 (0.35, 11.62) |
| Use of NSAID post-trauma | | Hansen (2017) | DVA | -- | 720 | Rx\_>6 | OR | 0.98 (0.69, 1.39) |
| Comorbidities | Charlson comorbidity score = 1-2 (ref: 0) | | Hansen (2017) | ICD10 | 1 year | 720 | Rx\_>6 | OR | 0.81 (0.55, 1.16) |
| Charlson comorbidity score ≥ 3 (ref: 0) | | Hansen (2017) | ICD10 | 1 year | 720 | Rx\_>6 | OR | 1.14 (0.45, 2.86) |
| Number of comorbidities = 2-3 (ref: <2) (algorithm based on Elixhauser) | | Hadlandsmyth (2018) | ICD9 | 1 year | 1,229 | Rx\_>6 | RR | 1.14 (0.98, 1.33) |
| Number of comorbidities = 4-5 (ref: <2) (algorithm based on Elixhauser) | | Hadlandsmyth (2018) | ICD9 | 1 year | 1,229 | Rx\_>6 | RR | 1.15 (0.97, 1.35) |
| Number of comorbidities = >5 (ref: <2) (algorithm based on Elixhauser) | | Hadlandsmyth (2018) | ICD9 | 1 year | 1,229 | Rx\_>6 | RR | 1.1 (0.89, 1.36) |
| Vascular | Cerebrovascular disease | | Kim (2018) | MA | 3 months | 54 | Rx\_3-6 | OR | 6.77 (0.71, 64.92) |
| Hypertension | | Kim (2018) | MA | 3 months | 54 | Rx\_3-6 | OR | 0.27 (0.04, 1.87) |
| Hypertension | | Inacio (2016) | ICD10 | 1 year | 593 | Rx\_3-6 | OR | 0.98 (0.59, 1.63) |
| Hypertension or ischemic heart disease | | Inacio (2016) | ICD10 | 1 year | 593 | Rx\_3-6 | OR | 0.66 (0.41, 1.07) |
| Renal disease | | Kim (2018) | MA | 3 months | 54 | Rx\_3-6 | OR | 0.95 (0.05, 18.17) |
| Venous thromboembolism | | Kim (2018) | MA | 3 months | 54 | Rx\_3-6 | OR | 2.66 (0.04, 72.63) |
| Endo/metab | **Diabetes** | | **Qureshi (2018)** | **ICD9** | **4 months** | **1,321** | **Rx\_3-6** | **OR** | **1.39 (NA, NA)** |
| **Diabetes with complications** | | **Inacio (2016)** | **ICD10** | **1 year** | **593** | **Rx\_3-6** | **OR** | **3.52 (1.05, 11.8)** |
| Diabetes without complications | | Inacio (2016) | ICD10 | 1 year | 593 | Rx\_3-6 | OR | 1.89 (0.78, 4.57) |
| BMI: overweight/obese (ref: normal) | | Hadlandsmyth (2018) | VHA | 1 year | 1,229 | Rx\_>6 | RR | 0.84 (0.7, 1) |
| BMI: unknown (ref: normal) | | Hadlandsmyth (2018) | VHA | 1 year | 1,229 | Rx\_>6 | RR | 0.81 (0.65, 1.02) |
| **Obesity** | | **Qureshi (2018)** | **ICD9** | **4 months** | **1,321** | **Rx\_3-6** | **OR** | **2.12 (NA, NA)** |
| Gastro | Liver disease (severe of failure) | | Inacio (2016) | ICD10 | 1 year | 593 | Rx\_3-6 | OR | 1.25 (0.59, 2.66) |
| Syst/  Rheum | **Inflammatory disease** | | **Qureshi (2018)** | **ICD9** | **4 months** | **1,321** | **Rx\_3-6** | **OR** | **1.85 (NA, NA)** |
| Rheumatoid arthritis or collage vascular disease | | Inacio (2016) | ICD10 | 1 year | 593 | Rx\_3-6 | OR | 1.01 (0.25, 4.71) |

*Note:* **Rx\_3-6** = opioid prescription 3-6 months post-event; **Rx\_>6** = opioid prescription > 6 months post-event; **OR** = Odds ratio; **HR** = Hazard ratio; **VHA**: Veterans Health Affairs; **ICD**: International Classification of Diseases (when available, the version number is written next to the ICD acronym); **PDD**: PearlDiver database; **MA**: medico-administrative records; **DVA**: Department of Veterans Affairs